

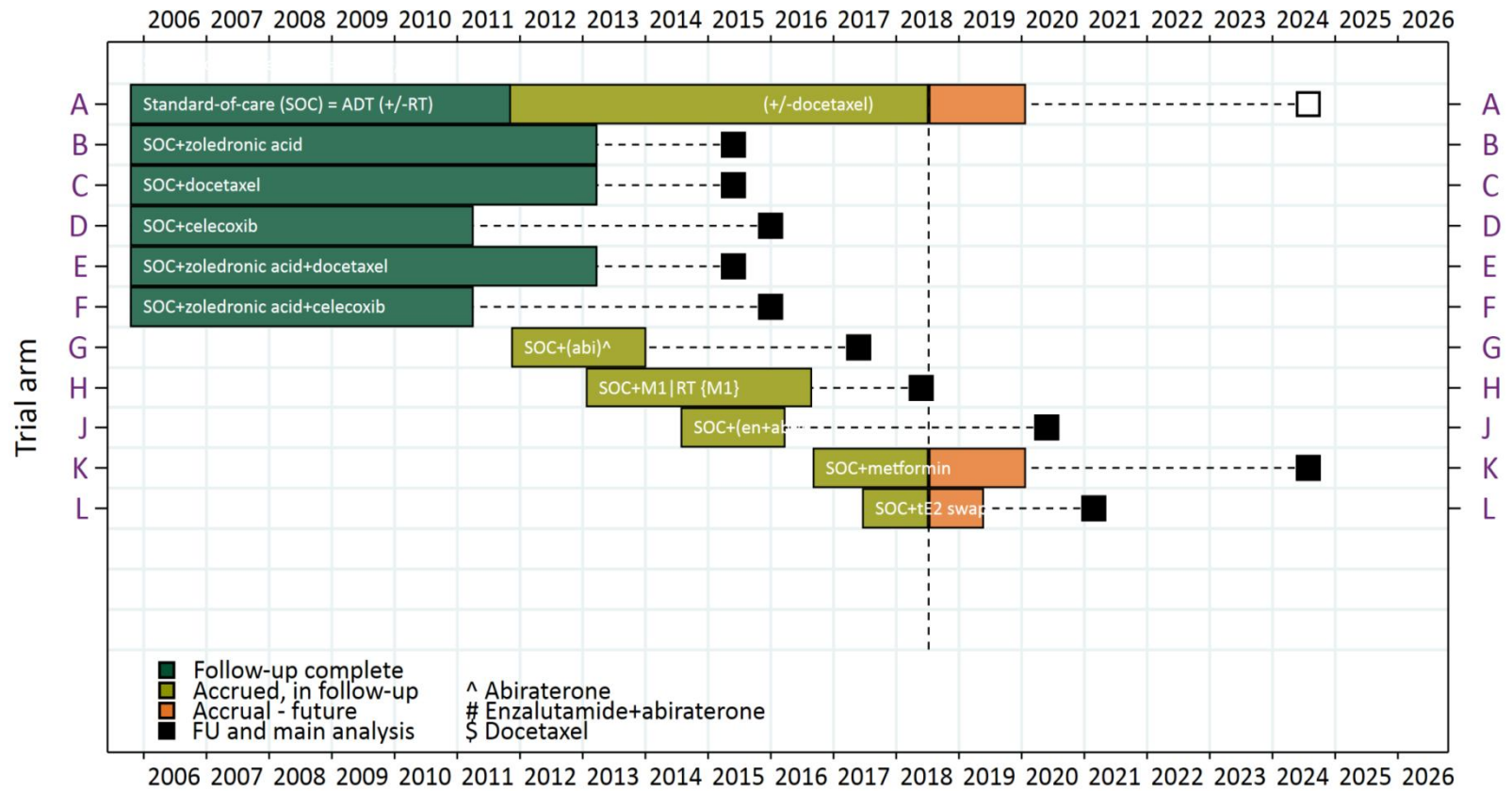
PHARMACY OVERVIEW

STAMPEDE

Systemic Therapy in **A**dvancing or **M**etastatic
Prostate Cancer: **E**valuation of **D**rug **E**fficacy

November 2018

STAMPEDE



Protocol Research Treatments

- Arm G – Abiraterone Acetate (Zytiga)
- Arm J – Abiraterone Acetate (Zytiga)
- Arm J – Enzalutamide (Xtandi)
- Arm K – Metformin
- Arm L – Transdermal Oestradiol (Progynova TS 100)

IMP Information

Arm G/J Zytiga

Abiraterone inhibits the enzymatic activity of steroid 17alpha-monooxygenase, a member of the cytochrome p450 family that catalyses the 17alpha-hydroxylation of steroid intermediates involved in testosterone synthesis. Administration of this agent may suppress testosterone production by both the testes and the adrenals to castrate-range levels.

Arm J Xtandi

Enzalutamide is an Androgen Receptor Antagonist, and Cytochrome P450 3A4 Inducer, and Cytochrome P450 2C9 Inducer, and Cytochrome P450 2C19 inducer. Enzalutamide inhibits the activity of prostate cancer cell ARs, which may result in a reduction in prostate cancer cell proliferation and, correspondingly, a reduction in the serum prostate specific antigen (PSA) level.

IMP Information

Arm K Metformin

Metformin inhibits complex I of the mitochondrial respiratory chain, thereby increasing the cellular AMP to ATP ratio and leading to activation of AMP-activated protein kinase (AMPK) and regulating AMPK-mediated transcription of target genes. This eventually prevents hepatic gluconeogenesis, enhances insulin sensitivity and fatty acid oxidation and ultimately leads to a decrease in glucose levels.

Arm L Progynova TS 100

Oestradiol hemihydrate diffuses through the cell membrane and binds to and subsequently activates the nuclear oestrogen receptor found in the reproductive tract, breast, pituitary, hypothalamus, liver, and bone. The activated complex binds to the oestrogen response element on the DNA and activates the transcription of genes involved in the functioning of the female reproductive system and secondary sex characteristics.

Ordering

Arm G Zytiga

- Abiraterone Acetate for Arm G patients are ordered through CSM (the distributor) using the order form.
- Abiraterone for Arm G is to be kept separate to Arm J Abiraterone and any pharmacy stock.
- Please find the order form on the STAMPEDE website here:

<http://www.stampetrial.org/centres/essential-documents/pharmacy/>

Arm K Metformin

- Metformin is to be ordered through the standard operating procedures for the pharmacy.

Arm J Zytiga and Xtandi

- Abiraterone Acetate & Enzalutamide for Arm J patients are ordered through Sharp (the distributor) using the order form.
- Abiraterone for Arm J is to be kept separate to Arm G Abiraterone and any pharmacy stock.
- Please find the order form on the STAMPEDE website here:

<http://www.stampetrial.org/centres/essential-documents/pharmacy/>

Arm L Progynova TS 100

- Progynova TS 100 Transdermal Oestradiol patches are ordered through AAH (the distributor) using standard site procedures. A discount will automatically be applied.

Receipt

Arm G Zytiga

- Log the stock on the accountability log in a timely manner & store the IMP appropriately.
- Check for signs of temperature excursion during shipping. If an excursion has occurred during transit please quarantine the IMP and contact the STAMPEDE Trial Team for further instructions.
- Acknowledge receipt of the delivery by emailing the enclosed form back to CSM.

Arm K Metformin

- Site Stock – Please follow any local site practices.

Arm J Zytiga and Xtandi

- Log the stock on the accountability log in a timely manner & store the IMP appropriately.
- Check for signs of temperature excursion during shipping. If an excursion has occurred during transit please quarantine the IMP and contact the STAMPEDE Trial Team for further instructions.
- Acknowledge receipt of the delivery by faxing or e-mailing the enclosed form back to Sharp.

Arm L Progynova TS 100

- Log the stock on the accountability log in a timely manner & store the IMP appropriately.

Accountability

Arm G Zytiga

- IMP accountability should be maintained on the Arm G Zytiga Accountability Log.
- Zytiga should be stored at room temperature and excursions outside of 15 - 30 degrees Celsius should be reported to the STAMPEDE trial team for further guidance.

Arm K Metformin

- Site Stock – Please follow any local site practices.

Arm J Zytiga and Xtandi

- IMP accountability should be maintained on the Arm J Zytiga Accountability Log and the Arm J Xtandi Accountability Log respectively for each IMP.
- Zytiga & Xtandi should be stored at room temperature and excursions outside of 15 - 30 degrees Celsius should be reported to the STAMPEDE trial team for further guidance.

Arm L Progynova TS 100

- IMP accountability should be maintained on the Arm L tE2 Accountability Log.
- Progynova TS should be stored below 30°C.

Dispensing

Arm G Zytiga

- Arm G Zytiga is to be prescribed from the STAMPEDE Arm G stock, and will arrive with an already affixed trial label.

Arm J Zytiga and Xtandi

- Arm J Zytiga and Xtandi is to be prescribed from the STAMPEDE Arm J stock, and will arrive with an already affixed trial label.

Arm K Metformin

- Metformin is to be prescribed from the pharmacy stock, with an affixed STAMPEDE trial specific label.
- Label templates can be found at:
<http://www.stampedetrial.org/centres/essential-documents/pharmacy/>

Arm L Progynova TS 100

- Progynova TS 100 is to be prescribed from the pharmacy stock, with an affixed STAMPEDE trial specific label.
- Label templates can be found at:
<http://www.stampedetrial.org/centres/essential-documents/pharmacy/>

Returns & Destruction

Arm G Zytiga

- Returns are not anticipated unless a patient is coming to a permanent stop of the medication.
- Any returns or expired stock must have trial team permission to be destroyed.
- Sites should document the destruction as appropriate within the Arm G Zytiga destruction log.

Arm K Metformin

- Any returns or expired stock can be destroyed without permission from the trial team, following the site's standard operating procedures.

Arm J Zytiga and Xtandi

- Returns are not anticipated unless a patient is coming to a permanent stop of the medication.
- Any returns or expired stock must have trial team permission to be destroyed.
- Sites should document the destruction as appropriate within the Arm J Zytiga and Xtandi destruction log.

Arm L Progynova TS 100

- Returns are not anticipated unless a patient is coming to a permanent stop of the medication.
- Any returns or expired stock must have trial team permission to be destroyed.
- Sites should document the destruction as appropriate within the Arm L tE2 destruction log.

More Information

For more detailed information, please see the STAMPEDE protocol, the STAMPEDE Pharmacy Information Sheet, the FAQ section of the website, or contact the trial team.



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