Payer/HTA requirements in metastatic breast cancer

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INTRODUCTION

- Triple-negative breast cancer (TNBC) represents 10%–20% of invasive breast cancers and has a very poor prognosis.1 There is a particular unmet need in TNBC, with a lack of clinical established targeted therapies2; chemotherapy is the only option for metastatic TNBC.3
- To facilitate access to new treatments, it is increasingly important to understand payer evidence needs in addition to regulatory evidence requirements.4
- Traditionally, payers have relied on hard endpoints such as overall survival (OS), and positive recommendations for reimbursement would ideally be supported by statistically significant improvement in OS. However, this is sometimes difficult due to long follow-up durations and post-study treatment.

OBJECTIVES

- To identify key health technology assessment (HTA) payer requirements and decision drivers/challenges in assessing new agents in TNBC by focusing on historical HTA submissions in metastatic breast cancer (MBC) as a proxy for TNBC (due to a lack of TNBC HTA assessments).

METHODS

- Assessments included for final analysis were original HTA assessments on drugs for the treatment of MBC published since 2003.
- Published assessments were identified via Quintiles’ HTA Accelerator Database.5 HTA agencies covered were NICE (UK), G-BA and IQWiG (Germany), HAS (France), PBAC (Australia), PCN (New Zealand), ASMR IV (Denmark), CSRs (China), ZIN (Netherlands), and TLV (Sweden).
- Key agency comments on the evidence in the submission were extracted, and cross-market and treatment analysis conducted to identify key differences or similarities across HTA agency valuation.

RESULTS

Payer decision drivers and evidence critique

- In total, 96 MBC reports from 9 agencies were identified; the primary elimination process showed 57 potentially relevant reports. After the secondary round of selection, 28 HTA reports on 8 drugs were included in the analysis.
- There were 38 recommendations based on 38 HTA assessments (1 HTA was a multiple technology assessment) and 19 (51%) positive, (8%), with restrictions (n = 12); ongoing with draft negative recommendation (n = 2); and no recommendation provided (n = 13).
- The 4 key treatments assessed by multiple agencies were trastuzumab/entanercept (Kadcyla), pertuzumab (Perjeta), eribulin (Halaven), and lapatinib (Tyverb/Ambex).
- Key decision drivers for positive recommendations included a lack of cost-effectiveness as a key driver for negative decisions (Figure 1a).
- Key criteria on submission were the most prominent negative critique on submissions that was model assumptions not justified or the relative treatment effect was unclear. The most common positive critique was superiority versus standard care/best supportive care in the primary endpoint (Figure 1b).

Clinical evidence requirements

- Most assessments were based on clinical evidence from randomised controlled trials (RCTs), with progression-free survival (PFS) or OS as primary (n = 9) and secondary (n ≥ 10) endpoints, respectively.
- All 12 pivotal RCTs mentioned in the HTA reports were 2-arm studies.
- New open-label RCTs commented on the potential of those trials to introduce bias in 10 of 27 assessments that included such a study. Six were appropriate comparators included.
- Use of an inappropriate comparator in the key RCTs was criticised in 18 of 38 assessments.
- Twenty-five submissions included health-related quality of life (HRQoL) data, of which 20 used the Functional Assessment of Cancer Therapy-Breast HRQoL instrument.6
- Lack of HRQoL data was critiqued as a data gap in 9 assessments. Figure 2 shows a trend toward more positive recommendations with sound tolerability and HRQoL data, but
- American Society of Clinical Oncology (ASCO) working groups’ guidelines consider significant improvements in median OS and PFS in previously untreated metastatic TNBC of 6.5-4.5 months, respectively, as clinically meaningful.

CONCLUSIONS

- Obtaining a positive HTA recommendation for new MBC drugs is challenging.
- Well-established HMs and acceptable ICERs are important factors in obtaining an favourable HTA opinion. However, model inputs and assumptions need robust validation in order to be accepted by HTA agencies, or they risk negative recommendations.
- Key drivers of positive HTA opinions include significant and clinically meaningful incremental improvements in OS and/or PFS.
- Despite efforts to clarify meaningful outcomes in oncology,10 there is no uniformly agreed HTA standard. For reimbursement evaluation, this ASCO framework defining clinically meaningful outcomes is limited and more elements need to be considered for adequate decision making.
- Obtaining statistically significant and mature OS data is challenging and cannot always be provided. Thus, other outcomes such as strong and adequately measured HRQoL should be a key factor to determine value.

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