# The Value of Looking Beyond Overall Survival: The Role of Oncology-Relevant Endpoints in HTA / Payer Decision-Making

HTA6

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## Key takeaways

**Enhanced use of oncology-relevant endpoints (OREs) in HTA / payer decisions can expedite access to beneficial medicines, optimise patient outcomes, and potentially cut healthcare costs**

**Progress in using OREs beyond OS requires stakeholder collaboration to overcome obstacles, ensuring HTA / payer decisions lead to optimal patient outcomes**

## Background

- Overall survival (OS) is a robust and clinically relevant measure of importance to patients that is universally accepted as evidence of the value of a medicine, especially for HTA bodies / payers
- However, reliance on OS in HTA body / payer decision-making for novel cancer medicines presents limitations
- OREs include OS, other clinical endpoints and PROs that capture outcomes of high importance in a given cancer type

## Aims

This research aims to better understand the role of OS and other OREs in decision-making of novel cancer medicines by HTA bodies / payers. The goal is to:

1. Identify current challenges and drawbacks related to the use of OS in clinical trials
2. Articulate the value of OREs in addressing these challenges
3. Define the barriers preventing the adoption of OREs other than OS, particularly by HTA bodies / payers
4. Suggest a set of cross-stakeholder and individual stakeholder actions to help ensure timely access to medicines that provide benefits to patients

## Methods

LITERATURE REVIEW OF NON-OS EPs AND PROs

13 INTERVIEWS WITH Ex-PAYERS, REGULATORS, HCPs & PAGs

Round-tables

CROSS STAKEHOLDER INTERVIEWS AND GROUP DISCUSSIONS

## Results

### 1. Challenges and drawbacks related to the use of OS

- Extending OS remains highly important across cancer types and stages, particularly in cancer settings where survival remains a high unmet need and OS data is more readily available
- However, reliance on OS data presents three key limitations:

1. It doesn't capture outcomes of high importance to patients beyond survival, particularly those that capture health-related quality of life (HRQoL)
2. Time to collect OS data is increasing as cancer prognoses improve, delaying patient access to novel medicines in instances where regulatory / reimbursement processes rely on OS
3. OS is vulnerable to confounding (i.e., the distortion of outcomes caused by factors not related to the medicine being investigated), diluting the impact of medicines being investigated and potentially preventing access to medicine

### 2a. Value of OREs

- The value of OREs should be considered and evaluated per cancer type / stage to ensure they are fit for purpose, measuring outcomes of high importance to patients, collecting core outcome sets per treatment setting and using standardised methodologies to collect them

Value of OREs

1. The ability to measure outcomes of high clinical importance and of high importance to patients, beyond survival
2. The ability to provide an early indication of efficacy in the absence of OS data
3. Benefits due to lower sensitivity to confounding

Find out more from our article

## Results (*cont.*)

### 2b. Classification of OREs

- Endpoints used in clinical trials can be classified according to the outcome types they are intended to measure. They can be broadly considered to measure time to event and response rates. In addition, PROs provide disease-agnostic, tumour-specific or symptom-specific measures

| | Time to event | | Response rate | | PROs | | |
|---|---|---|---|---|---|---|---|
| Definition | Time from randomisation until occurrence of a pre-defined, disease-specific event | | The proportion of patients who achieve a pre-defined outcome in response to a treatment; can be complete response, partial response or stable disease | | Information on the impact of disease, symptoms or treatment on patient's QoL; participation in activities of daily living and healthcare resource use | | |
| Segments | Mortality-related | Disease-state related | Tumour marker /Biomarker | Non-biomarker | Disease agnostic measures | Tumour-specific measures | Symptom-specific measures |
| Examples | • OS | • Progression-free survival (PFS)<br>• Time to progression (TTP)<br>• Disease-free survival (DFS)<br>• Event-free survival (EFS)<br>• Relapse-free survival (RFS)<br>• Metastasis-free survival (MFS)<br>• Time to next treatment (TTNT)<br>• Time to metastasis (TTM)<br>• Duration of response (DoR) | • Minimal / measurable residual disease (MRD)*<br>• ctDNA*<br>• Disease-specific biomarkers (e.g., AFP in hepatocellular carcinoma, beta HCG in non-seminomatous testicular cancer) | • Complete response<br>• Partial response<br>• Overall response rate (ORR)<br>• Pathological complete response (e.g., Breast Ca)<br>• Disease control rate<br>• Clinical benefit rate | • PROMIS<br>• EQ-5D<br>• SF-36<br>• MD Anderson Symptom Inventory (activities of daily living) | • QLQ-BR23** (breast)<br>• QLQ-CR2** (colorectal)<br>• QLQ-LC13** (lung)<br>• QLQ-C30**<br>• NSCLC-SAQ (lung)<br>• FACT-C (colorectal)<br>• FACT-G | • SBQ** (symptom burden)<br>• KESS (constipation)<br>• IIED / FSFI (sexual function)<br>• PDQ (pain) |

Notes: * Some biomarkers may be used as predictors of event-related outcomes, e.g., MRD for PFS and ctDNA for DFS ** Modules of the EORTC PROs tool ^ PROs can also be measures of time to event, e.g., time to deterioration, or response, e.g., percentage of patients with improved HRQoL

### 3. Barriers to acceptance of OREs

Key barriers include HTA/payer uncertainty, stakeholder misalignment, and data inconsistencies

1. A significant obstacle to wider ORE adoption beyond OS in regulatory and reimbursement decisions is the doubt about their ability to accurately measure the value of new medicines and the sustained benefit to patients and healthcare systems by meeting these endpoints
2. There is misalignment between stakeholder groups on the value of oncology-relevant endpoints; for example, regulators are more accepting, whereas many HTA bodies / payers continue to rely predominantly on OS
3. There is also misalignment within stakeholder groups; for example, some HTA agencies (e.g., NICE, G-BA) incorporate PRO measures into their decision-making processes while HTAs in other countries (e.g., Spain and Italy) give less recognition to PRO data
4. Inconsistencies in the way OREs are collected and the methodologies used to collect them are further driving uncertainties from regulators and HTA bodies / payers and make it more difficult to demonstrate the true value of these endpoints

### 4. Actions to drive acceptance of OREs

- Proposed actions target early cross-stakeholder dialogue to ensure suitable OREs are chosen for pivotal trials
- This addresses uncertainties hindering OREs' use in HTA body / payer decision-making in oncology, helping to ensure future assessments improve patient outcomes

**Understand outcomes of most importance to patients per cancer type and stage**
- Ensure alignment among stakeholder groups on these outcomes

**Select the appropriate OREs per cancer type and stage**
- Check if Overall Survival (OS) captures important outcomes
- If OS data is immature, define suitable OREs

**Ensure consistency of data collection**
- Determine the best outcome sets for these OREs
- Ensure data collection methods are scientifically validated

**Ensure appropriate evidence generation and dissemination**
- Assess existing evidence for these OREs' value and identify any additional required evidence

**Build a portfolio of fit-for-purpose OREs by cancer type and stage**
- Adopt the portfolio across all stakeholders
- Understand meaningful outcome magnitudes per endpoint
- Update the portfolio regularly as treatment landscape advances and patient-important outcomes evolve

ACCEPTANCE

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