
STAMPEDE

Pharmacy training session

Protocol v16.0

MRC Clinical Trials Unit at UCL

Overview

- Outline rationale and key aspects of the “transdermal oestradiol (tE2) comparison” within STAMPEDE
- Treatment administration
- IMP overview
 - Supply
 - Accountability
 - Destruction
 - Returns
- Activation timelines and requirements
- Other pharmacy updates

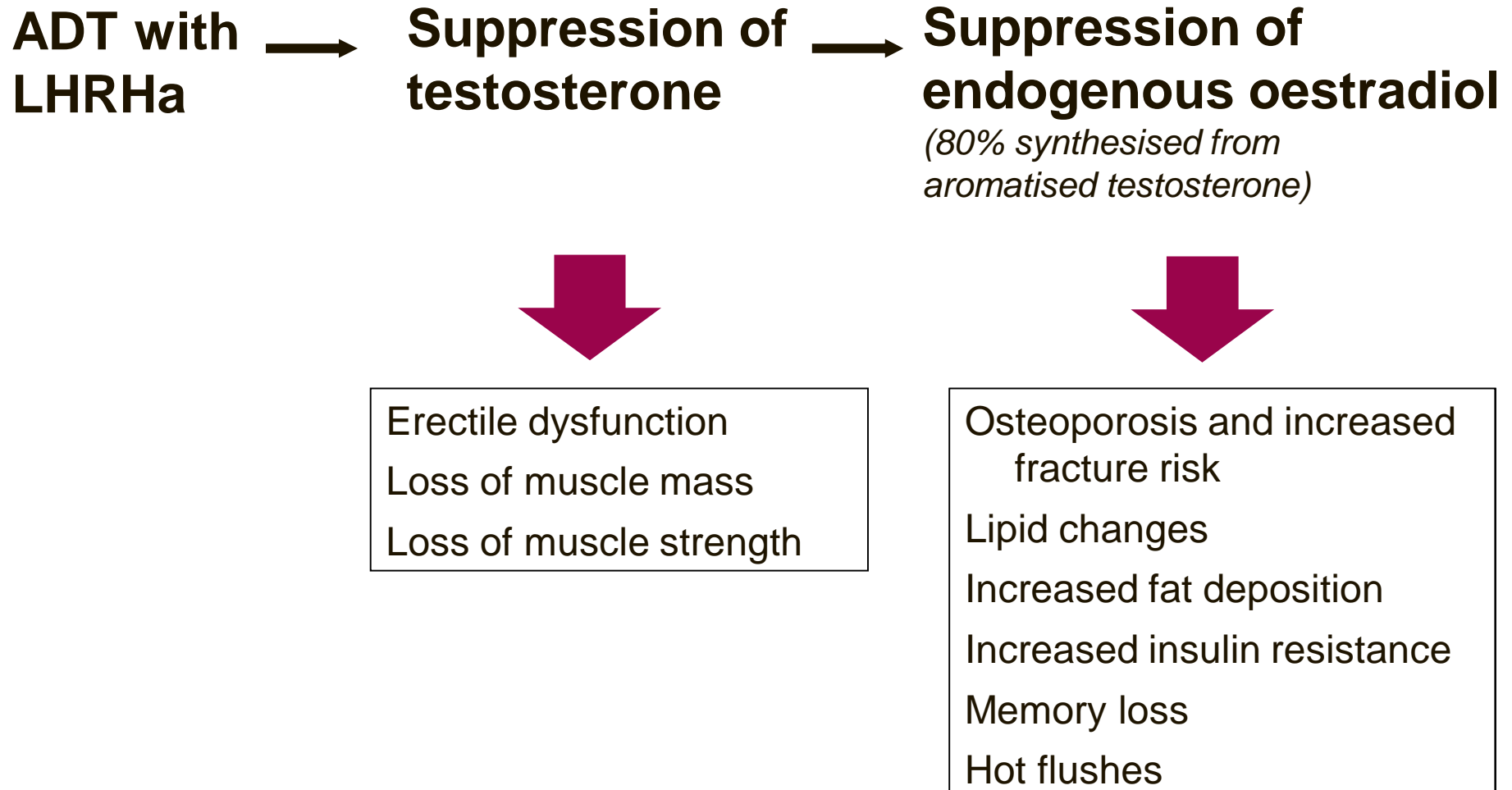
ADT vs hormone therapy definitions

in Protocol version 16.0

- **ADT** Androgen deprivation therapy given in the form of LHRH agonists/antagonists or alternatively, transdermal oestradiol
- **Hormone Therapy** All forms of hormone therapy given in the first line setting
 - includes LHRH, anti-androgens and transdermal oestradiol

Transdermal oestradiol: background & rationale

Toxicities due to sex hormone deficiency



Transdermal oestradiol

- Should avoid the toxicities associated with oestradiol deficiency seen with LHRHa
- Expected to mitigate the cardiovascular risk associated with oral oestrogen
- May possibly improve overall survival compared to LHRHa by:
 - reducing treatment-associated morbidity
 - potentially have additional direct anti-tumour effects

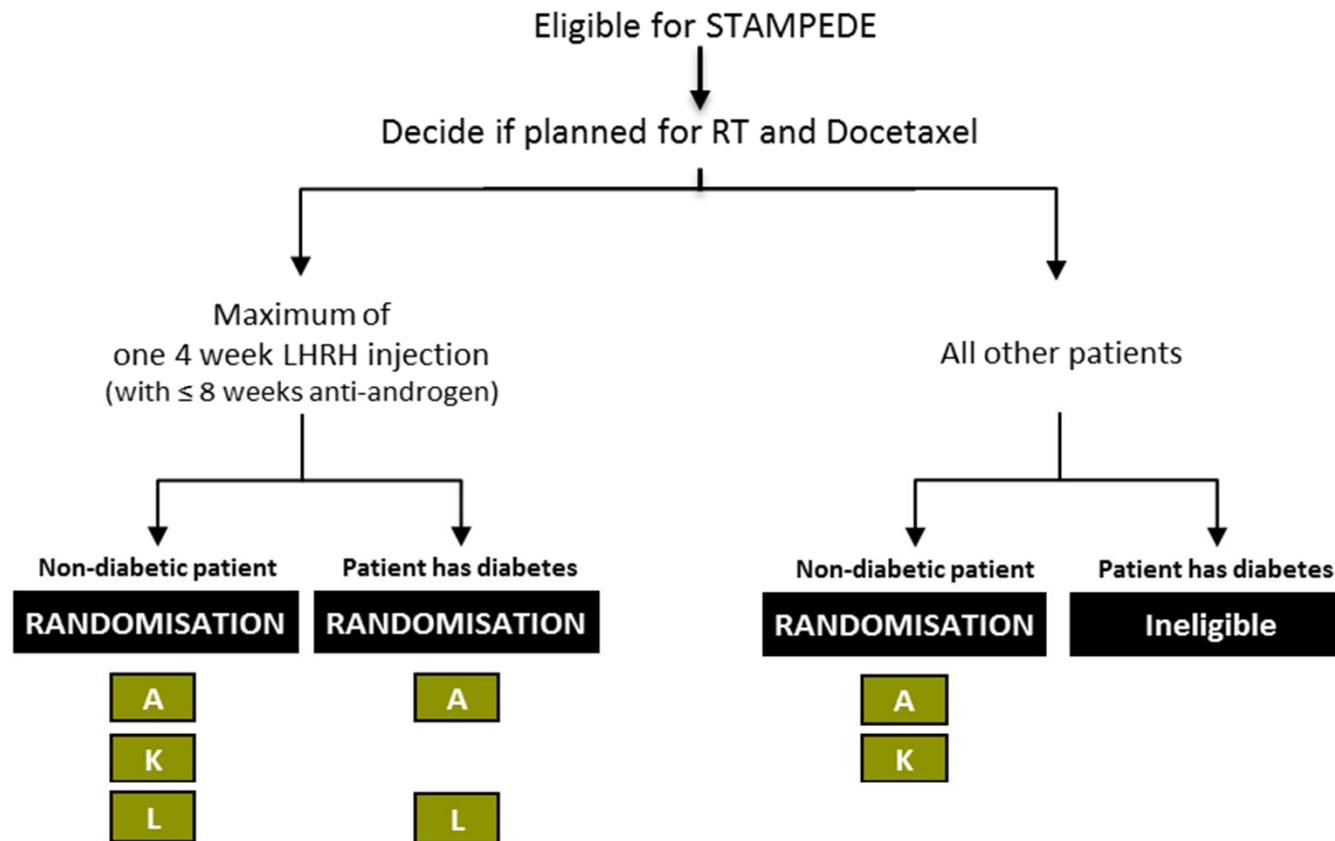
Transdermal oestradiol comparison

- Full details of scientific and clinical rationale in protocol.

**“Transdermal oestradiol
comparison”: design**

Arms open to recruitment in STAMPEDE

from Protocol version 16.0



Key

A	ADT ± RT ± DOC
K	ADT ± RT ± DOC ± metformin
L	tE2 ± RT ± DOC

RT = Radical radiotherapy for N0M0 pts
 DOC = Docetaxel for suitable pts
 ADT = Androgen deprivation therapy
 (LHRH agonist/antagonist or bilateral orchidectomy)
 tE2 = transdermal oestradiol

“Transdermal oestradiol comparison”: eligibility criteria

Inclusion criteria: “tE2 comparison”

- ≤8 weeks of anti androgen use
- Maximum one 4-week (or 1-month) LHRH injection
- Patient has not had a bilateral orchidectomy
- No cyproterone acetate prior to randomisation
- No prior radiologically confirmed deep vein thrombosis or pulmonary emboli
- No known thrombophilic disorders
- Not known to have porphyria

**Arm L treatment:
transdermal
oestradiol**

Transdermal oestradiol treatment

Starting treatment:

- Arm L patients should start tE2 treatment as soon as possible after randomisation, ideally within 1 week
- Discontinue any treatment started with LHRH and anti-androgens

Transdermal oestradiol treatment

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Administration:

- Delivered as Progynova TS 100 microgram/24 hours oestradiol patches
- Recommended anatomical sites: shoulder girdle, back, upper arms and buttocks. Alternate site of patch application.

Transdermal oestradiol treatment: Dose regimen

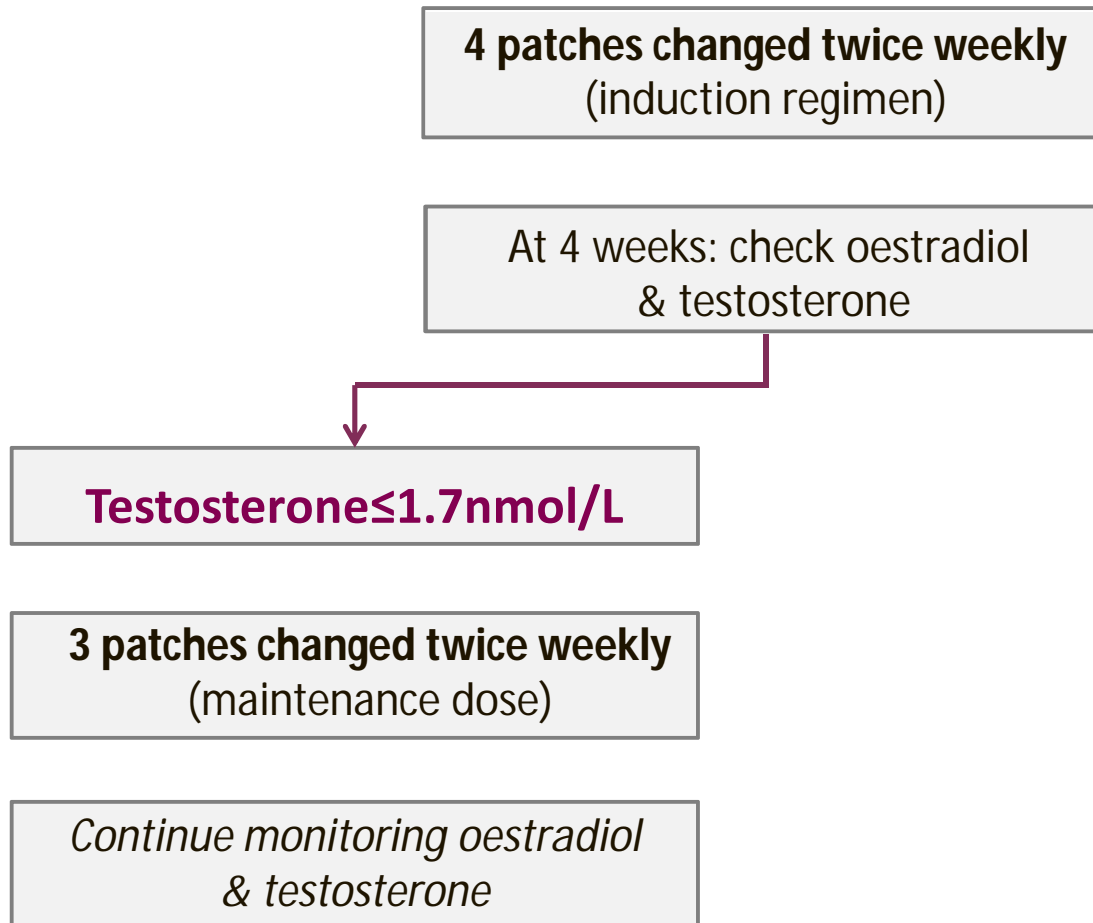
4 patches changed twice weekly
(induction regimen)

eg. Monday & Thursday

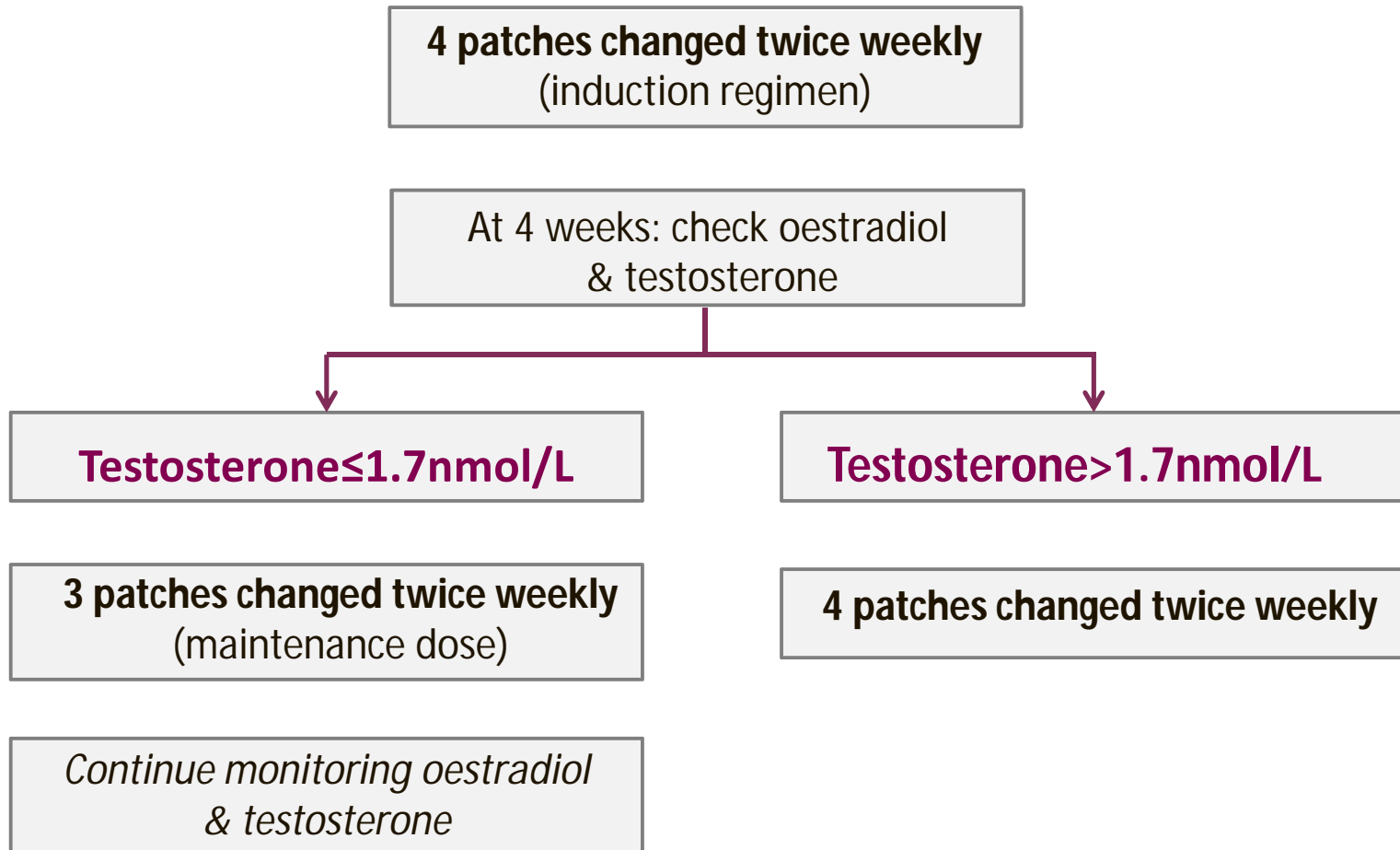
At 4 weeks: check oestradiol
& testosterone

NB. first f/up visit post-randomisation can be at 4 instead of 6 weeks

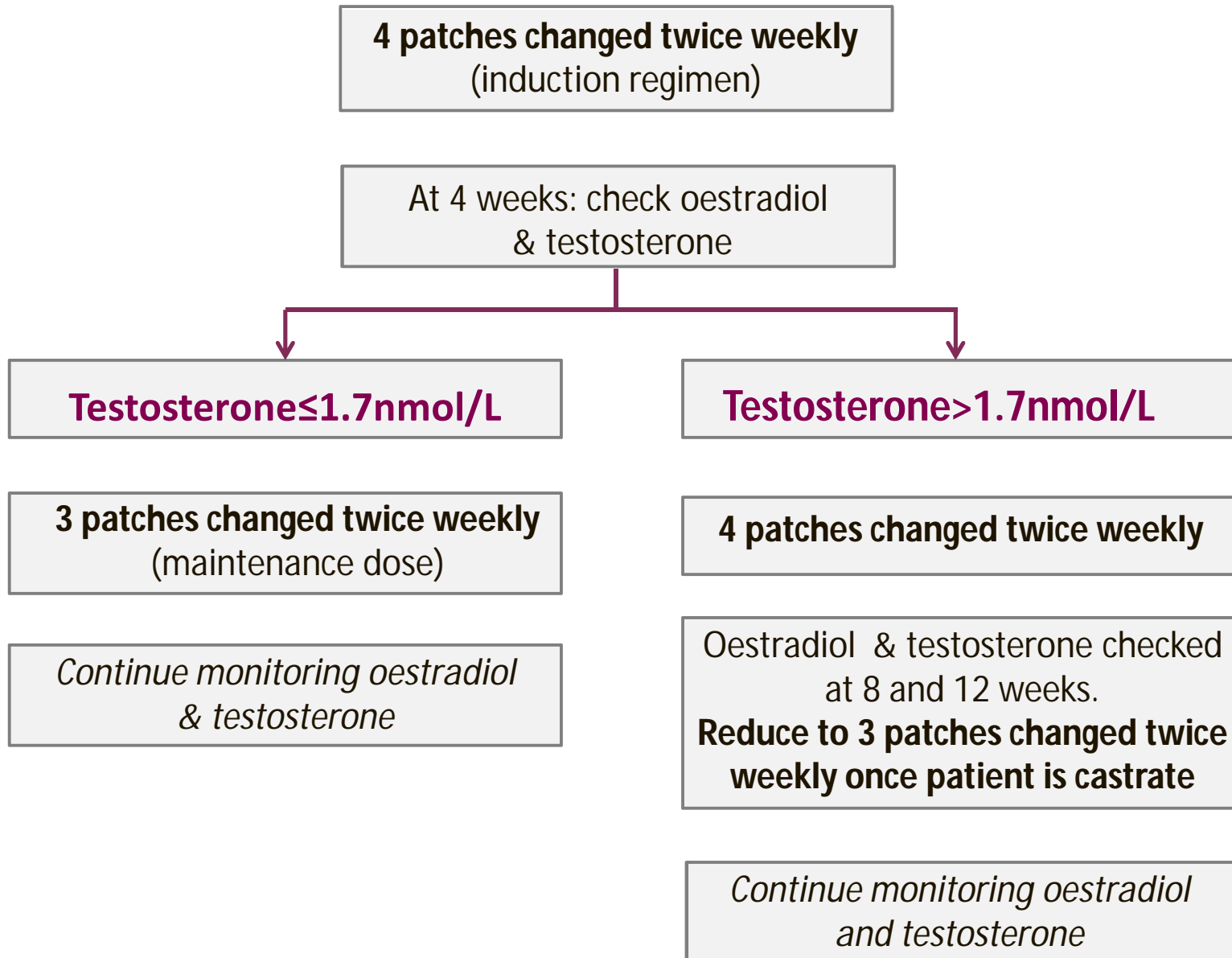
Transdermal oestradiol treatment: Dose regimen



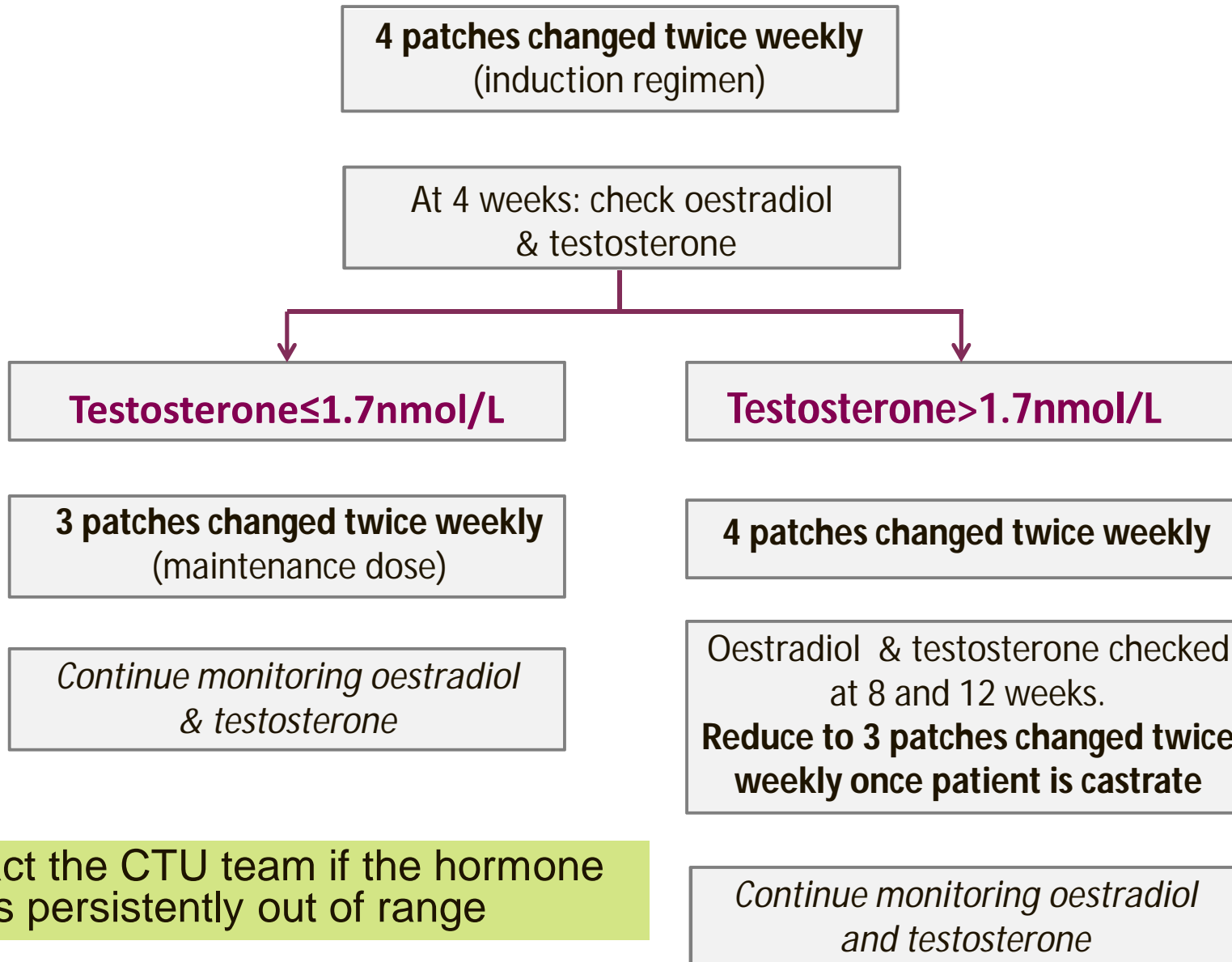
Transdermal oestradiol treatment: Dose regimen



Transdermal oestradiol treatment: Dose regimen



Transdermal oestradiol treatment: Dose regimen



Contact the CTU team if the hormone results persistently out of range

Transdermal oestradiol: Common toxicities

- **Skin problems** Mostly mild
Alternate site of patch application
Low dose steroid cream before applying patches

- **Gynaecomastia** Mostly mild
Note tamoxifen cannot be prescribed as it directly affects the action of the oestradiol patches

- **Hot flushes** Though less common than with LHRH

Transdermal oestradiol: Stopping trial treatment

- Treatment with tE2 can be discontinued for the following main reasons:
 - Unacceptable toxicity
 - Patient refusal
 - Intercurrent illness
 - Investigator decision
 - Cardiovascular event - discontinuation of treatment at discretion of clinician
 - Evidence of disease progression - switching to LHRH appropriate (lack of data on tE2 in combination with second-line agents)

IMP Overview

Transdermal oestradiol patches

- Progynova TS 100mcg/24 hours
- Manufactured by Bayer

Transdermal oestradiol patches - Ordering

- Order from AAH to qualify for 37% discount
- Can order from other wholesalers but discount has only been agreed with AAH
- Looking in to further financial support

Transdermal oestradiol patches - Labelling

- Trial specific labelling by the site pharmacist required before dispensing
- Template label provided in pharmacy pack (also available on STAMPEDE website)
- Use of alternative trial-specific labels developed by local pharmacy departments permitted but requires prior review and approval. Email alternative labels to mrcctu.stampede@ucl.ac.uk.

Transdermal oestradiol patches - Storage

- Store Progynova TS patches under 30°C and away from any other non-trial stock or returned or quarantined trial stocks.
- If storage temperature is exceeded the patches should be quarantined and the STAMPEDE team should be contacted to discuss the appropriate course of action

Transdermal oestradiol patches

- **Prescribing**

- As per local procedures and commissioning arrangements
- Ensure enough patches are prescribed up to next follow-up visit but not more than necessary

- **Accountability**

Pharmacy departments should use local Accountability Log templates for Arm L supplies.

- **Returns**

Not required unless specified by local procedures

Transdermal oestradiol patches - Destruction

- Authorisation for destruction is required from MRC CTU
- Email mrcctu.stampede@ucl.ac.uk for authorisation
- Destruction log template for Arm L supplies in the pharmacy pack

Other pharmacy updates

Temperature monitoring

- Abiraterone temperature monitoring during transit for arms G and J
- Check against temperature loggers received with each shipment
- Instructions for Libero C and TempTales in the pharmacy instructions and on the STAMPEDE website
- Contact MRC CTU if there has been a temperature deviation during transit
- Otherwise, no need to send back PDF from the TempTales

Arm G supplier

- BNC have changed names to CSM
- Change of email address: tmdreport@csmondemand.com

Activation

Activation process

- **Activation documentation sent to sites on 09-May-2017 and available on the STAMPEDE website**
- **Arm L activated on 20-Jun-2017**

Activation process

- **Activation process as per previous research comparisons**
 - Temporary suspension of recruitment if requirements not met by activation date
- **Activation requirements:**
 - Amendment acknowledgements
 - PI
 - Research Team
 - Pharmacy
 - Training attended

Contact Us

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Smarter studies
Global impact
Better health



Questions?