OPTIMA: a trial of less chemotherapy in high clinical risk early breast cancer.

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optima
personalised treatment of breast cancer
optimabreaststudy.com

Over 3100 patients now recruited into OPTIMA

Role for Surgeons and Breast Nurse Specialists

Surgeons and breast nurse specialists play an important role in facilitating OPTIMA recruitment

Your continuing support is vital for our ongoing success

Things you can do that help recruitment:	
Manage expectations about adjuvant treatment	• If you mention adjuvant chemotherapy, conveying that the benefit is uncertain helps patients keep an open mind. • For patients flagged as eligible, you might want to give them a heads up that the oncology consultation will include a discussion about OPTIMA.
Screen for OPTIMA at the MDT	• Please consider flagging for OPTIMA, patients with ER-positive HER2-negative breast cancer who would ordinarily be offered adjuvant chemotherapy.
Remember:	• The trial allows up to 8 weeks of pre-surgical endocrine therapy and pre-trial entry initiation of post-surgery endocrine therapy. • Patients receiving neo-adjuvant chemotherapy are ineligible.

Background

- Multi-parameter tumour gene expression assays (MPA's) are widely used to estimate individual patient residual risk in ER-positive HER2-negative node-negative EBC, allowing patients at low risk to safely avoid chemotherapy.
- TAILORx provides evidence for MPA utility in node-negative breast cancer.
- Patients with node-positive disease and favourable gene expression assay results can only safely avoid chemotherapy if the tests also predict chemotherapy sensitivity - evidence for this remains limited.
- RxPONDER provides <u>preliminary</u> evidence for MPAs use for 1-3 N+ postmenopausal patients
  - The result looks convincing but there is a large amount of statistical uncertainty.
  - Premature adoption would likely increase breast cancer mortality by 3% if the result is incorrect.
- **OPTIMA aims to validate MPA's as predictors of chemotherapy sensitivity in a largely node-positive population**.

Objectives

- To identify a method of selection that reduces chemotherapy use for patients with hormone sensitive primary breast cancer without detriment to recurrence and survival.
- To establish the cost-effectiveness of test-directed treatment strategies compared to standard practice.

Treatment in OPTIMA

- Chemotherapy & endocrine therapy are selected from menu of allowed regimens. Endocrine therapy for women premenopausal at trial entry includes ovarian function suppression; treatment may be deferred for patients with post-chemotherapy amenorrhoea.

Tools to support recruitment

- The OPTIMA guide for surgeons (updated in October 2021) is a handy 1-page guide down-loadable from the ABS website.
- The Eligibility Poster is available for MDT use.
- The Patient Flyer introduces patients to OPTIMA
- All are available on the OPTIMA website; the Trial Office can supply printed flyers.

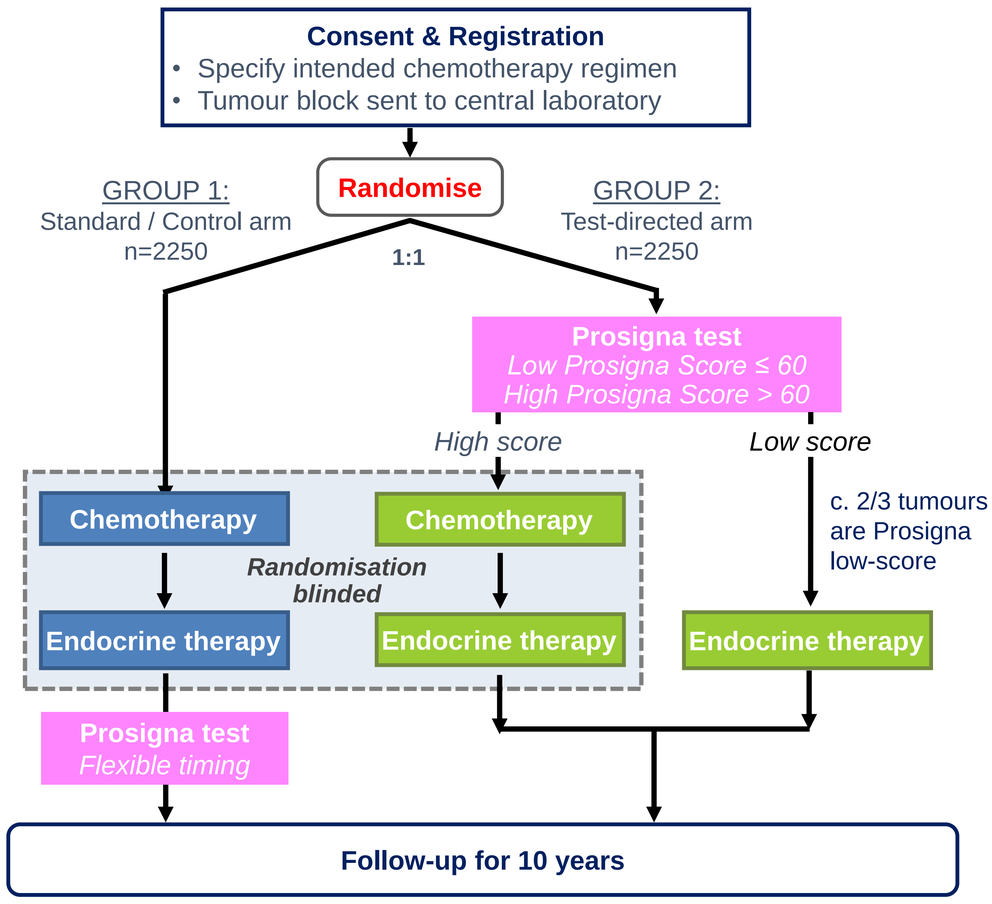
The OPTIMA website is a resource for both clinicians and patients: optimabreaststudy.com

Scan for OPTIMA website

Scan for OPTIMA animation

Trial Design

Trial population
- Female or Male age ≥ 40
- Excised primary breast cancer
- ER+ve (>10% staining), HER2-ve
- pN1-2 **OR** pN1mi & pT ≥ 20mm **OR** pN0 & pT ≥ 30mm



Primary outcomes
- Non-inferiority of recurrence (IDFS - Δ= -3%)
- Cost effectiveness evaluation of test-directed treatment

Key secondary outcome
- Non-inferiority of IDFS for patients with low-score tumors (Δ= -3.5%)

Additional secondary outcome measures
- DRFI, BCSS, OS, Health Resource use & Quality of Life

The continuing importance of OPTIMA

- It is the only trial that can answer the "premenopausal question"
  - Trials data showing premenopausal patients benefit from chemotherapy is likely confounded by treatment-induced menopause
  - 36% of the OPTIMA population is premenopausal
- It is the only trial that recruits patients with ≥4 involved nodes
  - If patients with 1-3 N+ and low test-score tumours can safely avoid chemotherapy, then this should also apply to those with higher nodal involvement
- It is the only trial that will include patients treated with adjuvant CDK4/6 inhibitors
  - Abemaciclib availability in the NHS is expected in late 2022
  - Approximately 50% of the Prosigna low-score population is likely to be eligible
- It will provide independent data on test use for 1-3N+ patients
  - Conclusive proof that tumour gene expression tests predict chemotherapy sensitivity will require meta-analysis

OPTIMA welcomes new sites: please inquire to OPTIMA@warwick.ac.uk

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