STAMPEDE trial (MRC PR08):

Arm J Pharmacy Training

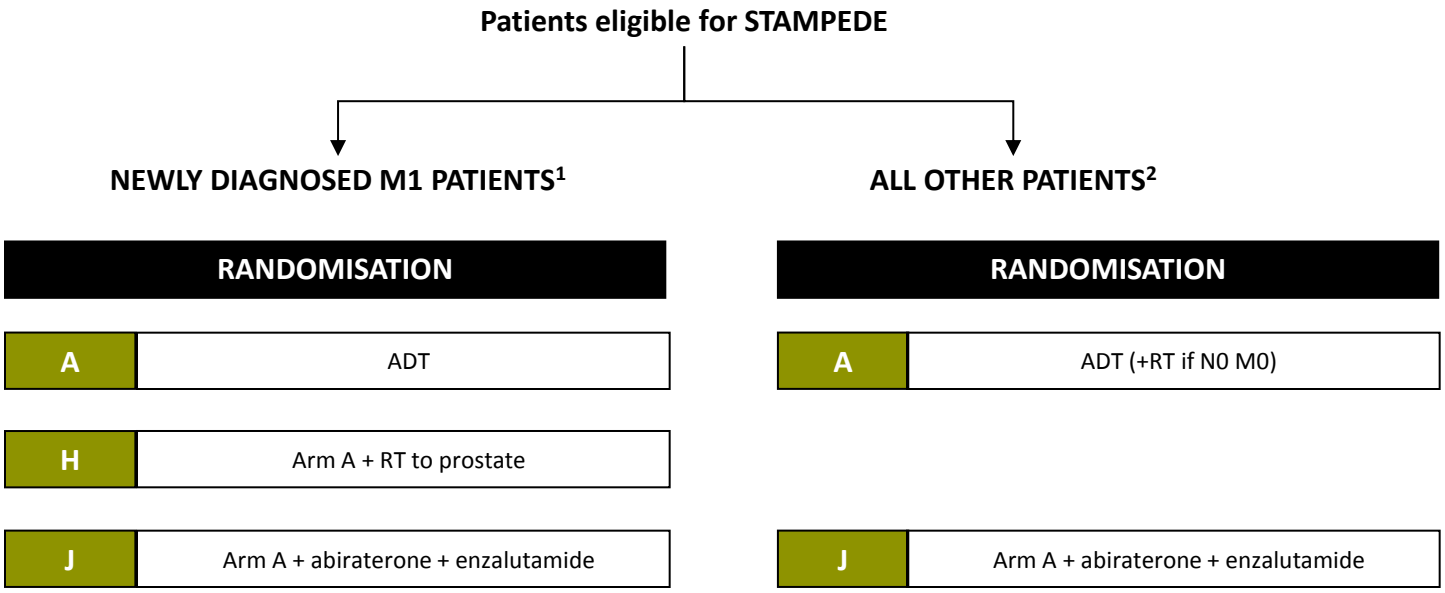
Overview

- Arm J Hypothesis and trial design
- Activation timelines and requirements
- Treatment administration and duration
- IMPs overview
  - Configuration
  - Drug ordering
  - Accountability
  - Destruction
  - Returns
- Other pharmacy updates

STAMPEDE: Hypothesis and set-up

- Will addition of enzalutamide and abiraterone to standard-of-care improve survival in hormone-naïve Pca?
- Free-of-charge IMP supply from Janssen and Astellas
- IMP distribution via Sharp Clinical Services UK

STAMPEDE: Eligibility and trial design



Please refer to protocol v12.0 and appendices v 11.0 for more details on eligibility

[1] except pts with a contra-indication to RT

[2] all suitable pts with newly diagnosed locally advanced disease should also have RT[1]

Activation timelines

- Activation in late June 2014
- REC approval received in February 2014
- MHRA approval received in April 2014
- IMP distributor in set-up

Activation process

- Pharmacy pack to be circulated to sites
  - Pharmacy instructions updated
  - New Pharmacy file self-assessment form

- IB and Pharmacy Pack confirmation to be faxed/emailed to STAMPEDE team

- Full activation plan to be communicated in due course

Arm J: Treatment administrations

- 4 x 250mg abiraterone (empty stomach) + 5 mg od prednisolone
- 4 x 40mg enzalutamide (with or without food)
- Trial treatment to start within 4 weeks of randomisation
- Any con-medication should be checked with trial team
- Standard-of-care RT (to be stratified at randomisation)
  - Mandatory for N0M0 patients
  - Optional for N+M0

Arm J: Assessment of Treatment Duration

- Different treatment duration for **M+** and **M0** patients

- **M+** patients, treatment should continue until **all progressions** occur:
  - PSA progression
  - Radiological progression
  - Clinical progression

- **N0M0** patients or **N+M0** patients planned for RT treatment should continue until:
  - 2 years or
  - Disease progression as defined for M+ patients, whichever is sooner

- **N+M0** patients **not planned for radical radiotherapy** should continue until:
  - Disease progression as defined for M+ patients

Arm J: Treatment duration

- Treatment should be stopped if new systemic therapy is introduced (eg anti-androgens)
- Post-progression dexamethasone 0.5mg can be given instead of prednisolone
- Selective discontinuation of either IMP depending on toxicity

IMP configuration: abiraterone

- Zytiga (Janssen)
  - 120 x 250mg tablets
  - bottle
  - pre-labelled

- Shelf life: 2 years
- Store between 15C and 30C
- IB version 10.0

! Arm G and Arm J abiraterone will be clearly labelled

! Pregnancy notification since IB version 9.0

IMP configuration: enzalutamide

- Xtandi (Astellas)
  - 120 x 40mg capsules
  - bottle
  - pre-labelled

- Shelf life: 2 years
- Store <25 C
- IB version 6.0

Arm J: IMP ordering

- Both IMPs can be ordered directly via Sharp (email, fax)
- Order form for both IMPs
- No starter packs (1st order = 1st patient randomised)
- Amount per order:
  - 9 bottles
  - 12 bottles
  - 16 bottles
- Re-order when stock is low and minimise waste
- Fax back distributor upon receipt

Arm J: IMP ordering

IMP	Contact	Details	Delivery Times
Zometa	MRC CTU Novartis	obu.medical@novartis.com	Allow 10 working days for delivery
Zytiga Arm G	B&C	F : +32 10 238 852 E : 144-Abirateroneiis@bnc-group.com	Allow 5 working days for delivery
Zytiga Arm J	Sharp	F : +44 (0)1873 8135999 E:	Allow 5 working days for delivery
Xtandi	Sharp	F : +44 (0)1873 8135999 E:	Allow 5 working days for delivery

Arm J: IMP dispensing and accountability

- Supply 1 month supply for the first 24 weeks
- 3 monthly supplies after 6 months if no toxicity
- Full accountability to be maintained
- Separate accountability log

Arm J: IMP returns and destruction

- No returns required unless
  - patient toxicity and
  - permanent termination of treatment
- Destroy returned stock & record on destruction log
- Any expired or unusable stock to be destroyed
  - According to local practice
  - To be recorded on destruction log

Arm J: IMP temperature control

- Temperature to be monitored throughout

- Any temperature excursion should be reported
  - Quarantine stock until further notice from team
  - Email mrcctu.stampede@ucl.ac.uk
    - Temperature log
    - Batch number of affected stock
    - If stock is for abiraterone Arm G or J

Other IMPs:
Zometa and Arm G Zytiga

Zometa

- Drug orders to continue as normal until patients complete treatment (2 years max)
- Refer to updated pharmacy instructions for further information
- Re-consent of patients undergoing treatment
  - see latest SmPC

Zytiga: Arm G

- Drug orders for **Arm G** patients via **B&C**
- Refer to updated pharmacy instructions for further information
- Letter to patients on new associated side effects
  - see latest IB version 10.0

Contact Details

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MRC

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ADDITIONAL SLIDES

Assessment of Treatment Failure

Types of progression:

1. Biochemical
2. Objective
   - Local
   - Lymph node
   - Distant metastatic
   - Skeletal related event

3. Symptomatic

Progression of each type need only be reported **once**

Complete an '**additional treatment update form**' if a patient receives additional treatment for a progression that you have already reported

Defining PSA Nadir & PSA Failure Categories

- PSA Nadir:
  - Lowest reported PSA level
  - Between randomisation and 24 weeks

- PSA Failure:
  - Depends on baseline PSA measurement and PSA nadir
  - 3 possible PSA failure categories, A, B and C

Reporting PSA Relapse

- Confirmatory PSA test between 1 week and 3 months later:
  - If value is ≥PSA progression value **then** report biochemical progression
- If clinician adds anti-androgens therapy before trial progression:
  - Report progression
- PSA progression emails are sent to sites approx. 3-monthly
  - Baseline and FU forms up to week 24 needed
  - Alternatively contact the trial team for help

STAMPEDE trial (MRC PR08):

Arm J overview

"Enzalutamide and abiraterone comparison" and trial update