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Economic Impact of 21-gene Recurrence Score testing on Early Stage Breast Cancer in Ireland

Introduction

- Breast cancer (BC) is the most frequently diagnosed cancer in Irish women, affecting ~2,700 patients (pts) per year.[1] Early-stage breast cancer (ESBC) accounts for ~70% of cases.[1]
- ~30% of stage I and 60% of stage II BC pts receive adjuvant (adj) chemotherapy (CT).[2] Adverse events from CT are not uncommon and can be serious.[3,4]
- The 21-gene BC assay is a genomic test, validated to predict the likelihood of CT benefit in oestrogen receptor positive (ER+), lymph node negative (N0) ESBC pts. Pts with low Recurrence Score results are considered at low risk for recurrence, and unlikely to benefit from the addition of CT to hormone therapy. Pts with high scores are at high risk for recurrence, and obtain maximum benefit from CT.
- Decision-impact studies estimate ≥30% change in adj treatment recommendation following testing with the 21-gene assay.[1,5–9] The main impact of testing is a reduction in use of adj CT in low risk pts and the addition of CT in a smaller number of high risk pts.
- **Ireland was the first public health care system in Europe to reimburse this test**.[10]

Objectives

Assess the impact of testing with the 21-gene assay in Ireland since its reimbursement, in particular:

1) **Change in adj CT treatment recommendation** following 21-gene testing
2) **Clinical characteristics associated with test score result** and **treatment recommendation**
3) **Economic impact** of the 21-gene assay on the Irish healthcare system

Methods

- **National, multi-site, retrospective, cross sectional, observational study**
- All ESBC pts tested with the 21-gene assay between **October 2011 and February 2013** were identified from pathology laboratory databases of 8 cancer centers in Ireland.
- Clinical data was retrieved from hospital pathology reports, hospital pharmacy databases and pt letters, and reported for all N0 pts.
- **Decision impact analysis**
  - **compared recommendations for adj CT pre-/post-21-gene testing**
  - **calculated net reduction in adj CT usage as a result of 21-gene testing**
- Lead BC medical oncologists in Ireland provided the **assumption** for the **pre-test treatment recommendation**, that **grade (G) 1 N0 pts would not have received CT (i.e. negative pre-test CT recommendation) and G 2/3 N0 pts would have received CT (i.e. positive pre-test CT recommendation).**
- **Budget impact analysis** compared the **cost of 21-gene testing with net savings in CT administration** resulting from testing N0 pts.
  - Calculated total cost per pt associated with CT administration was € 7,903 (see Table 1).*1
  - Costs were validated by an Irish hospital pharmacist and NCCP chief pharmacist.
  - List price for the **21-gene assay** was: € 3,180.*2

Table 1: Breakdown of CT administration costs

Parameter	*Cost*
CT drug costs	€ 515
G-CSF	€ 4,985
Administration & Monitoring	€ 1,646
Other Adverse Events	€ 756
Total	€ 7,903

Results

Clinical Characteristics

- 633 pts were tested with the 21-gene assay, including 41 (6.5%) node-positive (N1) pts tested as part of the RxPONDER trial.[11]
- Analysis focused on **592 N0 pts**, excluding N1 pts.
- Mean age **55.6 years** (SD: 9.7), mean tumour **size 1.97cm** (SD: 0.91).
- **53%** of pts had a **low** (0-17), **36%** an **intermediate** (18-30) and **10%** a **high test score** (≥31), with a comparable mean age in all groups.
- For clinical characteristics, see Table 2 and Figure 1.
- The most commonly prescribed CT regimen was docetaxel and cyclophosphamide (TC) across all test score groups (see Figure 2).

Table 2: Clinical Characteristics, by test score group

Variable	*Level*	*Overall*		*Low (0-17)*		*Intermediate (18-30)*		*High (31-100)*		*Unknown score*	
Overall		592	(100.0%)	312	(52.7%)	215	(36.3%)	57	(9.6%)	8	(1.4%)
Age	Mean	55.6	(9.7)	55.4	(9.4)	55.7	(9.8)	56.1	(10.9)	55.8	(10.9)
	≥50 yrs	426	(72.0%)	221	(70.8%)	159	(74.0%)	41	(71.9%)	5	(62.5%)
Tumour grade	Grade 1	76	(12.8%)	59	(10.0%)	16	(2.7%)	0	(0.0%)	1	(0.2%)
	Grade 2	384	(64.9%)	214	(36.1%)	146	(24.7%)	18	(3.0%)	6	(1.0%)
	Grade 3	129	(21.8%)	39	(6.6%)	52	(8.8%)	37	(6.3%)	1	(0.2%)
	Unknown	3	(0.5%)	0	(0.0%)	1	(0.2%)	2	(0.3%)	0	(0.0%)
Tumour size	Mean in cm (sd)	1.97	(3.91)	1.93	(0.91)	2.01	(0.94)	2.09	(0.84)	1.58	(0.77)
	Median in cm		1.80		1.70		1.80		1.90		1.65
Morphology	IDC	461	(77.9%)	233	(39.4%)	168	(28.4%)	54	(9.1%)	6	(1.0%)
	Non-IDC	131	(22.1%)	79	(13.3%)	47	(7.9%)	3	(0.5%)	2	(0.3%)
AJCC stage	IA	385	(65.0%)	208	(35.1%)	138	(23.3%)	32	(5.4%)	7	(1.2%)
	IIA	205	(34.6%)	102	(17.2%)	77	(13.0%)	25	(4.2%)	1	(0.2%)
	IIB	2	(0.3%)	2	(0.3%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
Presence of LVI	Yes	164	(27.7%)	81	(13.7%)	60	(10.1%)	19	(3.2%)	4	(0.7%)
ER	Positive	592	(100.0%)	312	(52.7%)	215	(36.3%)	57	(9.6%)	8	(1.4%)
PR	Positive	355	(60.0%)	204	(34.5%)	130	(22.0%)	14	(2.4%)	7	(1.2%)
LN	N0	577	(97.5%)	303	(51.2%)	209	(35.3%)	57	(9.6%)	8	(1.4%)
	N0 (i+)/N0(ITC)	15	(2.5%)	9	(1.5%)	6	(1.0%)	0	(0.0%)	0	(0.0%)
CT Received[3]	Yes	174	(29.4%)	12	(2.0%)	108	(18.2%)	52	(8.8%)	2	(0.3%)

Figure 1: Share of clinical characteristics, by test score group*4

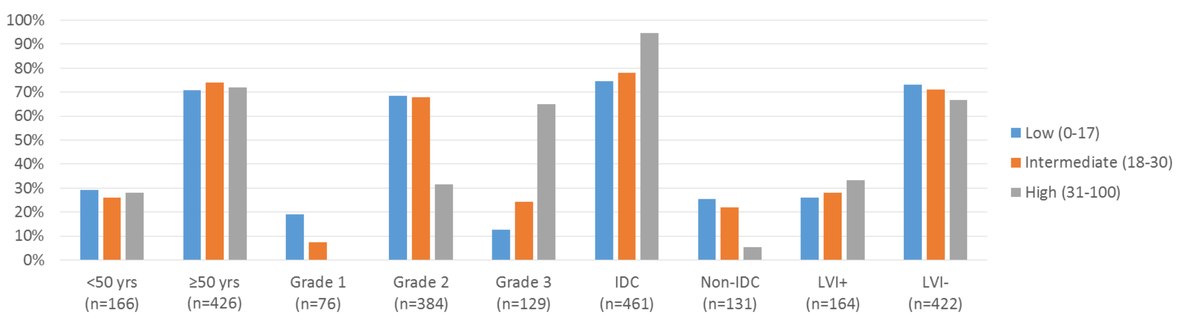
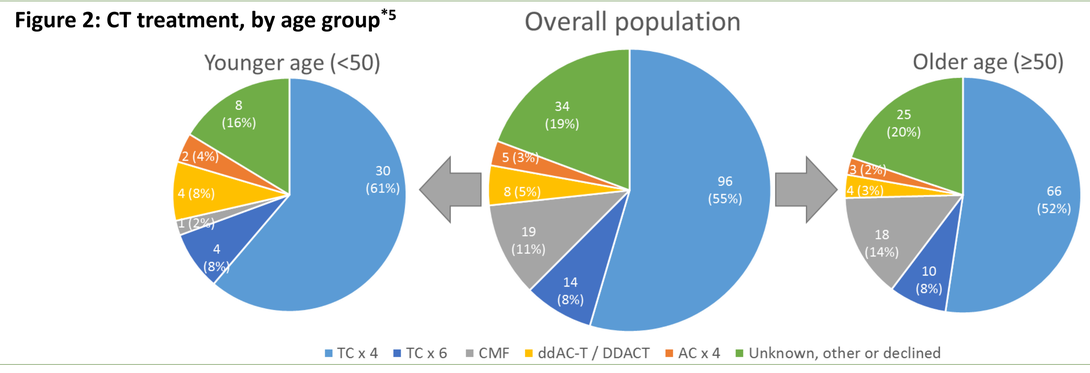


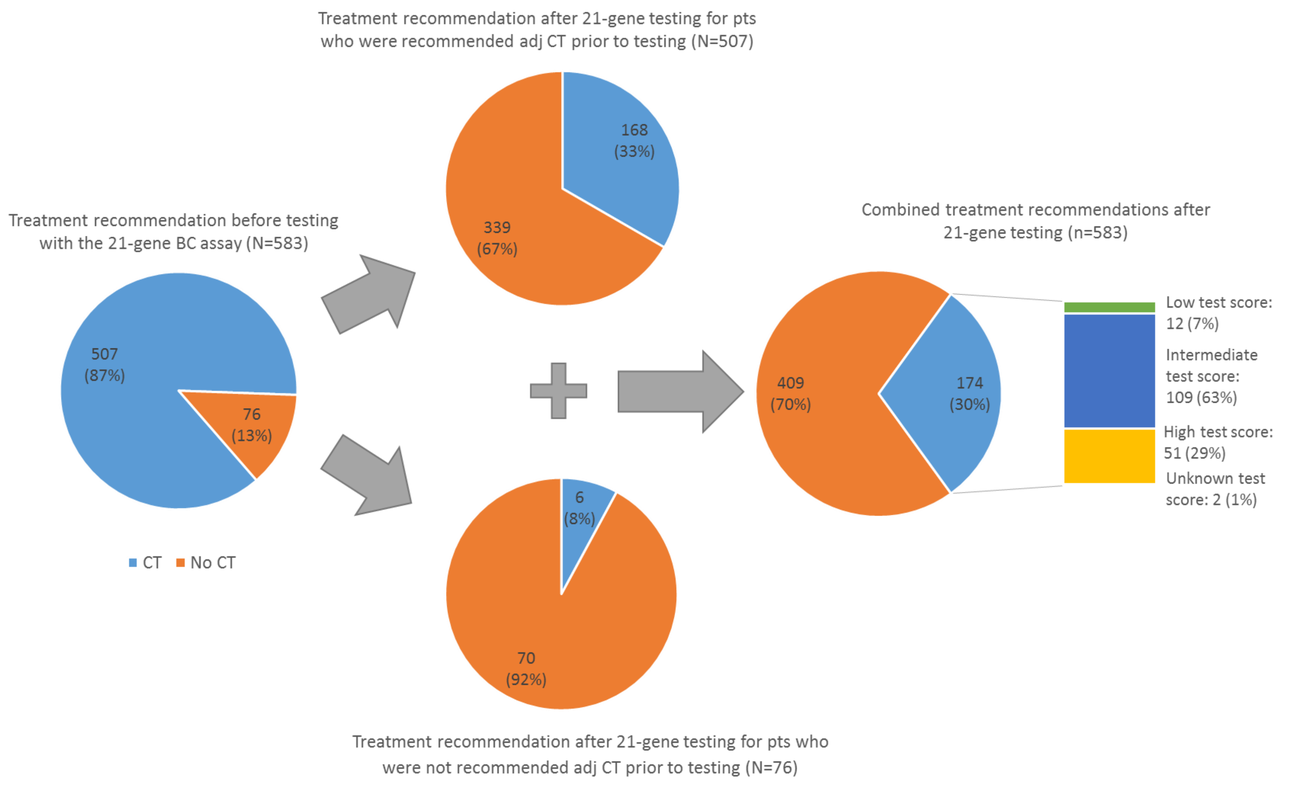
Figure 2: CT treatment, by age group*5



1) Change in adj CT treatment recommendation following 21-gene testing

- 9 pts were excluded from the analysis: 3 pts had an unknown grade (and therefore unknown pre-test CT recommendation), and 6 pts had an unknown post-test CT recommendation.
- Of the remaining 583 N0 pts, 76 G1 (13.0%) pts were assumed to have a negative pre-test CT recommendation and 507 G 2/3 pts (87.0%) a positive pre-test CT recommendation.
- **Post 21-gene testing, 174 pts (30%) were recommended CT compared with 507 pts pre- testing.**
- 12 (3.9%) of low risk pts, 108 (50.9%) of intermediate risk pts, 50 (90.9%) of high risk pts and 2 (25.0%) of those with an unknown test score received CT post testing. 2 pts declined CT.
- In total, **345 pts (59.2%) experienced a change in CT recommendation** after testing, including
  - 339 pts who were spared CT after 21-gene testing (who had a positive CT recommendation pre-test) and
  - 6 pts who were recommended CT after 21-gene testing (who had a negative CT recommendation pre-test). See Figure 3 for pre- and post-test CT recommendation.

Figure 3: CT recommendation pre- and post-21-gene testing *6



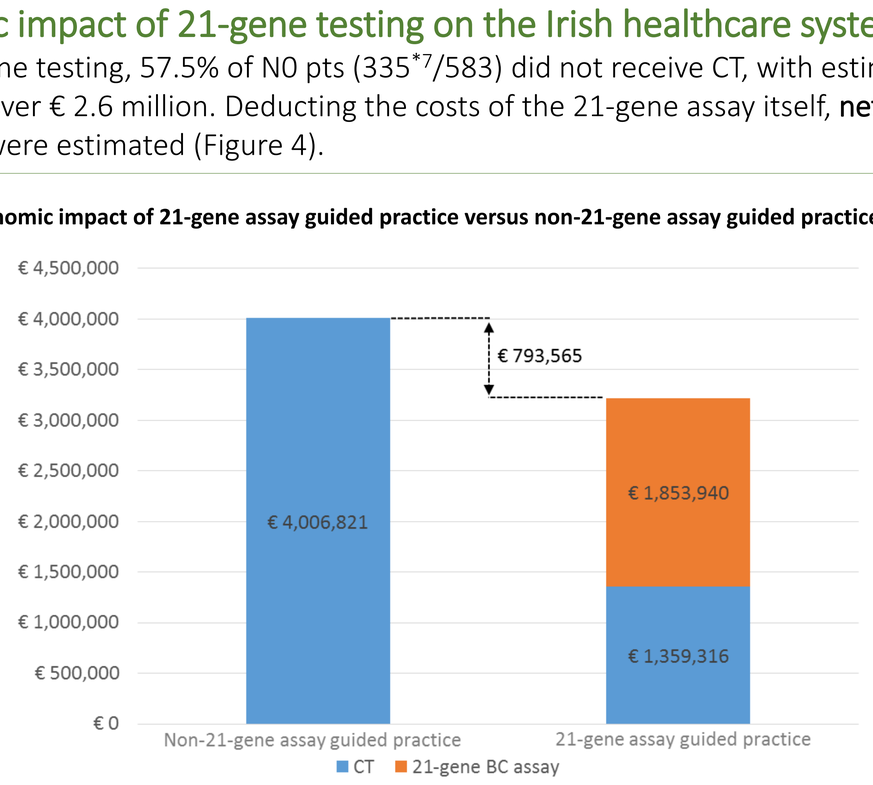
2) Clinical characteristics associated with test score result and treatment recommendation

- **IDC** morphology and **G3 tumours** were associated with a significantly **lower probability** of a **low test score** (relative risk [RR]: 0.84 and 0.51, respectively)
- **G 1/2 tumours** were associated with a higher chance of a **low test score** (RR: 1.57/1.98).
- The probability of pts receiving a **post-test CT recommendation increased significantly with G3 tumours** (RR: 2.06), and was significantly **lower for pts with G 1/2 tumours** (RR: 0.24/0.48).

3) Economic impact of 21-gene testing on the Irish healthcare system

- After 21-gene testing, 57.5% of N0 pts (335*7/583) did not receive CT, with estimated CT cost savings of over € 2.6 million. Deducting the costs of the 21-gene assay itself, **net savings of € 793,565** were estimated (Figure 4).

Figure 4: Economic impact of 21-gene assay guided practice versus non-21-gene assay guided practice in N0 pts



Conclusions

- Consistent with previously reported studies[5–8,12-13], this study **using real world evidence** demonstrates that the use of the **21-gene assay has a significant impact on adj treatment recommendations in a large number of N0 ER+ ESBC pts.**
- In the first 18 months after its introduction, the 21-gene assay led to a **57.5% net reduction in CT use in Irish pts with hormone sensitive N0 BC** (a 66% reduction in the pts who would have received CT without testing), with estimated **net savings of over € 790,000.**
- Further research is necessary to incorporate the long term impact of treatment decisions (i.e. BC recurrence and associated mortality) from 21-gene testing and the associated costs, short and long term impact on quality of life, and the potentially additional indirect societal costs.

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Footnotes

1. CT and G-CSF drug unit costs were taken from the 2012 NCCP reimbursement submission for the 21-gene BC assay. This submission was based on feedback obtained from oncologists / pharmacists at 5 of the 8 cancer centres in Ireland. The CT drug costs were based on a weighted average of the CT regimen prices (2014) according to the proportion of use of each regimen within the dataset (see Figure 2). Admin, monitoring, and AE costs were based on Diagnosis Related Groups (DRGs) obtained from Casemix 2010 Ready Reckoner Report. Hospitalisation rates were provided by oncologists, and percent of patients with AEs were collected from Docetaxel SmPC. Costs were inflated using Central Statistics Office (CSO) Health inflation factor and validated for 2014.
2. For the 21-gene BC assay, the test's list price was used, though the real price in Ireland is lower due to a confidential pricing agreement with the HSE.
3. Information on CT received provided for ALL 592 N0 pts, inclusive of those excluded from the decision impact analysis
4. Graph does not depict 8 patients with unknown score resullts.
5. One patient had an unknown age
6. 3 patients with unknown grade and 6 patients with unknown post-test CT recommendation were excluded from the graph.
7. Out of 507 pts with a positive pre-test CT recommendation, 172 pts actually received CT post 21-gene testing, leaving 335 pts who did not receive CT post 21-gene testing.