HTA87

Mapping accumulating evidence across multiple indications in oncology health technology assessment

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Objectives

An increasing number of oncology drugs are licenced for multiple indications but during an appraisal for a particular indication, health technology assessment (HTA) bodies typically ignore existing evidence in other indications. However, HTA-informed decisions about multi-indication oncology products can potentially be improved by making better use of evidence across, as well as within, indications.

Analytic approaches and policy decisions in a multi-indication context may be able to gain precision by considering a broader evidence-base, including more mature evidence from earlier indications that are considered clinically relevant.

Considering key features of multi-indication oncology HTA, we explored methods to present and summarise evidence, within and across indications, to inform policy makers, support evidence synthesis approaches or to guide expert elicitation.

Bevacizumab: A case-study

We identified all RCT evidence available for bevacizumab in the 7 indications licensed by either the EMA or FDA

- Trials were included:
  - if the treatment effect of bevacizumab could be isolated from background chemotherapy
  - if they were conducted in advanced or metastatic disease
- Excluded evidence from non-licensed and non-oncology indications

Features of interest of multi-indication evidence

- Multiple timepoints and the accumulation of evidence over time
- Multiple outcomes: OS and PFS
- Differences in trial populations and comparators
- Differences in relative sample size (Fig 2) and follow-ups between trials
- Uncertainty of evidence
  - Uncertainty can be defined in many ways. In Fig 2, we use the width of the CI of the reported HR.
- Maturity of evidence
  - Can be represented as a ratio of the number of events to the total trial participants in Fig 2.
  - Unfortunately, this measure is not always reported.

Fig 2: Modified time-summary plots for NSCLC

Time Summary Plots provide a graphical summary of the accumulation of evidence over time, within and across different indications (Fig 1). These can be modified to show study or outcome details (e.g., for NSCLC in Fig 2).

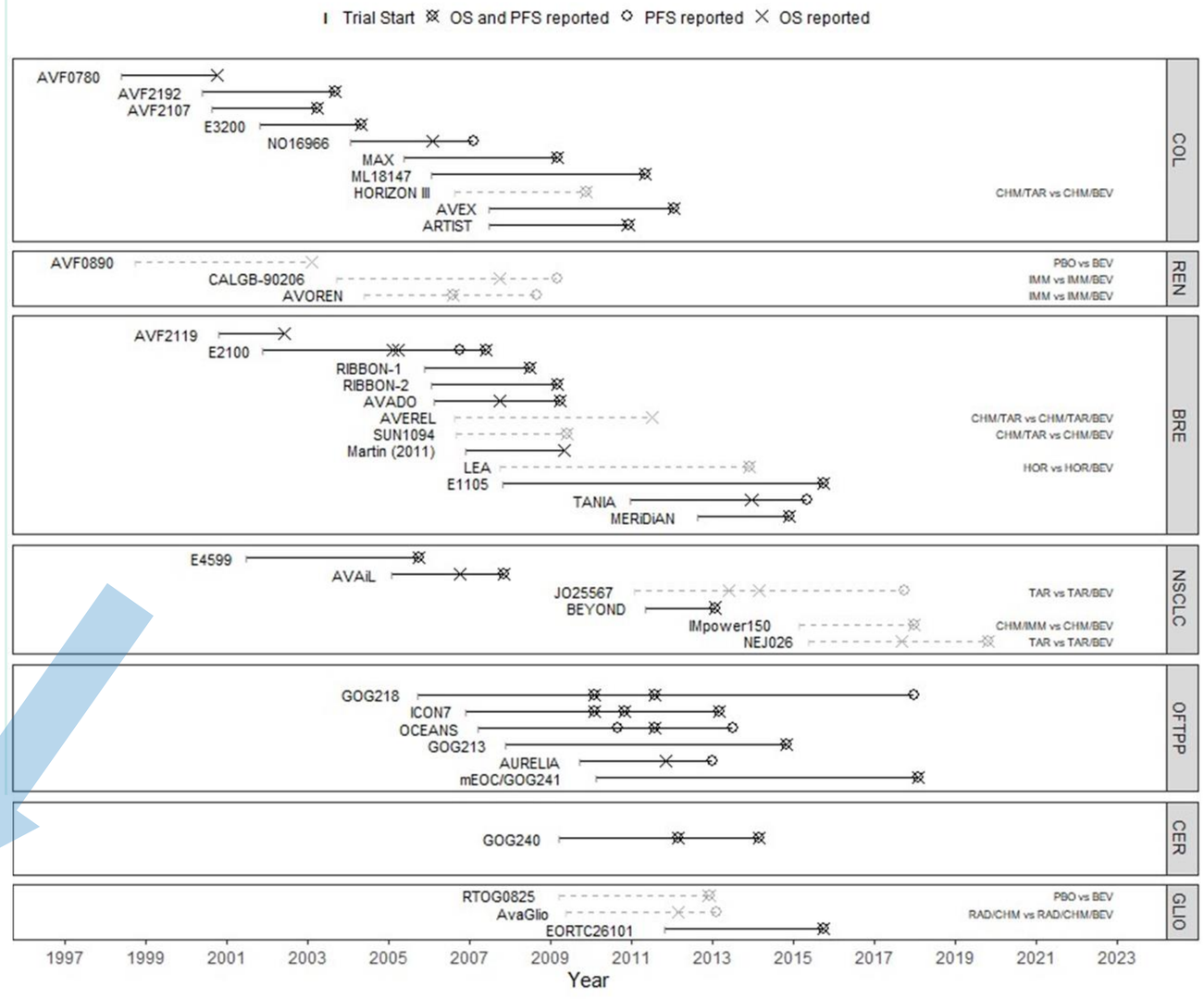
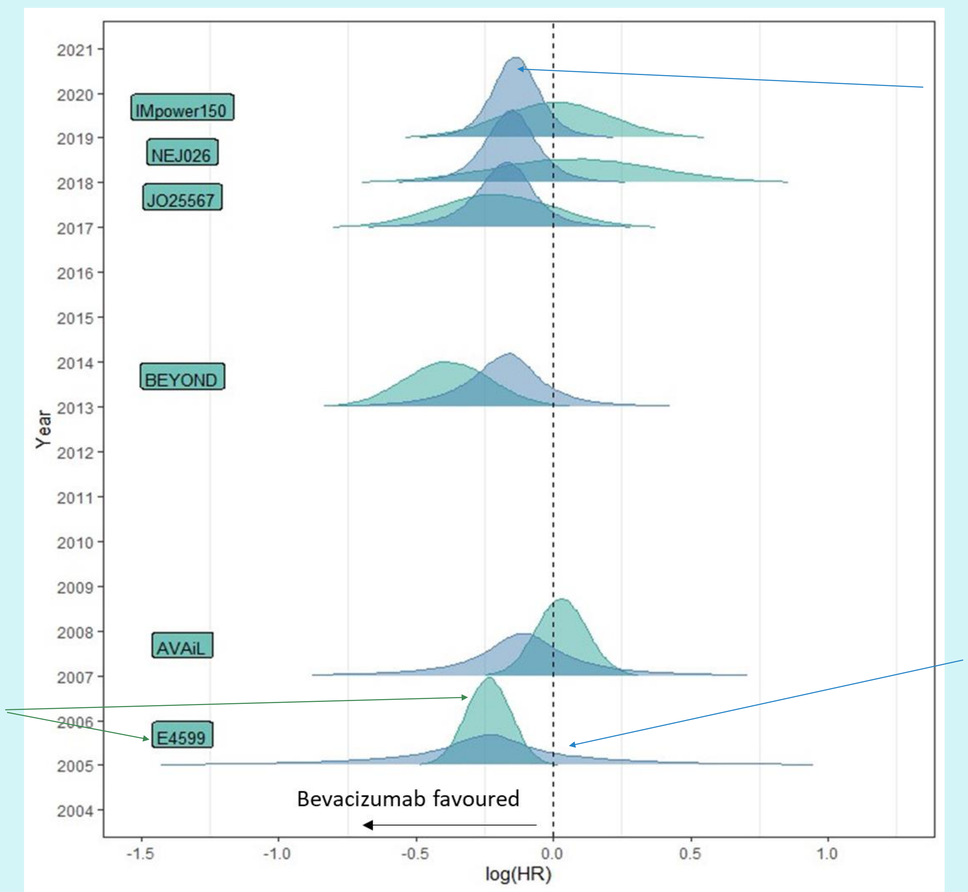


Fig 1: Time-summary plots

Ridgeline Plots can be used to show the density (assuming normal distribution) of the final reported lnHRs for OS and PFS within an indication (Fig 3) or to compare the density of HRs reported in trials to the results of a synthesis model (Fig 4).

The y-axis shows a representation of time. Multiple trials may report OS and PFS in the same year, but these are plotted distinctly

Fig 3: Ridgeline plot showing all colorectal trials



(1) A new trial reports the HR for OS

(2) A meta-analysis is conducted with all the NSCLC OS evidence available at that point and plotted

(3) The final meta-analysis includes all available NSCLC OS evidence. The narrow peak depicts improved precision in estimates.

Fig 4: Ridgeline plot showing all NSCLC trials and results of a random-effects cumulative meta-analysis for OS

Conclusion

There is a growing interest in the methods and approaches to the evaluation of multi-indication products. The representation of a broader and more complex evidence-base can be more effectively communicated using a range of visualisation approaches.

Specific elements of interest for analysts and policymakers can be further captured using modifications to these visual maps.

Abbreviations: BEV, bevacizumab; BRE, breast cancer; CHM, chemotherapy; COL, colorectal cancer; CER, cervical cancer; EMA, European Medicines Agency; FDA, food and drug agency; GLIO, glioblastoma; HOR, hormone therapy; IMM, immunotherapy; NSCLC, non-small cell lung cancer; OFTPP, ovarian, fallopian tube and primary peritoneal cancer; PBO, placebo; RAD, radiotherapy; REN, renal cell carcinoma; TAR, targeted therapy.

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