Early stage cost-effectiveness analysis

BRCA1-like predictive biomarker to detect triple negative breast cancers responsive to high dose alkylating chemotherapy

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Introduction: ineffective treatment for TNBC

40% of triple negative breast cancers (TNBCs) fail 1\textsuperscript{st}-line treatment\textsuperscript{1}

**Poor health outcomes**

- Early relapses and short post-recurrence survival\textsuperscript{1}

**Additional costs**

- Necessity to administer 2\textsuperscript{nd} and/or 3\textsuperscript{rd} line treatment

**Poor quality of life**

- i.e., utility score of relapse (0.44) vs. remission(0.79)\textsuperscript{2}

\textsuperscript{1} Liedtke JCO (2008), \textsuperscript{2} Lloyd (2006)
Introduction: personalized treatment for TNBC

BRCA1-like biomarker

Present in 68%\(^1\) of TNBCs

100 TNBC with BRCA1-like

HDAC\(^2\)

SC\(^3\)


89

90

35

35

\(\bar{X} = 155\%\)

HDAC is expensive

Requires stem cell transplantation with costs of €54,000/patient\(^4\)

Tests available in the NKI-AVL; aCGH & MLPA\(^*\)

Accuracy of the MLPA test is 86% (vs. aCGH)

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\(^1\) Lips BJC (2013), \(^2\) High Dose Alkylating Chemotherapy, \(^3\) Standard chemotherapy, \(^4\) Dutch Healthcare Authority (NZA), *Array comparative genomic hybridization, Multiplex ligation dependent probe amplification
Motivation and objective

Motivation

Effective but expensive strategy

BRCA1-like prevalence & positive predictive value (PPV) of the tests expected to influence cost-effectiveness

Objective

To estimate the minimum required BRCA1-like prevalence and minimum required PPV for a BRCA1-like test to be cost-effective when adopted in clinical practice
Methods: Markov model

- Markov model using Excel
- Comparison of 2 groups:
  Personalized HDAC treatment based on BRCA1-like testing versus no testing + standard chemotherapy
- 40-years old
- Simulation of hypothetical cohort of 10,000 patients
- Cycle length 1 year
- Time horizon 20 years
- Setting: the Netherlands
- Perspective: Societal
Methods: Outcomes

Expected cost-effectiveness (under base case assumptions)
method: deterministic CEA*

Driver of the ICER (prevalence, PPV)
method: one way SA*

Minimum required prevalence and PPV
method: threshold SA

* Cost effectiveness analysis, Sensitivity analysis
Methods: Decision tree

TNBC

BRCA1-like testing

BRCA1-like → HDAC

Non BRCA1-like → SC

Respondent

Non respondent

DFS

R

D

idem

Respondent (True BRCA1-like)

Non respondent (False BRCA1-like)

Respondent

Non respondent

Non respondent
## Methods: Key input parameters

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Baseline</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPV of the BRCA1-like test</td>
<td>100%</td>
<td>Assumption</td>
</tr>
<tr>
<td>Prevalence of BRCA1-like in TNBC</td>
<td>68%</td>
<td>Lips (2013)</td>
</tr>
<tr>
<td>Non BRCA1-like respondents to SC</td>
<td>35%</td>
<td>Vollebergh (2010)</td>
</tr>
<tr>
<td>TNBC respondents to SC</td>
<td>35%</td>
<td>Vollebergh (2010)</td>
</tr>
<tr>
<td>Utility of HDAC</td>
<td>0,610</td>
<td>Conner-S. (2010)</td>
</tr>
<tr>
<td>Utility of SC</td>
<td>0,620</td>
<td>Lidgren (2007)</td>
</tr>
<tr>
<td>MLPA test</td>
<td>€37</td>
<td>NKI-AVL</td>
</tr>
<tr>
<td>SC (5 x FEC*)</td>
<td>€9.844</td>
<td>NKI-AVL</td>
</tr>
<tr>
<td>HDAC (4 x FEC + 1 CTC*)</td>
<td>€75.472</td>
<td>NKI-AVL</td>
</tr>
</tbody>
</table>

**SURVIVAL**

Respondents: no events

Non respondents: Exponential f(x) with 95% patients relapsed or died from breast cancer in year 5

*Fluorouracil, Epirubicine and Cyclophosphamide/ Cyclophosphamide, carboplatin and thiotepa
### Results: Expected cost-effectiveness

**Threshold: €80,000/QALY**

<table>
<thead>
<tr>
<th>Years</th>
<th>Δ QALYs*</th>
<th>Δ costs*</th>
<th>ICER*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-0.03</td>
<td>€39,460</td>
<td>BRCA1-like dominated by current practice</td>
</tr>
<tr>
<td>2</td>
<td>0.14</td>
<td>€34,286</td>
<td>€251,079/QALY</td>
</tr>
<tr>
<td>5</td>
<td>0.29</td>
<td>€40,290</td>
<td>€136,806/QALY</td>
</tr>
<tr>
<td>10</td>
<td>0.80</td>
<td>€43,060</td>
<td>€53,929/QALY</td>
</tr>
<tr>
<td>20</td>
<td>1.71</td>
<td>€47,346</td>
<td>€27,719/QALY</td>
</tr>
</tbody>
</table>

* BRCA1-like testing strategy minus current clinical practice strategy.
Results: Driver of the ICER

One way SA - Prevalence (baseline assumptions)

One way SA - PPV (baseline assumptions)
Results: Minimum required prevalence and PPV

Threshold SA - on prevalence and PPV

- 20% prevalence, 20% PPV
- 40% prevalence, 40% PPV
- 60% prevalence, 60% PPV
- 80% prevalence, 80% PPV

prevalence 10.4% & PPV 57.8%
Results: Model parameter’s effect on the ICER

- Costs of septicemia
- Costs of heart failure
- Costs of MLPA test
- Utility of R health state
  - Utility of SC
- Costs of breast cancer death
- Probability of toxic death from heart failure
- Probability of toxic death from septicemia
- Utility of DFS health state
- Costs of R health state
  - Costs of SC
- Costs of DFS health state
  - Utility of HDAC
- Tp of breast cancer specific death
- Proportion of BRCA1-like respondents to SC
- Proportion of TNBC respondents to SC
- Tp of relapse free survival for non-respondents
  - Costs HDAC
Conclusions / Take home message

- Treating TNBC with personalized HDAC with a BRCA1-like test is expected to be CE vs. current practice (base case assumptions)
- CE is reached after a minimum of 10 years
- PPV and not prevalence, drives the ICER
- The lower bounds of PPV and prevalence for CE are 57.8% and 10.4% respectively

- CEA & SA → useful to guide product development
- Early CEA is an iterative process → Re-calculate the outcomes when new information on any of the uncertain parameters is available
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