OPTIMA: Optimal Personalised Treatment of early breast cancer using Multi-parameter Analysis, an international randomized trial of tumor gene expression test-directed chemotherapy treatment in a largely node-positive population.

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Background

- Multi-parameter tumor gene expression assays (MPAs) are widely used to estimate individual patient residual risk in ER-positive HER2-negative node-negative early breast cancer, allowing patients at low risk to safely avoid chemotherapy.
- TAILORx provides evidence for MPA use in node-negative breast cancer.
- Data to support test use for 1-3 node-positive postmenopausal patients are suggestive but definitive level 1 evidence remains lacking.
- No data exist to support test use for patients with ≥4 involved nodes.
- MPA trials conducted to date have demonstrated chemotherapy benefit for premenopausal women in lower risk MPA categories. This is potentially explained by imbalance arising from chemotherapy-induced menopause.
- OPTIMA is a UK-initiated RCT of test-directed chemotherapy use with a non-inferiority design that recruits patients at high clinical risk of recurrence.
- OPTIMA is currently recruiting in the UK, Norway & Sweden; additional international expansion is anticipated during 2021.

Patient characteristics (at 1 May 2021)

Characteristic		Invasive tumor size	
Number of participants	2123	<30mm	55%
Age: median (range)	56 (40-83)	≥30mm	45%
Menopausal status		**Nodal status**	
Premenopausal	36%	pN0 & pN1 mi	7%
Postmenopausal	63%	1N+	40%
Male	1%	2N+	23%
Grade		3N+	11%
Grade 1	5%	4N+	8%
Grade 2	62%	5-9 N+	11%
Grade 3	33%	Low Prosigna Score (≤60)	68%

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The bottom line

- OPTIMA, by mandating ovarian function suppression for premenopausal patients, is the only MPA trial that controls for chemotherapy-induced menopause.
- OPTIMA is the only MPA trial that recruits patients with higher-level (4-9) node involvement.
- OPTIMA will add to data generated by other trials in relation to postmenopausal patients with 1-3 involved nodes and with larger node negative tumors.
- OPTIMA welcomes additional collaborators from all nations

Further information can be found at optimabreaststudy.com

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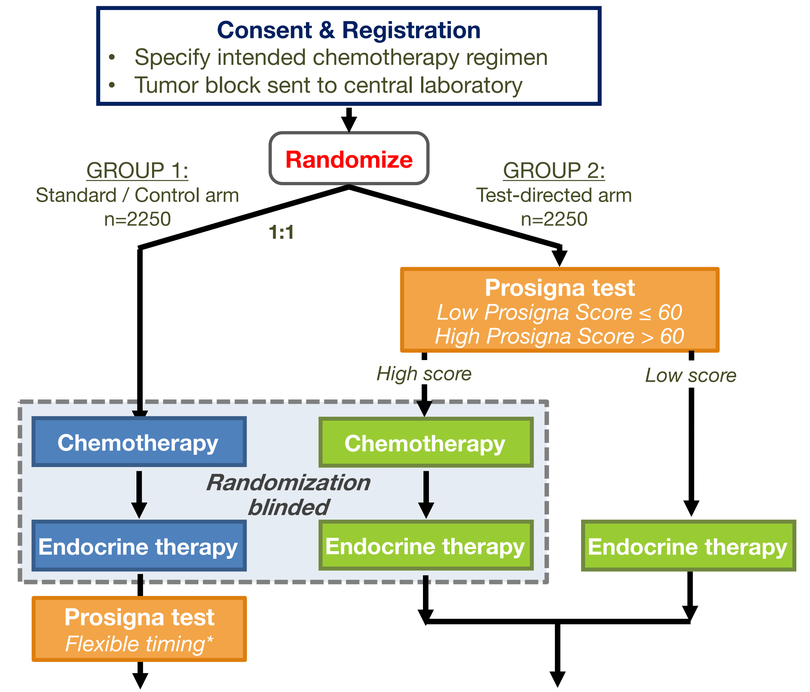
Trial Design

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

Treatment
- Chemotherapy from menu of standard regimens
- ET: Postmenopausal = AI; Premenopausal = OFS + AI or tam; Male = tam



Primary outcomes
- Non-inferiority of IDFS (Δ= -3%) -80% power if 15% 5yr control-arm event rate
- 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 **Requires control-arm testing*
- DRFI, BCSS, OS, Health Resource use & Quality of Life

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