Improving the understanding, acceptance and use of oncology–relevant endpoints in HTA body / payer decision-making

Introduction

Cancer continues to be one of the most pressing public health issues, putting burden on patients, their families and communities, and on healthcare systems. While cancer treatment has improved significantly, challenges remain in patient access to novel therapies. Regulatory agencies have evolved the criteria for bringing new oncology medicines to patients; however, a reliance on overall survival (OS) by some HTA bodies / payers can present barriers to medicines access in oncology. This infographic provides an overview of oncology-relevant endpoints and lays out current barriers to the acceptance of different endpoints in HTA body / payer decision-making, as well as potential actions to address these barriers.

What are oncology-relevant endpoints?

Oncology-relevant endpoints refer to OS as well as other endpoints used in oncology clinical trials that measure outcomes beyond survival (e.g., progression-free survival, event-free survival, pathological complete response and patient-reported outcomes (PROs)). They capture outcomes of importance to patients, clinicians and healthcare systems and should be considered per treatment setting, according to each cancer type and stage.

How are oncology-relevant endpoints classified?

Oncology-relevant endpoints can be broadly classified into three categories:

FIGURE 1: Classification of oncology-relevant endpoints

	Time to event	Response rates	Patient-reported^
Definition	Time from randomisation until occurrence of a pre-defined, disease-specific event. E.g., overall survival (OS), progression-free survival (PFS) and disease-free survival (DFS)	Proportion of patients who achieve a pre-defined outcome in response to a treatment; can be complete response, partial response or stable disease. E.g., overall response rate (ORR) and biomarkers, such as ctDNA	Impact of disease, symptoms or treatment on the patient's quality of life (QoL), participation in activities of daily living and healthcare resource use. These can be categorised into cancer-agnostic, cancer-specific and symptom-specific measures

* Some biomarkers may be used as predictors of event-related outcomes, e.g., ctDNA as a predictor of DFS

^ PROs can also be measures of time to event, e.g., time to deterioration, or response rates, e.g., percentage of patients with improved QoL

What is the value of oncology-relevant endpoints?

Traditionally, cancer medicines have been reimbursed based on their ability to extend patient survival, for which OS is used. OS is defined as the time from randomisation until death from any cause.[1] It is universally accepted as evidence of the value of a medicine, especially by HTA bodies / payers, due to its inherent objectivity.[2] OS remains a robust and clinically relevant measure and is particularly important in treatment settings where survival remains a high unmet need and OS data is readily available.[3]

However, reliance on OS poses three key challenges: as science advances and the ability to treat early-stage disease improves, time to collect OS data is increasing; OS fails to capture outcomes of importance to patients beyond survival; and OS's vulnerability to confounding may dilute the true benefit of a medicine being investigated. These challenges are increasingly recognised by regulators and clinicians, but less so by HTA bodies / payers.

FIGURE 2: Limitations of OS and how oncology-relevant endpoints beyond OS can address this

Limitations of OS	**Inability to reflect full value** 1 *Patients and physicians have health / treatment priorities not captured by OS, including effect on quality of life*	**Long duration of studies** 2 *OS benefit takes longer to demonstrate (more than 10 years in some treatment settings)*	**Susceptible to confounding*** 3 *Subsequent treatments, patient cross-over^ and non-cancer related deaths are increasingly confounding the OS benefit*
Limitations for patients	**Reduced access** *to therapies with improved outcomes beyond survival*	**Delayed access** *to potentially life-saving or life-extending therapies*	**Denied access** *to potentially life-saving or life-extending therapies*
How OREs beyond OS can address this	Oncology-relevant endpoints beyond OS can **reflect broader value** to patients, including reduced symptoms, improved function, and lower treatment burden	Oncology-relevant endpoints beyond OS such as progression-free survival and tumor response, can be **captured earlier** in clinical trials	Oncology-relevant endpoints beyond OS are captured before the use of subsequent therapies and can provide a **more direct measure** of treatment efficacy

* Results impacted by other variables

^ Patient cross-over occurs when patients switch from the control arm to the interventional arm of a trial, in cases where it can be assumed that the efficacy of an investigational medicine is not inferior to the control. Patient cross-over is an important cause of confounding for OS as it dilutes the additional OS benefit of the medicine being investigated. Sources: [2–5]

Which barriers to acceptance of oncology-relevant endpoints beyond OS exist?

Three barriers have been identified which prevent broader acceptance of oncology-relevant endpoints beyond OS in HTA body / payer decision-making:

Questions from HTA bodies / payers regarding the value of oncology-relevant endpoints beyond OS and how this translates into quantifiable and prolonged benefit to patients and healthcare systems.[7] This is particularly true for PROs as some HTA body / payers see these outcomes as more subjective and therefore less appropriate for use in isolation compared to more objectively measured oncology-relevant endpoints.[8]

Misalignment between and within stakeholder groups on the value of oncology-relevant endpoints beyond OS. Stakeholder groups include patient advocacy groups (PAGs), clinicians, academia, regulators, HTA body / payers and industry. For example, regulators can be more accepting of oncology-relevant endpoints beyond OS, whereas many HTA bodies / payers continue to rely predominantly on OS.[9,10] Furthermore, due to the subjectivity of PROs, HTA bodies / payers across countries may differ in the way they review and interpret such data in reimbursement decisions.[8] Misalignment can prevent focused evidence generation, which is needed to quantify the benefit of new medicines to patients and healthcare systems. This in turn makes it harder for HTA body / payers to recognise the importance of oncology-relevant endpoints beyond OS in their decision-making.

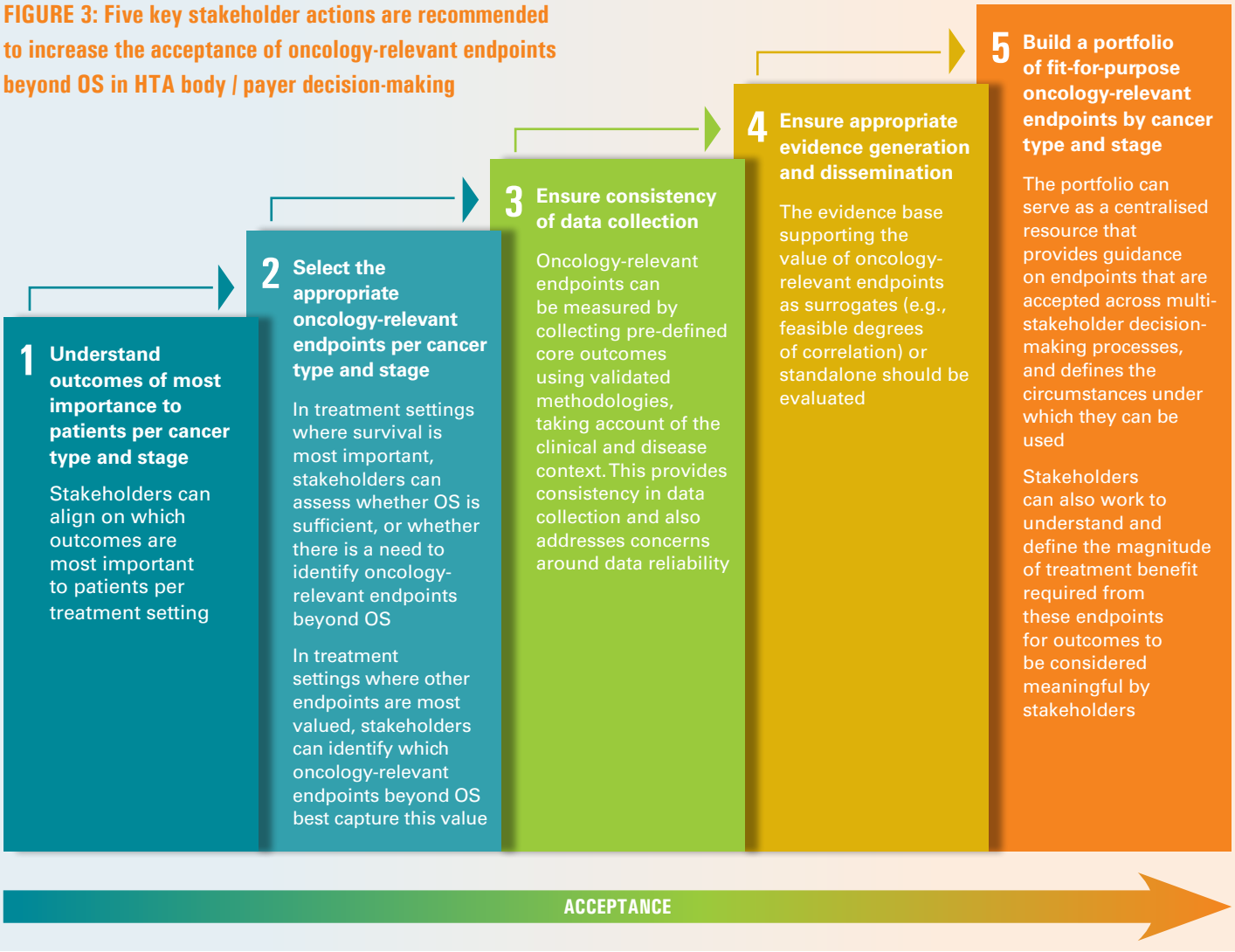
Inconsistencies in data collection and reporting of oncology-relevant endpoints beyond OS. Variations in the measures used to collect oncology-relevant endpoints can prevent their broader adoption in HTA body / payer decision-making. General tools are available that can be used across disease types; however, these fail to capture disease-specific outcomes of importance to patients. A wide variety of tools can collect disease-specific outcomes (e.g., pain, nausea, fatigue), but variability in the tools used and the specific outcomes collected limits comparability across trials. This in turn may limit the regulators' and HTA body / payers' confidence in PROs.[11–15]

What can stakeholders do to increase the acceptance of oncology-relevant endpoints beyond OS?

A stepwise approach including five key actions can be taken by stakeholders to address HTA body / payer concerns and ensure future HTA body / payer assessments result in the best outcomes for patients. As a first step, stakeholders can align on the outcomes which are most important per treatment setting and identify appropriate oncology-relevant endpoints to capture those. Once the oncology-relevant endpoints have been selected, abiding by the predefined and standardised methodologies to collect them is important to ensure consistency and comparability.

Stakeholders can then align on key uncertainties per treatment setting and define feasible evidence thresholds for oncology-relevant endpoints to be implemented. Subsequently, focused evidence generation can help to address uncertainties around the use of oncology-relevant endpoints and support their translation into patient-relevant and clinically relevant outcomes. These steps can help to build a portfolio of fit-for-purpose oncology-relevant endpoints per treatment setting.

FIGURE 3: Five key stakeholder actions are recommended to increase the acceptance of oncology-relevant endpoints beyond OS in HTA body / payer decision-making



Conclusion

Across settings, increased adoption of oncology-relevant endpoints beyond OS in HTA body / payer decision-making can help to provide timely access to life-improving or life-prolonging medicines, ensure optimal outcomes for patients and and potentially reduce healthcare costs.

Continued progress in incorporating oncology-relevant endpoints beyond OS depends on the collaboration of all stakeholders to overcome barriers and to ensure that HTA body / payer decision-making can result in the best outcomes for patients.

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This infographic has been developed as part of an EFPIA project to drive awareness of the use of oncology-relevant endpoints in HTA body / payer decision-making. The infographic was developed with the support of L.E.K. Consulting and was informed by a thought piece based on a literature review as well as 13 qualitative interviews with clinicians, patient advocates and former HTA body / payers to better understand the value of oncology-relevant endpoints, and the challenges facing their adoption. The findings were discussed and refined at three roundtables with the project's sounding board.

The findings were published in a white paper: "Improving the understanding, acceptance and use of oncology–relevant endpoints in HTA body / payer decision-making" which can be accessed here: https://www.efpia.eu/media/t2nlhr0k/improving-the-understanding-acceptance-and-use-of-oncology-relevant-endpoints.pdf