TODAY'S RESEARCH FOR TOMORROW'S HEALTH

Rapid Review of Published Economic Evaluations of Larotrectinib and Entrectinib: Current Practices to Overcome Challenges in Health Technology Assessment of Tumor-Agnostic Treatments

HTA151

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INTRODUCTION

- Tumor-agnostic treatments target cancer based on its genetic and molecular characteristics, regardless of the tumor's histology.
- This approach introduces variability in target patient populations and treatment settings, necessitating reliance on nonrandomized, single-arm trials that provide limited data on clinical outcomes and create uncertainty in cost parameters.[1]
- The lack of sufficient evidence at the time of market entry presents significant challenges for health technology assessment (HTA) agencies in evaluating the cost-effectiveness of these treatments.[1]

OBJECTIVES

- This study aimed to review published economic evaluations of two tumor-agnostic therapies, larotrectinib and entrectinib.
- The primary objective was to summarize existing practices for addressing the challenges associated with this treatment type

METHODS

- A rapid literature review adhering to PRISMA principles[2] was conducted using PubMed, Embase, CEA Registry, PROSPERO, and Cochrane Library, covering all available records up to June 2024.
- The review included scientific articles and conference presentations evaluating the cost-effectiveness of larotrectinib and entrectinib in tumor-agnostic indications.
- General characteristics of the economic evaluations were extracted, and efforts to address challenges were carefully examined, with a specific focus on the heterogeneity caused by investigating multiple tumor types and the limitations of clinical input data.

RESULTS OF THE LITERTURE SEARCH

- A total of 151 records were identified and screened by titles and abstracts. Of these, 14 proceeded to full-text screening, and 9 were considered relevant to this study.
- Among these, six independent model-based economic analyses were identified[3-8], while the remaining three were country adaptations and updates of these analyses.

Characteristics of studies

- Among the six primary analyses, three investigated entrectinib[3,5,6] and three examined larotrectinib[4,7,8]. Five analyses employed a partitioned survival approach[3-5,7,8], and one used microsimulation method[6]. All models applied extrapolations over a lifetime horizon relying on progression free survival (PFS) and overall survival (OS) data.
- All analyses reported pooled cost per quality-adjusted life years (QALYs) for the tumor types investigated, with only one study also calculating tumor-specific incremental cost-effectiveness ratios (ICERs)[8].
- All assessments included tumor-specific standard of care as the comparator. To construct the comparator arm in the model, three studies relied on literature data[3,5,7], one used real-world data[6], one employed a non-responder control[8], and one analysis utilized three different approaches (historical control based on literature, intra-cohort comparison, and non-responder control)[4].
- The inclusion of companion diagnostic tests varied in studies: one assessed both costs and outcomes[6], showing significant cost-effectiveness impact, another included only testing costs[3], while the remaining four studies did not consider testing in the analyses[4,5,7,8].

Observed practices to overcome challenges in HTA

POOLED AND TUMOR SPECIFIC ICERs ✓

WEIGHTING BASED ON TUMOR PREVALENCE ✓

- When tissue specific input is used
- When calculating pooled results

TUMOR-SPECIFIC STANDARD OF CARE AS COMPARATOR ✓

CONSTRUCTION OF COMPARATOR ARM ✓

- Historical control based on literature
- Use of Real World Data (RWD)
- Intra-cohort comparison (progression in a previous treatment line)
- Non-responder controls from clinical trials

INCLUSION OF COMPANION DIAGNOSTIC TESTS ✓

CONCLUSION

- There is substantial heterogeneity in the published economic evaluation methods for assessing tumor-agnostic treatments.
- Utilizing multiple approaches in parallel is recommended to enhance the robustness of results and scenario analyses are crucial to understand the impact of different methods on cost-effectiveness results.
- Understanding the differences between economic evaluation approaches is crucial to support future HTA decisions in tumor-agnostic treatments.

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