NCRI
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NCRI Prostate Cancer Clinical Studies Group

Annual Report 2015-16

Partners in cancer research

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NCRI Prostate Cancer CSG Annual Report 2015-16

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

Achievements:

1. STAMPEDE docetaxel comparison: This trial tested the use of 'early' docetaxel, as part of first line treatment in 2,000 men with advanced prostate cancer. It showed an overall survival benefit for early docetaxel, which has now become standard of care.
2. CHHIP: Three radiotherapy fractionations schemes were compared in this 3000 patient trial. As a result, the standard of care has changed from 37 fractions over 7.5 weeks to 20 fractions over four weeks. This represents a big improvement in both patient convenience and resource use.
3. TO-PARP: This phase II trial of olaparib demonstrated for the first time that a PARP inhibitor was active in the treatment of metastatic castrate-refractory prostate cancer (mCPRC), and it provided evidence for using DNA repair defects as a predictive biomarker. Until now, we have used a 'one size fits all' approach to treating mCRPC

Two other important prostate cancer trials, PROMIS and ProtecT, have been analysed and the results are due to be presented in 2016. The results are not available at the time of writing but are likely to impact on clinical practice.

Challenges:

1. Developing precision medicine trials: The results of the TO-PARP trial have given a strong impetus to the development of biomarker-driven trials. Good progress has been made and we anticipate a funding application for the first such trial in prostate cancer before the end of the year.
2. Surgical trials: Surgical trials are not well represented in the portfolio. We considered proposals to study the role of radical prostatectomy in men with locally advanced prostate cancer. While this is an important unanswered question, we concluded, after lengthy deliberation, that such a trial would not be feasible. The Localised disease subgroup is looking into new methodologies to conduct surgical trials and has also prioritised the evaluation of minimally-invasive ablative (surgical) procedures as a strategic aim.

2. Structure of the Group

The structure of the Group has not changed since the last report. The current membership is listed in Appendix 1. The CSG has been large, with up to 28 members. The size of the Group will be reduced this year as some members come to the end of their term and are not replaced. Until now, oncologists have heavily outnumbered surgeons, and priority will be given to strengthening surgical representation.

3. CSG & Subgroup strategies

Main CSG

The CSG has two main strategic aims: First, to develop biomarker-driven trials in advanced disease, and second, to address over-diagnosis of localised prostate cancer.

We have made significant progress towards developing biomarker-driven trials. The results of the TO-PARP trial of olaparib in mCRPC, led by Johann De Bono, were published in the New England Journal of Medicine in 2015. This has provided the first good evidence for a predictive biomarker in prostate cancer treatment. The response rate to olaparib in patients whose tumours had a known DNA repair defect was 88%, compared to just 3% in those without such a defect. Building on these data, we are now developing a trial of a PARP-inhibitor in biomarker-selected patients with hormone-naïve metastatic prostate cancer. The proposal is to embed this trial within the STAMPEDE program that will facilitate accrual from over 100 centres. This proposal has been developed in collaboration with both Prostate Cancer UK and Cancer Research UK in an unprecedented example of collaboration between investigators and two of our major funding bodies.

Our aim to tackle over-diagnosis of localised disease is at an earlier stage of development. Key data were published in 2015 from the STHLM3 study, led by Henrik Gronberg, which has shown that a multiplex biomarker panel performed better than PSA alone in the prostate cancer diagnostic pathway. The data suggested that as many as 32% of prostate biopsies could be safely avoided, leading to a 17% reduction in the detection of low-grade cancers, without compromising detection of high-grade cancers. There is now a need to validate these results in UK populations. The localised subgroup is working on a proposal to do this, in close collaboration with Prostate Cancer UK, NCRI SPED and NCRI Primary Care CSG.

Localised Disease Subgroup (Chair, Mr Hashim Ahmed)

Aims:

1. To reduce over-diagnosis - The Subgroup is working with NCRI SPED and NCRI Primary Care CSG to develop an application to conduct a validation study in the UK of the STHLM3 study. If successful, this will be a prime example of how CSGs might work together.
2. To promote surgical trials - We are working with a new PI, Greg Shaw, to develop a protocol to evaluate a new surgical technique that might improve nerve-sparing during radical prostatectomy called Neurosafe. The Chair is working with members of the CSG such to evaluate novel trial designs such as the MAMS design and the cohort-multiple RCT described by Clare Relton.
3. To evaluate minimally-invasive strategies within multi-centre studies - The role of ablative therapies is increasing and might be a strategy to reduce the harms of therapy. The Chair

is working on an RCT to evaluate focal ablative therapy within a possible multi-arm multi-stage trial design.

4. To encourage, nurture and enable young/new investigators to the field.

Advanced Disease Subgroup (Chair, Dr Robert Jones)

Following a review of the group's strategy in the previous year, 2015/16 has focussed on moving towards delivery of this strategy. The main project in which the Subgroup is engaged is now the development of an umbrella stratified medicine trial in advanced prostate cancer (APC), formerly known as STRATOSPHERE. By planned rotation, the membership structure of the Subgroup has changed to reflect this: we welcomed David Waugh (laboratory science) and Matt Sydes (biostatistics, MRC CTU) to the group. David is science lead for this project and Matt is part of the biostatistics team, building on his major role in STAMPEDE. Simon Chowdhury remains the overall lead for the project.

Broad design principles are now agreed: the study will be embedded in STAMPEDE, with a cohort of patients, identified by a DNA-damage mRNA expression signature, to be randomized to rucaparib or control being the first study embedded within the umbrella. This builds on the ground-breaking work of Professor De Bono working in collaboration with other ECMCs in the UK. The main STAMPEDE trial will remain an important study for 'biomarker negative' patients, those with locally advanced disease and those sites without the resources to conduct more complex trials. The addition of the metformin arm of STAMPEDE was funded during the year, and there are ongoing discussions regarding future arms.

4. Task groups/Working parties

Not applicable.

5. Patient recruitment summary for last 5 years

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	2418	2140	2256	2044	6.9	6.2

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	2416	2475	2260	2363	5.6	5.8
2013/2014	3811	2826	3629	2826	9.0	7.0
2014/2015	4164	2836	4021	2786	9.9	6.9
2015/2016	3469	4025	3328	3892	8.23	9.62

In the last year, 14 trials closed to recruitment and 19 opened. Recruitment to non-interventional studies has remained stable. There has been a modest increase in recruitment to interventional

trials. Our top recruiting trial is STAMPEDE, which has supported nine different treatment comparisons and has now accrued over 8,000 patients. We regard STAMPEDE as an excellent example of what can be achieved using a Multi-Arm, Multi-Stage (MAMS) design.

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

We have established a good relationship with the Primary Care CSG in our efforts to tackle over-diagnosis of prostate cancer. Hashim Ahmed, Chair of the Localised Disease Subgroup has presented to the Primary Care CSG. Chris Parker and Richard Neal, the respective Chairs of the two CSGs, have met on several occasions to discuss this project. Rhian Gabe, a member of the Primary Care CSG, is now a member of the Localised Disease Subgroup. Hashim Ahmed also sits on the NCRI SPED Advisory Group and has presented ideas on the next generation of research questions in diagnosis and screening of prostate cancer. Much of this will be influenced by the CaP and PROTECT, as well as PROMIS studies.

Two CSG members, Simon Crabb and Chris Parker, have joined the EORTC GU Group in the last year. The new Chair of the EORTC GU group is Silke Gillessen, whom we know well, not least because she leads the Swiss involvement in STAMPEDE. This track record of collaboration should facilitate closer working with the EORTC Group in future.

The four Urologic CSGs held a joint national trials meeting in January 2016 to present recent trial results and to discuss future trials. This was well attended (approximately 170 people) and received excellent feedback.

7. Funding applications in last year

Table 3 Funding submissions in the reporting year

Cancer Research UK Clinical Research Committee (CRUK CRC)			
Study	**Application type**	**CI**	**Outcome**
July 2015 (CTAAC)			
HEXPROP: A phase III trial of HDR or External Beam Prostate Cancer Dose Painting with or without Pelvic node radiotherapy for men with high risk localised cancer	Outline application	Dr Emma Hall	Full application invited
STAMPEDE: Systemic Therapy in Advancing or Metastatic Prostate cancer: Evaluation of Drug Efficacy. A three-stage multi-arm, randomised controlled trial	Full application *Amendment*	Professor Nicolas James	Funded
PATCH: Prostate Adenocarcinoma: TransCutaneous Hormones - amendment	Full application *Amendment*	Professor Paul Abel	Approved (no cost)
STAMPEDE: Systemic Therapy in Advancing or Metastatic Prostate cancer: Evaluation of Drug Efficacy. A three-stage, multi arm, randomised controlled trial	Sample collection application	Professor Nicolas James	Funded
December 2015			
Genetic profiling of urine samples for improved diagnosis and prognosis of prostate cancer	Sample collection application	Dr Emanuela Volpi	Not funded
QuiPCaM: Wnt signalling a key pathway in determining the aggressiveness of prostate cancer	Feasibility application	Dr Aamir Ahmed	Not funded

- a Quantitative Prostate Cancer Marker comparative analysis within different ethnicities			
Developing a new epigenetic-based diagnostic and prognostic blood test for prostate cancer	Feasibility application	Dr Dmitry Pshezhetskiy	Not funded
May 2016			
PIVOTALboost: A phase III trial of prostate alone vs pelvic lymph node IMRT with or without prostate boost for intermediate and high risk localised prostate cancer	Full application	Dr Emma Hall & Dr Isabel Syndikus	Funded
STAMPEDE: Systematic Therapy in Advancing or Metastatic Prostate Cancer: Evaluation of Drug Efficacy – Establishing a STAMPEDE Biorepository	Full application	Professor Nicholas James & Professor Malcolm Mason	Not funded
Development of a detection method for multiple endogenous androgens for prostate cancer screening via molecular imprinting and comprehensive 4D gas chromatography	Full application	Dr Nicholas Turner	Not funded

8. Collaborative partnership studies with industry

There are 12 open industry studies in the portfolio.

The collaboration with Janssen and Astellas on the STAMPEDE study has been notably successful. Over 1900 patients were accrued ahead of schedule to the comparison of standard care +/- (abiraterone + enzalutamide). It is a major achievement to get more than one pharmaceutical company to collaborate on the same study to test combinations of their products.

There are ongoing discussions with several industry partners about future trials in prostate cancer, but the details cannot be shared at this stage.

9. Impact of CSG activities

There have been two major changes to routine clinical practice in the last year as a result of CSG trials. First, the addition of 'early' docetaxel to androgen deprivation has become standard of care for men with newly diagnosed advanced prostate cancer. This change was effected very promptly, with NHS England commissioning early docetaxel just three months after publication of the STAMPEDE trial data. Second, the standard fractionation for radical prostate radiotherapy has changed from 74Gy in 37 fractions to 60Gy in 20 fractions, as a result of the CHHIP trial. Given that around 10,000 men undergo prostate radiotherapy in the UK annually, this represents a huge reduction in resource use.

During the last year, the CSG has advised NICE on the following technologies:

- Enzalutamide for pre-docetaxel CRPC
- Radium-223 for CRPC
- Abiraterone for pre-docetaxel CRPC
- Cabazitaxel for CRPC

The CSG has provided reviews of the funding applications submitted to CRUK listed above. We have also agreed to provide the same service to Prostate Cancer UK for future applications.

The CSG has reviewed a draft research call from Prostate Cancer UK concerning validation of the STHLM3 biomarker panel.

Chris Parker and Simon Chowdhury are members of the Prostate Cancer Advisory Group, which brings together prostate cancer clinicians, patient representatives, the voluntary sector and the Department of Health. A top priority of this group has been to highlight the forthcoming changes to the prostate cancer diagnostic pathway, in particular with the increasing use of pre-biopsy MRI. The NIHR-HTA PROMIS trial, of which Chris Parker and Hashim Ahmed, are co-PIs will impact on this issue when the results are presented at ASCO and subsequently published later this year.

10. Consumer involvement

We are very sorry to report the death of Allister Murphy. Allister was extremely committed to his work on the CSG, and made a very full contribution over several years, in addition to his work for many other prostate cancer organisations. He made a significant impact to the work of the CSG, not least in strengthening our motivation to tackle advanced disease. Here are some excerpts from his last report:

"Involvement: I attended the NCIN conference in Belfast and contributed to the debate regarding Degarelix. I met with the Northern Ireland Health Minister, Simon Hamilton, and discussed the establishment of a Cancer Drugs Fund for Northern Ireland as well as reform of the IFR process.

What help is required from CSG? Support for a national based approach to treating prostate cancer. General public seen unaware of huge need for blood and platelets to treat cancer patients. Need to raise awareness on this subject on a national scale.

Take away message to CSG: "Research is the only cure".

We are pleased to welcome a new consumer member, Derek Price, to the Group. Derek has yet to attend his first CSG meeting. At present, he is the only consumer member. We will make sure that he is well mentored, and we will appoint a second consumer member this year.

11. Open meetings/annual trials days/strategy days

A Joint Urological CSG trials meeting was held in London in January 2016. Some of the feedback is shown below:

HOW DO YOU RATE THE OVERALL QUALITY OF THE MEETING?
Excellent 55
Good 11
Satisfactory 0
Poor 0

HOW DO YOU RATE THE RELEVANCE OF THIS MEETING TO YOUR CONTINUING PROFESSIONAL DEVELOPMENT NEEDS?
Highly relevant 45
Mostly relevant 20
Little relevance 1
Not relevant 0

WAS THERE ADEQUATE TIME FOR DISCUSSION?
Yes 62

No 4

HOW DID YOU FIND THE CONTENT OF THE PRESENTATIONS OVERALL?
Excellent 48
Good 18
Satisfactory 0
Poor 0

HOW DID YOU FIND THE LENGTH OF THE MEETING?
Too long 3
Just right 61
Too short 0

12. Priorities and challenges for the forthcoming year

Priorities:

- Establishing biomarker-driven trials in advanced prostate cancer - A proposal is being prepared to test the PARP inhibitor, rucaparib, in patients with newly diagnosed metastatic disease whose tumours have a DNA repair defect. An application to Cancer Research UK will be submitted this year. We hope that this will be the first of many biomarker driven trials, as more predictive biomarkers are identified in mCRPC.
- Tackling over-diagnosis - The STHLM3 trial has shown that a multiplex biomarker panel can safely reduce over-diagnosis of low-grade disease. The results of the PROMIS study, expected at ASCO 2016, are eagerly awaited. They may show that MRI, used as a triage test prior to biopsy, could also reduce over-diagnosis. It will be a major priority to determine how best to incorporate both multiplex biomarker panels, together with MRI, in the diagnostic pathway.
- To open new comparisons within the STAMPEDE trial - STAMPEDE is the flagship trial for the Prostate CSG. It has recruited over 8,000 patients and, using an innovative MAMS design, has addressed 9 treatment comparisons to date. The local radiotherapy in M1 disease comparison is due to complete recruitment of 1,800 patients shortly. The trial will then be a two arm randomised trial comparing standard of care +/- metformin. In order to achieve the advantages of a multi-arm design, it will be a priority to open new comparisons within the trial. Potential interventions include radium-223 and Prostvac.

Challenges:

- Surgical trials - We recognise that surgical trials are not well represented in the portfolio. Partly for that reason, we had planned to develop a trial of radical prostatectomy in locally advanced disease. However, having considered the details of several proposals, we decided that it would not be feasible to do so. We shall try to develop other surgical trials. We will aim to boost surgical representation on the CSG. As a first step, one of the new trainee members is, for the first time, an urologist. The Localised Disease Subgroup is working on developing surgical trials and new methodologies in comparative surgical trials.
- International collaboration - Some progress has been made to address this area with the appointment of Simon Crabb and Chris Parker to the EORTC GU group. We are now looking for suitable trial concepts on which to collaborate. This has proved challenging in

the past because it is possible to do large scale phase III trials of several thousand patients in the UK alone, without the need for international collaboration.

- Consumer involvement - For sad and unavoidable reasons, we do not have any experienced consumer members on the Group. We will need to help the new members to become established and make a full contribution.

13. Appendices

Appendix 1 - Membership of main CSG and subgroups

Appendix 2 – CSG and Subgroup strategies
A – Main CSG Strategy
B – Localised Disease Subgroup Strategy
C – Advanced Disease Subgroup Strategy

Appendix 3 - Portfolio Maps

Appendix 4 - Publications in previous year

Appendix 5 - Major international presentations in previous year

Dr Chris Parker (Prostate Cancer CSG Chair)

Appendix 1

Membership of the Prostate Cancer CSG

Name	Specialism	Location
Dr Stefan Symeonides*	Clinical Fellow	Edinburgh
Dr Nicholas van As	Clinical Oncologist	London
Professor Nick James	Clinical Oncologist	Warwick
Professor Malcolm Mason	Clinical Oncologist	Cardiff
Dr Chris Parker (Chair)	Clinical Oncologist	London
Dr John Staffurth	Clinical Oncologist	Cardiff
Mr Allister Murphy	Consumer	Belfast
Mr Derek Price	Consumer	Solihull
Professor Ros Eeles	Geneticist	London
Dr Mehran Afshar*	Medical Oncologist	Birmingham
Dr Johann de Bono	Medical Oncologist	London
Dr Simon Chowdhury	Medical Oncologist	London
Dr Simon Crabb	Medical Oncologist	Southampton
Dr Robert Jones	Medical Oncologist	Glasgow
Dr Simon Pacey	Medical Oncologist	Cambridge
Mr Roger Wheelwright	Nurse	Poole
Professor Daniel Berney	Pathologist	London
Mr Vincent Gnanapragasam	Surgeon	Cambridge
Dr Tristan Barrett	Radiologist	Cambridge
Professor Gary Cook	Radiologist	London
Dr Suniel Jain	Radiologist	Belfast
Dr Emma Hall	Statistician	London
Mr Matthew Sydes	Statistician	London
Mr Hashim Ahmed	Surgeon	London
Mr Rakesh Heer	Surgeon	Newcastle
Mr Sanjeev Madaan	Surgeon	Kent
Mr Prasanna Sooriakumaran	Surgeon	Oxford

*denotes trainee member

Membership of the Subgroups

Localised Disease Subgroup		
Name	**Specialism**	**Location**
Dr Ann Henry	Clinical Oncologist	Leeds
Dr Anita Mitra	Clinical Oncologist	London
Dr John Staffurth	Clinical Oncologist	Cardiff
Mr Christof Kastner	Consultant Urologist	Cambridge
Dr Mehran Afshar*	Medical Oncologist	Birmingham
Professor Daniel Berney	Pathologist	London
Dr Shonit Punwani	Radiologist	London
Dr Athene Lane	Senior Research Fellow	Bristol
Dr Rhian Gabe	Statistician	London
Mr Hashim Ahmed (Chair)	Surgeon	London
Mr Paul Cathcart	Surgeon	London
Professor Frank Chinegwundoh	Surgeon	London
Mr Rakesh Heer	Surgeon	Newcastle

Advanced Disease Subgroup		
Name	**Specialism**	**Location**
Dr Stefan Symeonides*	Clinical Fellow	Edinburgh
Dr Dan Ford	Clinical Oncologist	Birmingham
Dr Satinder Jagdev	Clinical Oncologist	Leeds
Dr Zafar Malik	Clinical Oncologist	Wirral
Professor David Waugh	Director, CCRCB	Belfast
Dr Simon Chowdhury	Medical Oncologist	London
Dr Simon Crabb	Medical Oncologist	Southampton
Dr Johann De Bono	Medical Oncologist	London
Dr Rob Jones (Chair)	Medical Oncologist	Glasgow
Dr Jonathan Shamash	Medical Oncologist	London
Mr Matthew Sydes	Statistician	London
Mr Prasanna Sooriakumaran	Surgeon	Oxford

*denotes trainee member
**denotes non-core member

Appendix 2

CSG & Subgroup Strategies

A – Main CSG Strategy

Overall goals:

1. To minimise the harms from the investigation and treatment of localised prostate cancer
2. To maximise the quality of life and overall survival of patients with advanced prostate cancer

Aims:

- To promote a clinical research culture within urology: encouraging young urologists to develop an interest in clinical trials
- To promote international collaborations on prostate cancer trials
- To foster links with the British Uro-oncology Group (BUG) and the British Association of Urological Surgeons (BAUS) Section of Oncology
- To work with the bladder, testis and renal CSGs to encourage clinical research in the uro-oncology community
- To foster a harmonised approach to tissue biomarker collection for future translational studies accompanying clinical trials
- To support consumer involvement in clinical research: establishing links with the Prostate Cancer Support Federation
- To strengthen links with Prostate Cancer UK

B – Localised Disease Subgroup Strategy

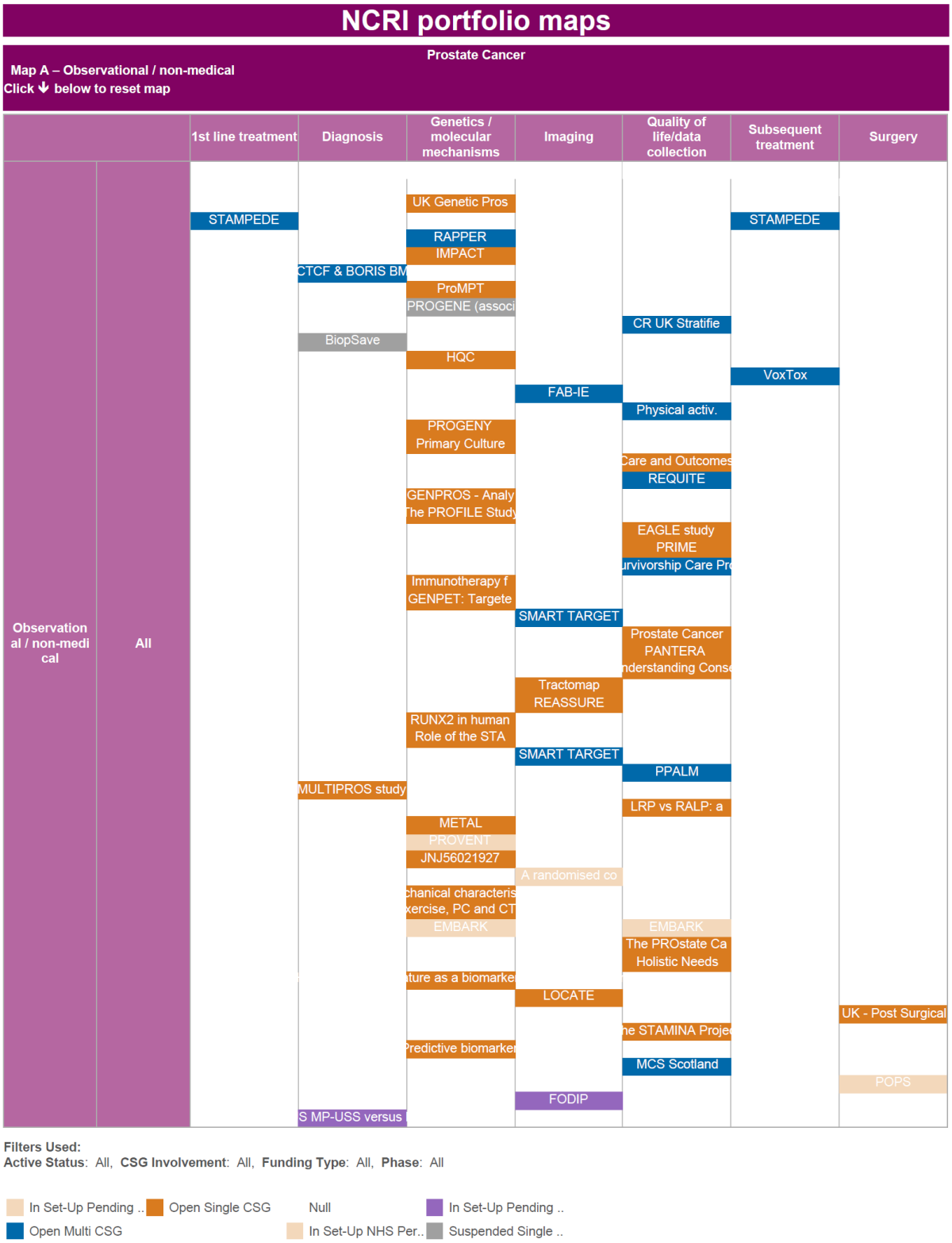
- To evaluate the use of individualised risk assessment models using multiplex tissue biomarkers in the diagnostic pathway. The aims of such an intervention are to reduce unnecessary biopsy, reduce the detection of low-grade disease while maintaining (or improving) the detection of high-grade disease.
- To minimise the morbidity of prostate biopsy, while improving the detection of high-grade disease.
- To evaluate the role of MRI in the diagnostic pathway
- To evaluate novel methodologies to improve surgical trial success in accrual
- To evaluate novel strategies to reduce harms of current treatment in men requiring therapy
- To increase the number of new investigators becoming trial PIs.

C – Advanced Disease Subgroup Strategy

- To build on the success of STAMPEDE, introducing new treatment comparisons into the trial
- To identify intermediate endpoints to hasten clinical development of new agents
- To collaborate with the Supportive and Palliative Care CSG
- To focus on translational science with an overarching focus to progress the theme of personalized medicine in advanced prostate cancer.
- To engage with the ECMC network.

Appendix 3

Portfolio maps



NCRI portfolio maps

Prostate Cancer

Map B – Metastatic
Click ↓ below to reset map

		1st line treatment	Diagnosis	Genetics / molecular mechanisms	Imaging	Quality of life/data collection	Subsequent treatment	Surgery
Refractory metastatic	All	PATCH				CR UK Stratifie	PATCH	
							SAPROCAN	
							AT13148 Phase I	
							TOPARP	
							MELCAP	
							ZD3965 in adv can	
							ledronic acid and I	
							CANTATA	
		DCVAC						
							abiraterone acetate	
			SWE					
							ProCAID	
							Radium-223	
						Risk of Seizure		
							masit. V docet.	
							RE-AKT	
							Enzalutamide +/- B	
		MAdCaP						
		CANC - 3641						
		ASURE Radium-2						
							Add-Aspirin	
							ENZAMET	
							Tasquinimod	
		Ipilimumab						
		LETERONE VS E						
		VANCE						
		Oral RXDX-101						
		PREMISE						
Refractory psa ..	All							
Sensitive metastatic	All	n mHSPC CANC -						

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

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

NCRI portfolio maps

Prostate Cancer

Map C – Localised
Click ↓ below to reset map

		1st line treatment	Diagnosis	Genetics / molecular mechanisms	Imaging	Quality of life/data collection	Subsequent treatment	Surgery
Localised	All	ACT' SURVEILL PATCH INDEX DELINEATE ProSpare II The PACE Study TAK-385 CaNCaP02 - CAmb PART Add-Aspirin ENZARAD			PET /MRI preRad [18F] DIHYDRO-T ciclovine (18F) PET		PATCH RADICALS SPARTAN	
Locally advanced	All	ProSpare II ODM Add-Aspirin Oral RXDX-101			FORECAST [18F] DIHYDRO-T		RADICALS AdUP SPARTAN	

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

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

Appendix 4

Publications in the reporting year

TRAPEZE

Nicholas D. James; Sarah J. Pirrie; Ann M. Pope; Darren Barton; Lazaros Andronis; Ilias Goranitis; Stuart Collins; Adam Daunton; Duncan McLaren; Joe O'Sullivan; Christopher Parker; Emilio Porfiri; John Staffurth; Andrew Stanley; James Wylie; Sharon Beesley; Alison Birtle; Janet Brown; Prabir Chakraborti; Syed Hussain; Martin Russell; Lucinda J. Billingham. Clinical Outcomes and Survival Following Treatment of Metastatic Castrate-Refractory Prostate Cancer With Docetaxel Alone or With Strontium-89, Zoledronic Acid, or Both: The TRAPEZE Randomized Clinical Trial. JAMA Oncology 2016 [epub ahead of print]

STAMPEDE

James ND, Sydes MR, Clarke NW, Mason MD, Dearnaley DP, Spears MR, Ritchie AW, Parker CC, Russell JM, Attard G, *et al.* Addition of docetaxel, zoledronic acid, or both to first-line long-term hormone therapy in prostate cancer (STAMPEDE): survival results from an adaptive, multiarm, multistage, platform randomised controlled trial. Lancet 21 Dec 2015

ND James, MR Spears, NW Clarke, DP Dearnaelyt, MD Mason, CC Parker, AWS Ritchie, JM Russell, F Schiavone, G Attard, JS De Bono, A Birtle, DS Engeler, T Elliott, D Matheson, J O'Sullivan, D Pudney, N Srihari, J Wallace, J Barber, I Syndikus, MKB Parmar, MR Sydes. Failure-Free Survival and Radiotherapy in PatientsWith Newly Diagnosed Nonmetastatic Prostate Cancer: Data From Patients in the Control Arm of the STAMPEDE Trial. JAMA Oncology (2015) epub ahead of print

James ND, Spears MR, Clarke NW, Dearnaley DP, De Bono JS, Gale J, Hetherington J, Hoskin PJ, Jones RJ, Laing R, Lester JF, McLaren D, Parker CC, Parmar MK, Ritchie AW, Russell JM, Strebel RT, Thalmann GN, Mason MD, Sydes MR.Survival with Newly Diagnosed Metastatic Prostate Cancer in the "Docetaxel Era": Data from 917 Patients in the Control Arm of the STAMPEDE Trial (MRC PR08, CRUK/06/019. Eur Urol. 2015 Jun;67(6):1028-38

R. Davda, S. Hughes, R. Jones, S.J. Crabb, J. Troup, H. Payne. Chemotherapy at First Diagnosis of Advanced Prostate Cancer Revolution or Evolution? Findings from a British Uro-oncology Group UK Survey to Evaluate Oncologists' Views on First-line Docetaxel in Combination with Androgen Deprivation Therapy in Castrate-sensitive Metastatic and High-risk/Locally Advanced Prostate Cancer. 2016. Clinical Oncology. *In press.*

James ND, Spears MR, Clarke NW, Dearnaley DP, De Bono JS, Gale J, et al. Survival with Newly Diagnosed Metastatic Prostate Cancer in the "Docetaxel Era": Data from 917 Patients in the Control Arm of the STAMPEDE Trial (MRC PR08, CRUK/06/019). Eur Urol. 2015;67(6):1028-38

James ND, Spears MR, Clarke NW, Dearnaley DP, Mason MD, Parker CC, et al. Failure-Free Survival and Radiotherapy in Patients With Newly Diagnosed Nonmetastatic Prostate Cancer: Data From Patients in the Control Arm of the STAMPEDE Trial. JAMA Oncol. 2015:1-10

Vale CL, Burdett S, Rydzewska LHM, Albiges L, Clarke NW, Fisher D, et al. Addition of docetaxel or bisphosphonates to standard of care in men with localised or metastatic, hormone-sensitive

prostate cancer: a systematic review and meta-analyses of aggregate data. The Lancet Oncology. 2015

James ND, Sydes MR, Clarke NW, Mason MD, Dearnaley DP, Spears MR, et al. Addition of docetaxel, zoledronic acid, or both to first-line long-term hormone therapy in prostate cancer (STAMPEDE): survival results from an adaptive, multiarm, multistage, platform randomised controlled trial. The Lancet. 2016;387(10024):1163-77

Active Surveillance

Henderson DR, de Souza NM, Thomas K, Riches SF, et al. Nine-year Follow-up for a Study of Diffusion-weighted Magnetic Resonance Imaging in a Prospective Prostate Cancer Active Surveillance Cohort. Eur Urol. 2015 Oct 16. pii: S03022838(15)00980.

Simpkin AJ, Donovan JL, Tilling K, Lane JA, Martin RM, Albertsen PC, Bill-Axelson A, Carter HB, Bosch R, Ferrucci L, Hamdy FC, Holmberg L, Metter EJ, Neal DE, Parker CC, Metcalfe C. BJU Int. 2016 Jan 22. doi: 10.1111/bju.13422. [Epub ahead of print]

PROMIS

El-Shater Bosaily A, Parker C, Brown LC, Gabe R, Hindley RG, Kaplan R, Emberton M, Ahmed HU; PROMIS Group. The University College London/Medical Research Council/National Institute of Health Research-Health Technology Assessment PROMIS Trial: An Update. Eur Urol Focus. 2015 Sep;1(2):212-214. PubMed. PMID: 26839919; PubMed Central PMCID: PMC4694096.

El-Shater Bosaily A, Parker C, Brown LC, Gabe R, Hindley RG, Kaplan R, Emberton M, Ahmed HU; PROMIS Group. PROMIS--Prostate MR imaging study: A paired validating cohort study evaluating the role of multi-parametric MRI in men with clinical suspicion of prostate cancer. Contemp Clin Trials. 2015 May;42:26-40.doi: 10.1016/j.cct.2015.02.008. Epub 2015 Mar 3. PubMed PMID: 25749312; PubMed Central PMCID: PMC4460714

CROP trial

Boyd, K et al. A decision-analytic cost-effectiveness model to compare prostate cryotherapy to androgen deprivation therapy for treatment of radiation recurrent prostate cancer. 2015. BMJ Open (in press)

CHHiP Trial

Wilkins A, Mossop H, Syndikus I et al. Hypofractionated radiotherapy versus conventionally fractionated radiotherapy for patients with intetmediate risk prostate cancer: 2 year patient reported outcomes of the randomised, non-inferiority, phase 3 CHHIP trial. Lancet Oncology (2015) 16(16):1605-1616 Dec 2015

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Appendix 5

Major international presentations in the reporting year

ProCAID

Simon J. Crabb, Alison J. Birtle, Karen Martin, Nichola Downs, Megan Bowers, Ian Ratcliffe, Mary Ellis, Gareth Griffiths, Stuart Thompson, Vincent Khoo, Robert J. Jones. ProCAID: A phase I clinical trial to combine the AKT inhibitor AZD5363 with docetaxel and prednisolone (DP) chemotherapy for metastatic castration resistant prostate cancer (mCRPC). ASCO, Genitourinary Cancers Symposium, San Francisco, 2016

SAKK 08/11

R. Cathomas, S. Crabb, H. Kenner, M. Mark, C. Rothermundt, T. Elliott, R. Winterhalder, P. Von Burg, S. Berardi Vilei, S. Hayoz, D. Rauch, E. Roggero, F. Stenner, D. Berthold, A. Erdmann, N. Fischer, G. Manetsch, S. Gillessen. Orteronel (Ort) maintenance therapy in patients (pts) with metastatic castration resistant prostate cancer (mCRPC) and non-progressive disease after first-line docetaxel (Doc) therapy: Results of a multicenter randomized double-blind placebo-controlled phase III trial (SAKK 08/11). ESMO Annual Meeting, Vienna, 2015