2025 ESMO BREAST CANCER
Annual Congress

CLINICAL OUTCOMES IN THE OPTIMA PRELIM (OPTIMAL PERSONALISED TREATMENT OF EARLY BREAST CANCER USING MULTI-PARAMETER ANALYSIS) STUDY

OPTIMA is registered as ISRCTN42400492 and approved by the UK NHS HRA London Surrey Research Ethics Committee.

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DECLARATION OF INTERESTS

Rob Stein

Financial Interests:

- GSK: Stocks/Shares: Personal; Value <5000 GBP
- Veracyte Inc: Research Grant (Institutional); Supplementary support for the OPTIMA trial

Other

- Veracyte Inc: Other; Sponsorship for international meeting attendance

BACKGROUND

Tumour multiparameter gene expression assays (MPAs) are widely used to guide chemotherapy decisions – “test-directed chemotherapy”

OPTIMA is an ongoing RCT designed to validate MPA use in high clinical-risk ER+ve HER2-ve EBC

OPTIMA prelim is the feasibility part of the OPTIMA trial

- Patients were recruited from October 2012 – August 2014
- We have previously reported the feasibility outcomes*
- OPTIMA prelim demonstrated frequent disagreement between different MPA tumour assessments¶

We report the clinical outcome data from OPTIMA prelim for the first time

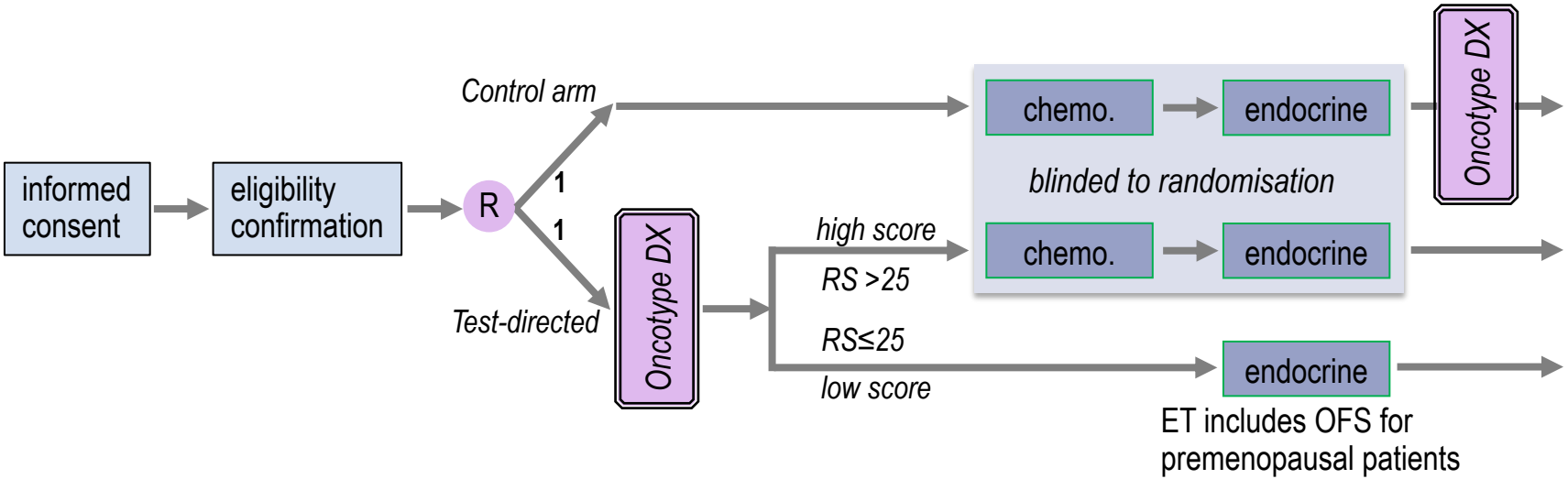
*Stein 2016 Health Technol Assess 20(10), Hall 2017 Value Health 20:1311

¶Bartlett 2016 J Natl Cancer Inst 108(9):djw050

OPTIMA PRELIM DESIGN

Main eligibility criteria

- Women age ≥40 with excised breast cancer
- ER-pos & HER2-neg
- Nodes: ▸1-9N+,
  ▸N0 & pT ≥30mm
- Neoadjuvant treatment prohibited

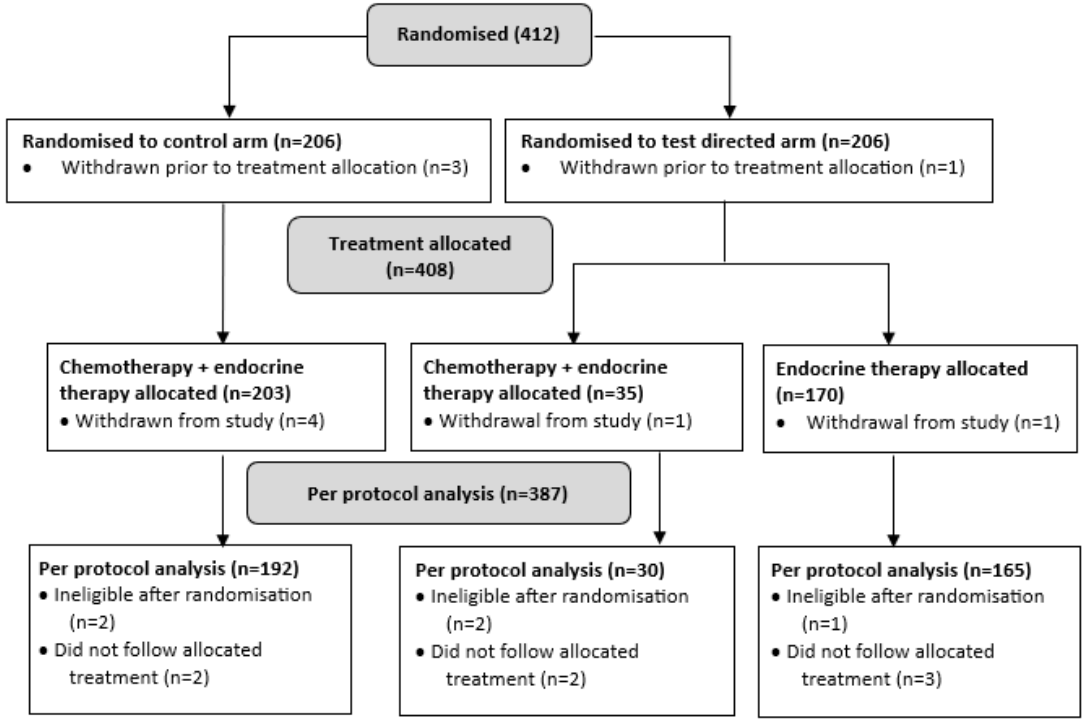


CONSORT DIAGRAM

Patients were randomised October 2012 – August 2014

Analysis of comparative MPA performance (RFI) in ITT population with complete test data (n=383)

Analysis of clinical outcomes (IBCFS) in per protocol (PP) population (n=387)



IBCFS = Invasive breast cancer free survival; RFI = Recurrence free interval

PATIENT & TUMOUR CHARACTERISTICS (PP POPULATION)

Characteristic	Control arm	Test directed arm	Total
number PP	192	195	387
age (range)	58 (40-78)	57 (40-78)	58 (40-78)
premenopausal	60 (31%)	64 (33%)	124 (32%)
postmenopausal	132 (69%)	131 (67%)	263 (68%)
grade 1-2	139 (72%)	148 (76%)	287 (74%)
grade 3	53 (28%)	47 (24%)	100 (26%)
median tumour size (range) mm	27 (2-150)	26 (7-170)	26 (2-170)
nodes: 0 / micromets	36 (19%)	36 (18%)	72 (18%)
1-3	132 (69%)	134 (69%)	266 (69%)
4-9	24 (12%)	25 (13%)	49 (13%)
RS >25	34 (18%)*	30 (15%)	64 (17%)
RS ≤25	157 (82%)	165 (85%)	322 (83%)

* Oncotype DX assay failed for 1 patient

EVENTS

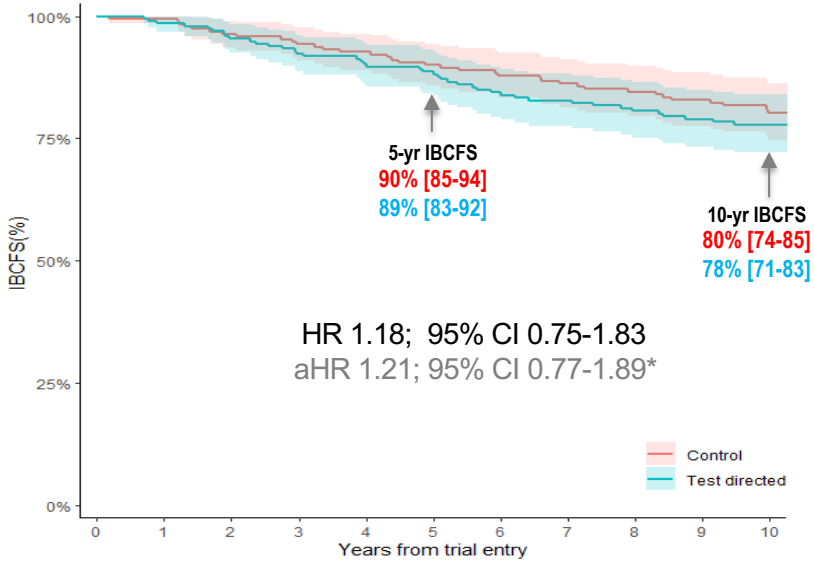
Median follow-up 10.0 years (IQR 9.9-10.1 years)

Outcome	Control arm	Test directed arm	Total
Number at risk	192	195	387
Breast cancer recurrence (all)	23 (12%)	29 (15%)	52 (13%)
loco-regional only*	2 (1%)	11 (6%)	13 (3%)
distant recurrence (± loco-regional)	21 (11%)	18 (9%)	39 (10%)
Non-breast malignancy	9 (5%)	12 (6%)	21 (5%)
Death (all)	30 (16%)	30 (15%)	60 (16%)
breast cancer	18 (9%)	16 (8%)	34 (9%)
other cancer	8 (4%)	5 (3%)	13 (3%)
non-cancer	4 (2%)	9 (4%)	13 (3%)
IBCFS events	36 (19%)	42 (22%)	78 (20%)
RFI events	24 (13%)	29 (15%)	53 (14%)

* includes contralateral new 1° breast cancer

INVASIVE BREAST CANCER FREE SURVIVAL (IBCFS)

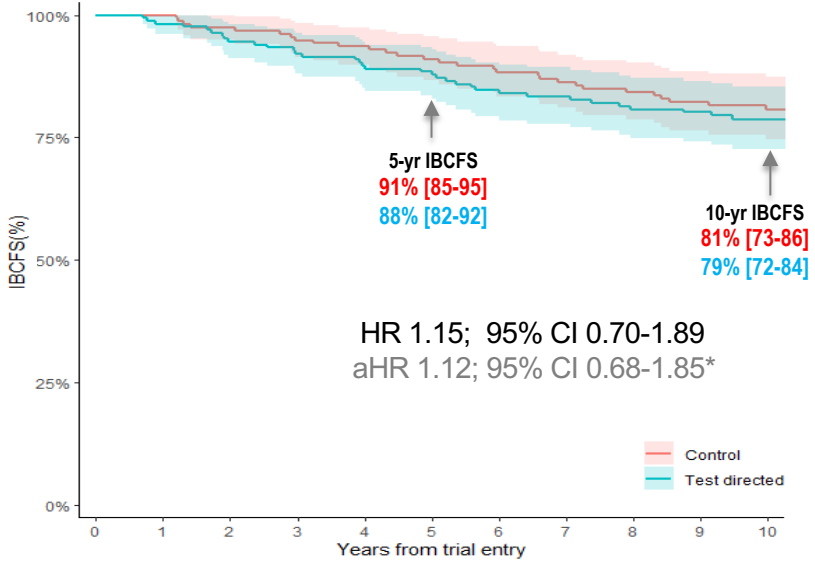
IBCFS - Complete PP population



Number at Risk

Control	192	190	184	180	176	168	161	157	153	148	79
Test directed	195	192	186	180	174	168	157	153	148	143	87

IBCFS - Oncotype DX RS ≤25 PP population



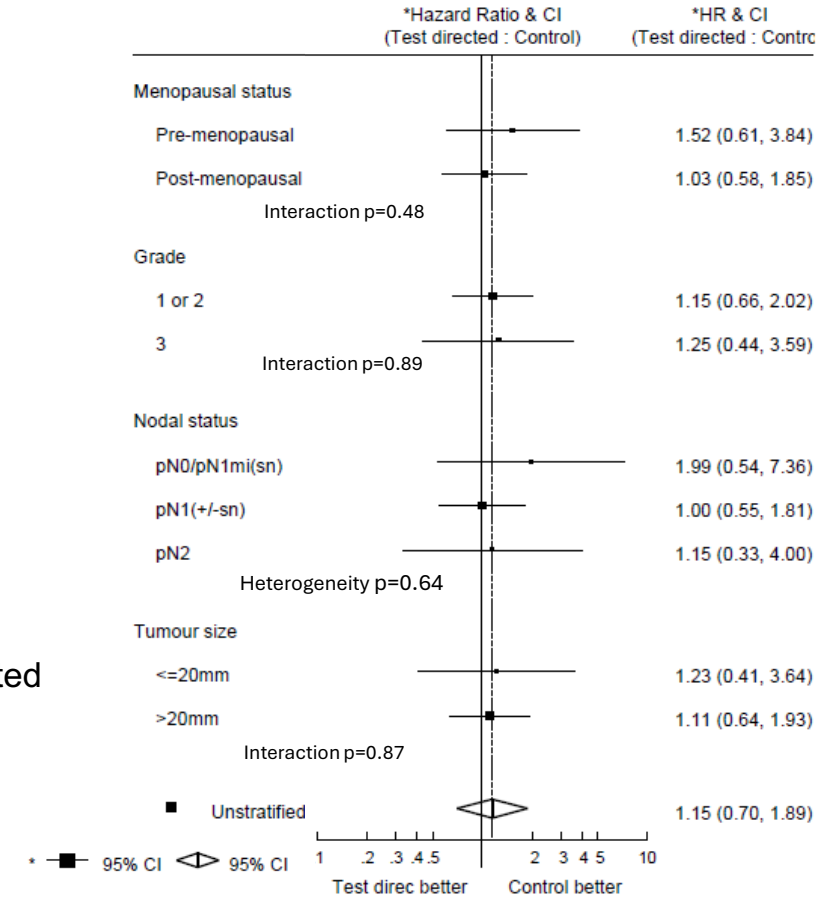
Number at Risk

Control	157	156	152	148	146	139	132	129	125	121	68
Test directed	165	162	156	152	146	142	133	130	125	123	76

*HR adjustment factors (aHR): menopausal status, age, nodal status, tumour size, tumour grade reported lymphovascular invasion and intended chemotherapy

SUBGROUPS

Oncotype DX RS ≤25 PP population

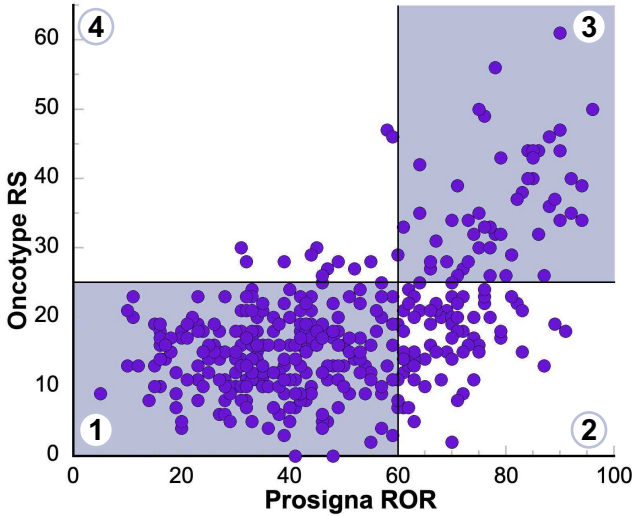


No significant heterogeneity in effect were detected across subgroups

COMPARISON OF ONCOTYPE & PROSIGNA PERFORMANCE

383 patients with both Oncotype DX & Prosigna results in the ITT population analysed

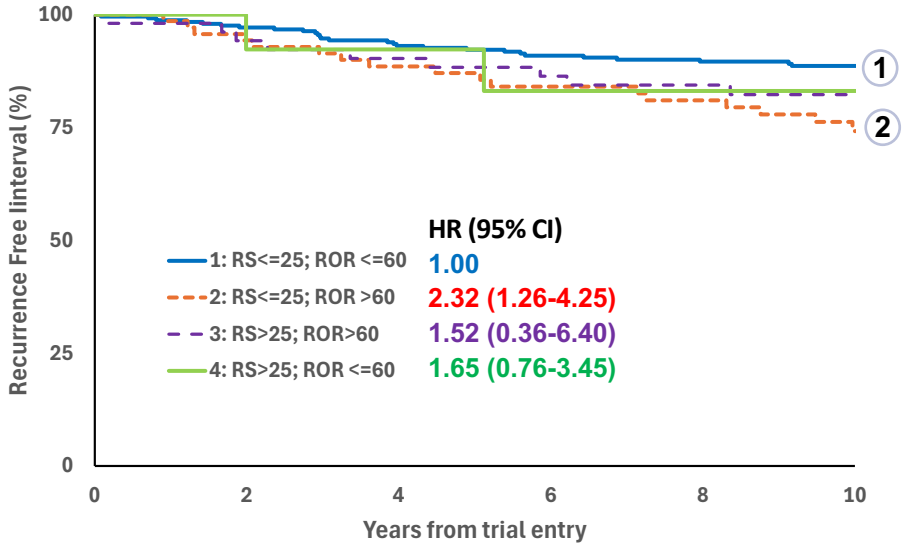
- All patients with RS>25 treated with chemo + ET
- 50% with RS ≤25 treated with ET only



Characteristic	1 RS <=25 & ROR <=60	2 RS <=25 & ROR >60	3 RS >25 & ROR >60	4 RS >25 & ROR <=60
number	247	71	52	13
premenopausal	91 (37%)	15 (21%)	10 (19%)	2 (15%)
postmenopausal	156 (63%)	56 (79%)	42 (81%)	11 (85%)
grade 1-2	222 (90%)	44 (62%)	12 (23%)	7 (54%)
grade 3	25 (10%)	27 (38%)	40 (77%)	6 (46%)
tumour size (mm) median (range)	25 (2-170)	27 (12-80)	29 (8-95)	24 (10-50)
Nodes: 0/ micro.	51 (21%)	12 (17%)	8 (15%)	1 (8%)
1-3	168 (68%)	49 (69%)	36 (69%)	10 (77%)
4-9	28 (11%)	10 (14%)	8 (15%)	2 (15%)

PROGNOSTIC ACCURACY OF THE TESTS

10-year RFI prediction by Oncotype DX and Prosigna subgroups



No. at risk:

RS<=25;ROR<=60	247	239	226	208	197	119
RS<=25;ROR>60	71	66	61	56	53	23
RS>25;ROR<=60	52	49	46	44	42	19
RS>25;ROR<=60	13	12	11	9	9	9

% Event Free

Oncotype DX	Prosigna - ROR ≤60 (n=260)	Prosigna - ROR >60 (n=123)	Subtotal
RS>25 (n=65)	83% (47-96) n=13 (4)	82% (69-90) n=52 (3)	83% (71-90)
RS≤25 (n=318)	89% (84-92) n=247 (1)	74% (62-83) n=71 (2)	85% (81-89)
Subtotal	88% (84-92)	78% (69-84)	n=383

Group 2 vs Group 1 RFI Event Risk

HR 2.32 [1.26-4.25], p=0.0067

aHR 1.97 [1.01-1.97]

HR adjustment factors (aHR): menopausal status, nodes, grade, intended chemotherapy, tumour size

CONCLUSIONS

1. There was no difference in outcome between trial arms after 10 years follow-up
   - This result is exploratory as OPTIMA prelim was not powered to demonstrate non-inferiority - it neither supports nor refutes other trial results
2. We did not identify any safety issue from test directed treatment use in a small sample (n = 124) of premenopausal women treated with optimal endocrine therapy
3. The Prosigna test identified a group of patients (22%) who had adverse outcomes despite low Oncotype DX recurrence score tumours
   - This is consistent with findings from larger datasets using research versions of the tests*

The OPTIMA main trial result is expected in mid 2026 and will include a non-inferiority analysis of test-directed chemotherapy and more information about its safety for premenopausal women

* **Bartlett 2021 NPJ Breast Cancer 7(1):90**; Van Alsten 2024 JCO Precis Oncol 8e2400137; Paul 2025 Nat Commun 16(1):226

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- The OPTIMA team

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