Surrogate Survival Endpoints: Are They Sufficient to Support Access?

Navisha Doolub, Raquel Fernandez Dacosta, Alex Grosvenor, George Wang, Richard Macaulay

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Precision Value & Health offers a range of specialized, yet complementary capabilities across the commercialization continuum for pharmaceutical products.

Richard Macaulay  Vice President, Global Pricing & Market Access, PRECISIONadvisors

Richard is responsible for the growth and development of consultative, analytic, and data services supporting life science products' commercial performance. Our team excels at understanding the ever-changing and complex healthcare market and helping clients solve issues including access strategy, stakeholder mapping, value communication, strategic pricing, and product positioning.
Surrogate Survival Endpoints: Are they Sufficient to Support Access?

Agenda

1. Evolving oncology landscape
2. Payer challenges
3. HTA outcomes
4. Conclusions
Oncology drugs are being increasingly developed as earlier-line therapies

Evolving oncology treatment landscape

Typical treatment pathway

Resectable cancer
- Neo-adjuvant
- Surgery
- Adjuvant

Recurrent / metastatic cancer
- 1L chemotherapy
- 2L chemotherapy

Traditional focus for cancer drug development
- The risk/benefit of traditional chemotherapies limits their use to the palliative setting

New focus for cancer drug development
- Newer therapies (e.g. I-Os) with long-term OS benefits & favorable safety can justify earlier use
Developing oncology drugs for early-stage use can create challenges for payers.

**Payer challenges for oncology therapies in the neo-/adjuvant setting (vs. the metastatic setting)**

<table>
<thead>
<tr>
<th>Challenge</th>
<th>Impact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Larger population</td>
<td>Higher budget impact</td>
</tr>
<tr>
<td>Lower unmet need</td>
<td>Lower willingness to pay</td>
</tr>
<tr>
<td>Longer treatment</td>
<td>Higher per patient costs</td>
</tr>
<tr>
<td>Retreatment?</td>
<td>Uncertain budget impact</td>
</tr>
</tbody>
</table>

**Key challenge**

Lack of overall survival data

*Use surrogate OS endpoints (e.g. MFS, DFS, EFS)*

**Key question**

Patient relevant? Correlate to OS gain?

OS = the key payer efficacy metric
This research examined how early-stage oncology drugs were assessed by payers.

Research objectives & methodology

**Identify** any EC-approved therapy for neo-/adjuvant cancer

(1\textsuperscript{st} Jan 2011 to 30\textsuperscript{th} May 2021)

**Corresponding HTA guidance** identified for

- HAS
- NICE
- SMC
- G-BA
- CADTH
- PBAC
- Medicinrådet

Key information extracted with a focus on **surrogate OS endpoint critique**
9 drug:indication pairings were identified with neo-/adjuvant oncology indications

<table>
<thead>
<tr>
<th>Brand name</th>
<th>INN</th>
<th>Indication</th>
<th>EC-approval date</th>
<th>Primary endpoint</th>
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<tbody>
<tr>
<td>HERCEPTIN</td>
<td>Trastuzumab</td>
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<td>HER2+ Breast</td>
<td>DFS</td>
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<tr>
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<td>pCR</td>
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<td>Nivolumab</td>
<td>Adj</td>
<td>- Mel</td>
<td>RFS</td>
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<tr>
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<td>Dabrafenib + trametinib</td>
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<td>BRAF+ Mel</td>
<td>RFS</td>
</tr>
<tr>
<td>KEYTRUDA</td>
<td>Pembrolizumab</td>
<td>III</td>
<td>- Mel</td>
<td>RFS</td>
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<tr>
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<td>Trastuzumab emtansine</td>
<td>Adj</td>
<td>HER2+ Breast</td>
<td>iDFS</td>
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</tbody>
</table>
51 HTA outcomes of early-stage oncology therapies were identified

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<th>HTA appraisal</th>
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</thead>
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<td>DFS</td>
<td>ASMR I</td>
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<tr>
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<td>Adj</td>
<td>DFS</td>
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<tr>
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<td>Neo</td>
<td>pCR</td>
<td>SMR insuff</td>
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<td>Adj</td>
<td>iDFS</td>
<td>ASMR III Major</td>
</tr>
</tbody>
</table>

HTA outcome key
- Positive
- Moderate/conditional
- Negative
- Not assessed
Acceptability of early-stage oncology therapies varied by **surrogate endpoint**

- Payer assessments were most positive where:
  - the **magnitude** of the surrogate benefit were **greater**
  - **early OS** data showed significant benefits or a clear numerical trend

- Nevertheless, there were some **trends** regarding acceptability of **endpoints across payers**
  - Although clearly valued **less than OS**, RFS and DFS were deemed patient relevant by payers, much **moreso than pCR**
Acceptability of early-stage oncology therapies varied by **HTA body**

- NICE and SMC appeared the most supportive of **access for oncology drugs using surrogate endpoints**, followed by G-BA, with CADTH the least.

- Some assessments (e.g. NICE & G-BA) were **conditional** and contingent on more **mature follow-up data** being provided for reassessment.

- PBAC imposed flow-on restrictions **limiting retreatment** with I-Os in later lines of therapy.
Early-stage cancer therapies supported by surrogate survival endpoints have achieved some payer access, with variations between different endpoints & payers

Summary and conclusion

Oncology therapies approved and reimbursed in metastatic cancer are being increasingly investigated in the early-stage setting using surrogate survival metrics as primary endpoints.

HTA bodies have generally given quite favorable assessments to these early cancer therapies, deeming some surrogate endpoints patient relevant or correlated to OS.

There are, nevertheless, clear trends in payer willingness to accept these endpoints between different surrogate endpoints and between different HTA bodies.

Further, such therapies may be more likely to be subject to reimbursement conditional on further evidence generation [e.g. CDF] and/or later-line restrictions.
THANK YOU!
we look forward to staying in touch

richard.macaulay@precisionvh.com

PRECISION advisors
a precision value & health team