SUB STUDIES OVERVIEW

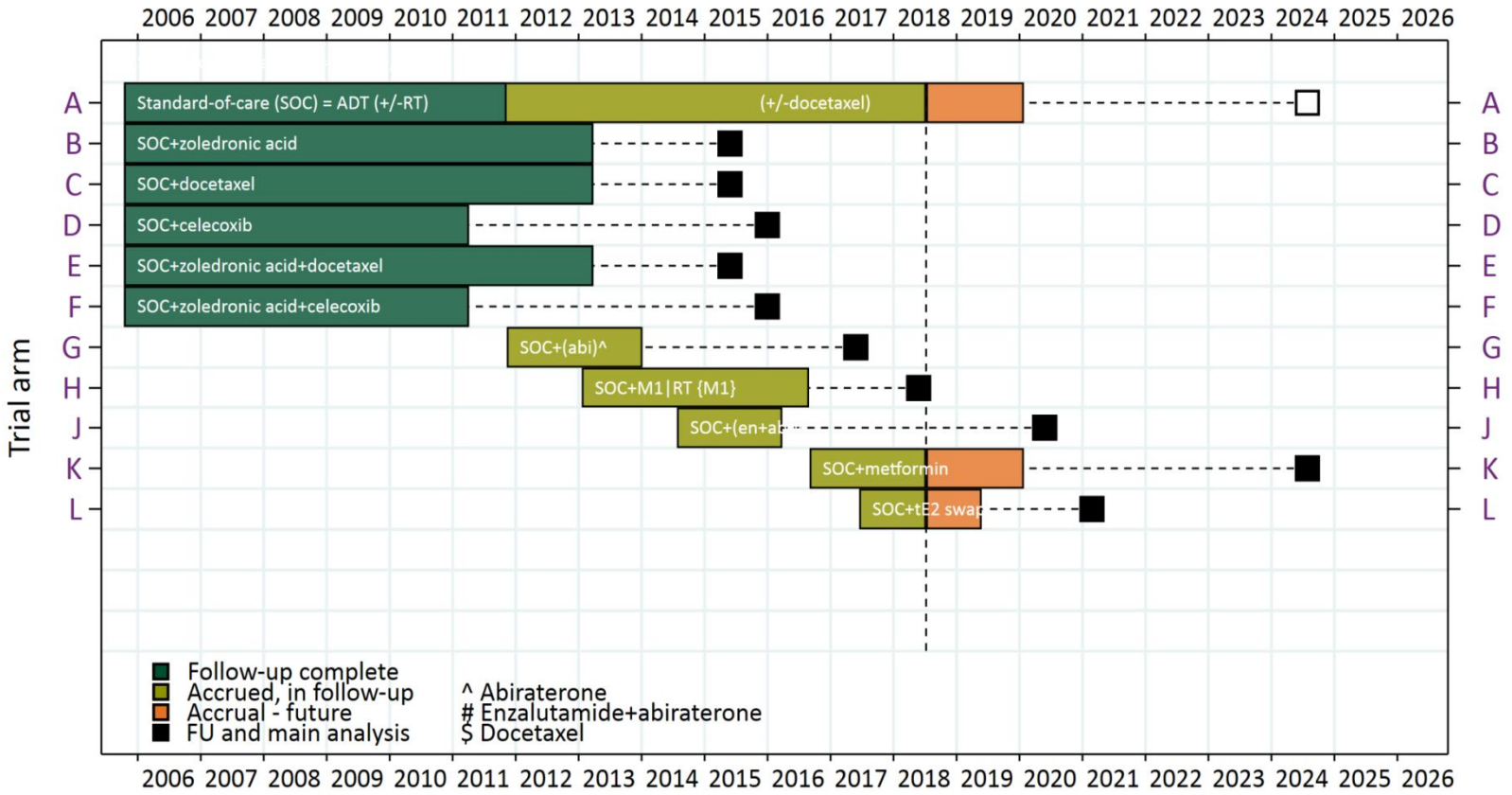
STAMPEDE

Systemic **T**herapy in **A**dvancing or **M**etastatic

Prostate Cancer: **E**valuation of **D**rug **E**fficacy

November 2018

STAMPEDE


2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017 2018 2019 2020 2021 2022 2023 2024 2025 2026
Trial arm
A
B
C
D
E
F
G
H
J
K
L
Standard-of-care (SOC) = ADT (+/-RT)
(+/-docetaxel)
SOC+zoledronic acid
SOC+docetaxel
SOC+celecoxib
SOC+zoledronic acid+docetaxel
SOC+zoledronic acid+celecoxib
SOC+(abi)^
SOC+M1|RT {M1}
SOC+metformin
Follow-up complete
Accrued, in follow-up
Accrual - future
FU and main analysis
^ Abiraterone
# Enzalutamide+abiraterone
$ Docetaxel

Additional Research Consent

Consent for additional research has been recorded in two places:

1. STAMPEDE Consent form (part L) version 13.0 and earlier

I have read the Additional research patient information sheet relating to the Molecular Genetics Sub-studies and I agree to (see K and L)

K. I agree to donate a droplet of blood sample which will be stored and may be used for research in the future. I understand this is a gift. ☐

L. After my initial diagnosis I give my authority for my remaining samples to be used for additional research analyses. I understand this is a gift ☐

2. From Mar-2016 onwards consent for participation in additional sub-studies is collected on a separate additional research consent form (part C)

C. I give my consent for my remaining tissue, including prostate biopsy or surgical samples, to be used for additional research analyses. I understand that this may require the anonymised samples to be transferred outside of Europe and analysed by researchers (including both academic and commercial collaborators). This may include genetic analysis or use in animal models. I will not benefit financially from this work and will not be contacted with any results arising from it.

Combined Consent

Consent to the main study and to optional additional research will now be captured on the one consent form.
Following this amendment:
Section B: Q15

15. I have read the Additional Research participant information sheet and I give my consent for my remaining prostate cancer tumour sample (including prostate biopsy or surgical samples) to be used for additional prostate cancer research. I understand that this may require the anonymised samples to be transferred outside of Europe and analysed by researchers (including both academic and commercial collaborators). This may include genetic analysis or use in animal models. I will not benefit financially from any resulting arising from this research.

Germline DNA Analysis
(Saliva Samples)

Aims

- To examine the germline (inherited) genetic changes present in mean with high-risk localised or metastatic prostate cancer.
- How does inherited genetic profile influence treatment response and prostate cancer outcome?

Eligibility

- **All** patients enrolled in STAMPEDE are eligible to participate in this sub-study
- Patients must be provided with the additional research PIS
- Informed consent must be obtained using additional research consent form prior to Saliva collection; using consent form version 18.0
- Saliva sample can be collected at any time point during the study

Saliva Collection

A single saliva sample will be collected from patients who have consented.

Please ensure that patient does not eat/drink/chew gum/brush their teeth for **30 minutes before sample collection**. For full details refer to STAMPEDE Sample Collection and Handling manual v7 (Section 1).

- A repeat sample may be requested in cases where quality of DNA is insufficient.
- Saliva collection Oragene kits are supplied to all sites upon request
- Please email trial team mrcctu.stampede@ucl.ac.uk should you require more kits

Kit Contains:

- 1x Saliva Collection Kit (Oragene DNA)
- 1x White Postal Tube
- 2x Sample ID Labels
- 1x Plastic Envelope
- 1x Pre-Paid padded envelope

Shipping Saliva Samples

Reminders:

- Please do not send saliva samples without a trial ID on the samples and saliva CRF
- Saliva kits are not sent automatically at randomisation, please email trial team mrcctu.stampede@ucl.ac.uk should you require more kits
- Please ensure to use older kits before expiry date
- Do not sent consent form with the samples
- Ensure to send in **consent forms to MRC CTU**

Shipping Checklist:

1. Place labelled Oragene tube inside the postal tube and secure the screw cap. Complete Saliva CRF
2. Place Postal tube into the plastic polyseal bad and seal
3. Place both postal tubes into the transport box
4. Place the plastic polyseal bag and the saliva pathology form into the prepaid padded envelope

Where to post samples:

Professor Ros Eeles
STAMPEDE SALIVA
Institute of Cancer Research
15 Cotswold Place
Sutton
Surrey SM2 5NG

Please send a copy of the saliva form to MRC CTU at UCL

Circulating Tumour DNA Analysis
(Sequential Blood Samples)

What is ctDNA?

- Circulating tumour DNA is genetic material arising from cancer that circulates in the blood of prostate cancer patients

Why are serial blood samples collected?

- To identify and assess genetic changes associated with treatment failure
- To develop biomarkers that will help identify which patients benefit (or experience toxicity) from particular prostate cancer treatments

Eligibility

- As of Nov 2018 activation of protocol v19.0 **ONLY** patients allocated to the "Abiraterone and Enzalutamide comparison" are eligible to participant in this sub-study.
  - ✓ Arm A: SOC (contemporaneous to Arm J)
  - ✓ Arm J: SOC+ Enz + Abi

*Randomised between 29-Jul-2014 and 31-Mar-2016

- **Please DO NOT** collect samples for patients in other arms (i.e. K and L) or Arm A's that are not contemporaneous to Arm J, even if they are due a sampling time point.

Blood Collection Time points

Time points for sequential blood sampling by disease stage

ASSESSMENT POINT	CONSENTED TO PREVIOUS VERSIONS OF CONSENT FORM		CONSENTED TO CURRENT VERSION OF THE PARTICIPANT TREATMENT AND ADDITIONAL RESEARCH CONSENT FORM	
	M1 PATIENTS	M0 PATIENTS	M1 PATIENTS	M0 PATIENTS
Pre-progression				
48 weeks (+/- 12 weeks)	X		X	
72 weeks (+/- 12 weeks)	X		X	
84 weeks (+/- 12 weeks)	X		X	
At progression	X	X		
Biochemical			X	X
Radiological			X	X
Clinical			X	X
End of first-line treatment				
End of first line treatment in absence of progression		X	X	X
Immediately prior to starting second line treatment [2]	X	X	X	X

KEY:

Timepoints introduced from protocol v.16.0 only applicable for patients who have provided consent on Current version of Participant Treatment and Additional Research Consent Form

X **Progression** samples are the most important. If biochemical, clinical and radiological progression occur at different times please provide a sample at each time point.

[2] If second line treatment is started at the same visits as progression is confirmed, only collect one sample

Blood Collection Logistics

Blood kits are supplied to sites.

Please contact the STAMPEDE team on mrcctu.stampede@ucl.ac.uk if additional supplies are required.

- Confirm consent prior to blood collection
- Collect 2x 10ml of blood in streck™ tubes provided and invert 8-10 times.
- Please do not under fill tubes
- Ensure blood tubes are labelled and blood form is completed
- Store blood samples at room temp DO NOT refrigerate
- Post samples together with blood form within a maximum of 2 days
- Email ci.stampedeblood@ucl.ac.uk when samples are posted

Shipping Blood Samples

Reminders:

- **Progression** samples are the **most important**
- If biochemical, clinical and radiological progression occurs at different times please provide a sample at each time point
- Please ensure **consent forms are sent to MRC CTU**, very important to ensure GCP compliance and HTA regulations
- Blood kits are not sent automatically at randomisation, please email trial team mrcctu.stampede@ucl.ac.uk should you require more kits
- Please do not sent blood samples without a trial ID on the samples and blood CRF

Shipping Checklist:

1. 2x 10ml Streck blood tubes labelled with Trial ID, DOB and Date of Collection
2. Completed Blood CRF
3. Place streck blood tubes into a postal tube
4. Place both postal tubes into the transport box

Where to post samples:

STAMPEDE BLOOD
UCL Cancer Institute
UCL ECMC GCLP Facility
Paul O'Gorman Building
72 Huntley Street
London
WC1E 6DD

Please send an email to ci.stampede@ucl.ac.uk to inform the lab that a samples have been sent.
Send a copy of the Blood CRF to MRC CTU at UCL.

Tissue Sample Analyses

The STAMPEDE protocol (from version 3.0, approved in 2006) has specified that FFPE tumour blocks will be retrieved from sites at the point at which additional analyses are planned

Aim of additional analyses:
Through the analysis of tumour blocks we hope to be able to maximise the information that can be learnt about the treatments tested in STAMPEDE and inform new therapeutic approaches. Specifically, this project aims to identify predictive and prognostic biomarkers that can inform treatment selection.

Analyses are now planned for patients randomised to:

- **Docetaxel-containing comparisons**
  - Arms A, C and E randomised between 05-Oct-2005 and 31-Mar-2013
- **Abiraterone comparison**
  - Arms A and G randomised between 15-Nov 2011 and 17-Jan-2014

Required Agreements

Clinical Trial Agreement variation is required to permit reimbursement.

Supporting Documents available via website:

- STAMPEDE Sample & Handling Manual (Section 3)
- Tissue Sample Form
- Pathology Request Letter (requires personalising)
- Accountability Log (optional, for site use only)

Tissue Samples

Samples to be collected

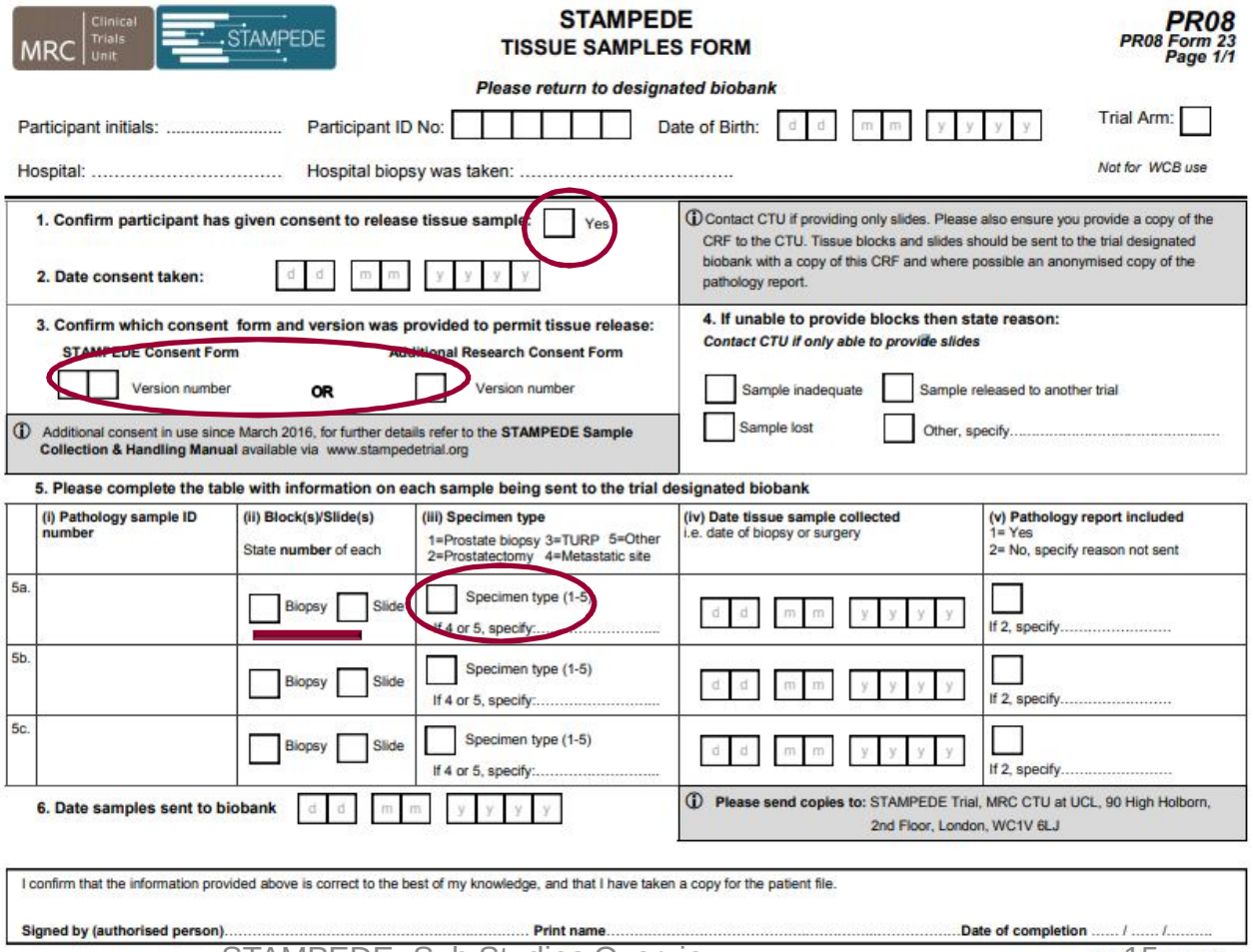
- Select proportion of STAMPEDE patients
- Samples will be requested in manageable batches
- Transfer required to the designated biobank within **4-6 weeks** of the request

Requesting Stored Samples

- FFPE tumour blocks- pre-trial entry prostate cancer samples are required i.e. those obtained (ideally) within 6-12 months of randomisation to the trial.
- Slides: max of 1 representative H&E slide per block
- Anonymised copy of the pathology report
- Complete Tissue Sample CRF
  - 1 copy to be sent to the designated biobank with the blocks
  - 1 copy to be sent to the MRC CTU at UCL
  - 1 copy retained at site

Following analysis, all remaining usable tissue can be returned upon request. Please email the STAMPEDE team to arrange this.

Tissue Sample Form



STAMPEDE
TISSUE SAMPLES FORM

PR08
PR08 Form 23
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Please return to designated biobank

Participant initials: ..... Participant ID No: ☐☐☐☐☐☐ Date of Birth: d d m m y y y y Trial Arm: ☐

Hospital: ..... Hospital biopsy was taken: ..... *Not for WCB use*

1. Confirm participant has given consent to release tissue samples ☐ Yes

2. Date consent taken: d d m m y y y y

ⓘ Contact CTU if providing only slides. Please also ensure you provide a copy of the CRF to the CTU. Tissue blocks and slides should be sent to the trial designated biobank with a copy of this CRF and where possible an anonymised copy of the pathology report.

3. Confirm which consent form and version was provided to permit tissue release:

STAMPEDE Consent Form ☐☐ Version number **OR** **Additional Research Consent Form** ☐ Version number

ⓘ Additional consent in use since March 2016, for further details refer to the **STAMPEDE Sample Collection & Handling Manual** available via www.stampedetrial.org

4. If unable to provide blocks then state reason:
Contact CTU if only able to provide slides

☐ Sample inadequate ☐ Sample released to another trial
☐ Sample lost ☐ Other, specify.....

5. Please complete the table with information on each sample being sent to the trial designated biobank

	(i) Pathology sample ID number	(ii) Block(s)/Slide(s) State number of each	(iii) Specimen type 1=Prostate biopsy 3=TURP 5=Other 2=Prostatectomy 4=Metastatic site	(iv) Date tissue sample collected i.e. date of biopsy or surgery	(v) Pathology report included 1= Yes 2= No, specify reason not sent
5a.		☐ Biopsy ☐ Slide	☐ Specimen type (1-5) If 4 or 5, specify:.....	d d m m y y y y	☐ If 2, specify.....
5b.		☐ Biopsy ☐ Slide	☐ Specimen type (1-5) If 4 or 5, specify:.....	d d m m y y y y	☐ If 2, specify.....
5c.		☐ Biopsy ☐ Slide	☐ Specimen type (1-5) If 4 or 5, specify:.....	d d m m y y y y	☐ If 2, specify.....

6. Date samples sent to biobank d d m m y y y y

ⓘ **Please send copies to:** STAMPEDE Trial, MRC CTU at UCL, 90 High Holborn, 2nd Floor, London, WC1V 6LJ

I confirm that the information provided above is correct to the best of my knowledge, and that I have taken a copy for the patient file.

Signed by (authorised person)..... **Print name**..... **Date of completion** ..... / ..... /.....

June 2015 Version 5.0

Materials & Shipping

- Shipping supplies can be provided:
  - Padded envelopes with pre-paid postage
  - Plastic bags
  - Sticker for labelling the plastic bag with Trial ID
  - Slide mailers
- If possible please use 1 polyseal plastic bag per patient.
- Place the sticker on the plastic bag **not** the block and place the slide mailer containing the accompanying slide inside the plastic bag.
- Place all polyseal bags inside the padded envelope and seal it with tape

Checklist: Please ensure you send the following:

1. Polyseal bag containing all available FFPE blocks labelled with the Trial ID
2. Slide mailer labelled with Trial ID containing representative H&E slide
3. Completed Tissue Samples CRF
4. Anonymised pathology report

Post samples to the designated biobank

The address will be pre stamped on packing you will receive.

Please send an email to the STAMPEDE team with a list of trial ID's for all blocks that have been sent to the designated biobank for tracking purposes

What to do if…

Blocks are not available:

- Complete the tissue sample CFR and send only to MRC CTU at UCL stating the reason of unavailability in question 2.

More than 1 block is available:

- Please send all blocks, or the 3 containing the most tissue

Slides are available:

- Send a max of 1 representative H&E slide per block

Invoicing

Confirmed receipt by Wales Cancer Bank

Email invoice: mrcctu.stampede@ucl.ac.uk

Please include:

- FAO Blocks Project- Mazna Anjum
- Instructions for payment
- List of trial IDs invoicing for

More Information

For more detailed information, please see the STAMPEDE protocol, Sample Collection & Handling Manual, the FAQ section of the website, or contact the trial team

mrcctu.STAMPEDE@ucl.ac.uk