A Review of the Use of Clinical Expert Opinion to Inform Survival Curve Extrapolations in Single Technology Appraisals of New Cancer Drugs by NICE, UK

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INTRODUCTION

For immature survival data, extrapolation approaches are required to estimate the full survival benefit over a lifetime time horizon. Various extrapolation approaches are available; each will result in different survival estimates. Different methods, including clinical expert opinion, can be used to assess the plausibility of extrapolated curves. The Technical Support Document (TSD 14) published by the National Institute for Health and Care Excellence (NICE) Decision Support Unit (DSU), provides guidance on methods to be used when extrapolating survival data (1).

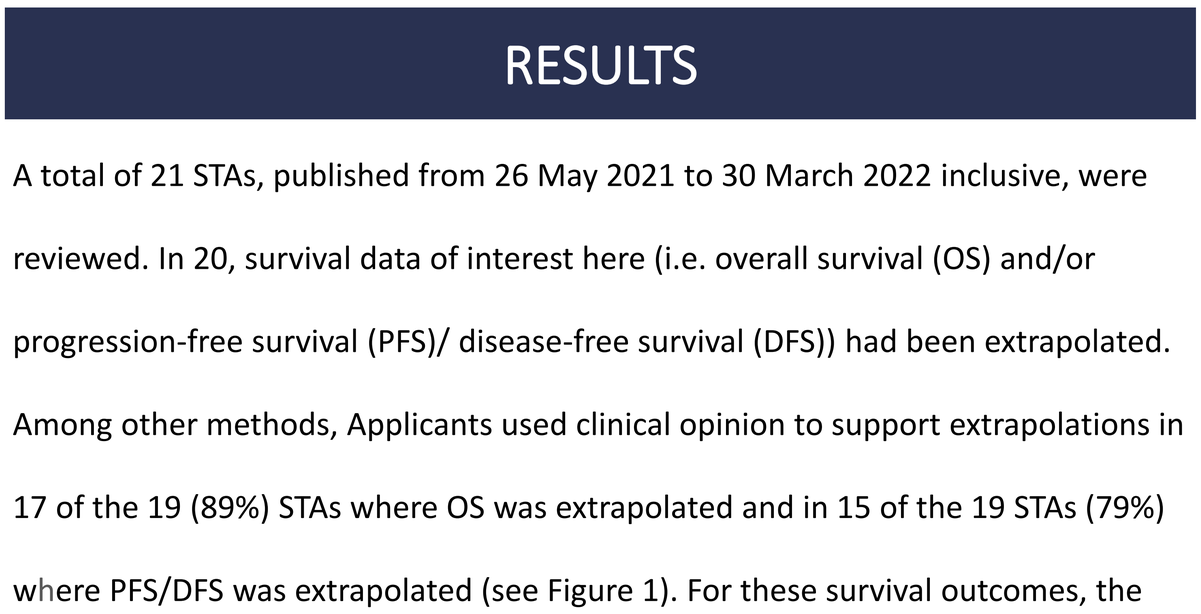
METHODS

Single Technology Appraisals (STAs) for new cancer drugs, published by NICE, UK, were reviewed. The publicly available Applicant Submissions and Evidence Review Group (ERG) reports were accessed at www.nice.org.uk. Pre-specified data was extracted using a data collection instrument programmed in Microsoft Forms® and analysed in Microsoft Excel®.

RESULTS

A total of 21 STAs, published from 26 May 2021 to 30 March 2022 inclusive, were reviewed. In 20, survival data of interest here (i.e. overall survival (OS) and/or progression-free survival (PFS)/ disease-free survival (DFS)) had been extrapolated. Among other methods, Applicants used clinical opinion to support extrapolations in 17 of the 19 (89%) STAs where OS was extrapolated and in 15 of the 19 STAs (79%) where PFS/DFS was extrapolated (see Figure 1). For these survival outcomes, the Applicants' chosen base case extrapolations aligned with the clinical opinion received in all relevant STAs, except in one STA for PFS.

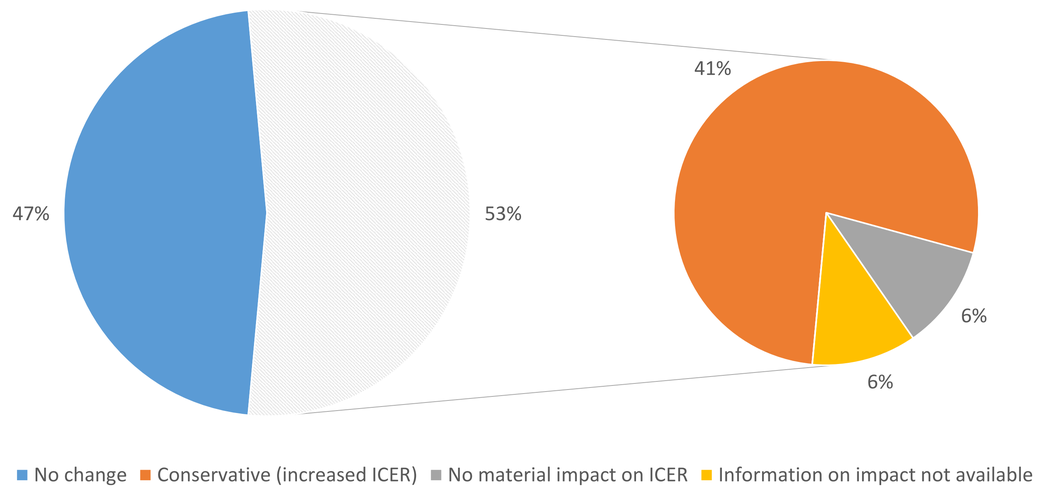
Figure 1: Methods used by Applicants to justify extrapolations of OS curves (n=19) and PFS/DFS curves (n=19) in STA submissions to NICE (26 May 2021 to 30 Match 2022 inclusive)



Note: STA: Single Technology Appraisal, OS: overall survival, DFS: disease-free survival, PFS: progression-free survival.

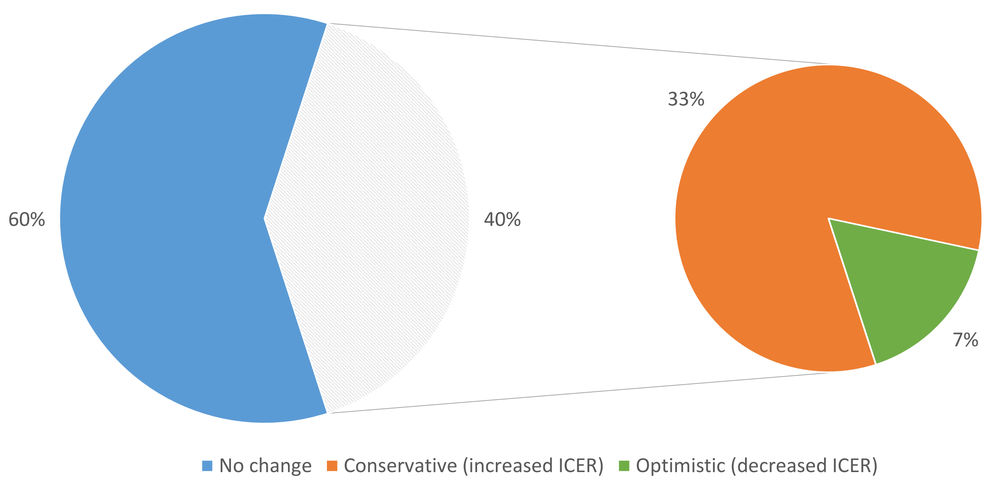
Where clinical opinion was sought, the ERG-preferred extrapolation did not align with the Applicant's base case extrapolation in 9 of 17 STAs (53%) for OS (see Figure 2) and 6 of 15 STAs (40%) for PFS/DFS (see Figure 3). When compared to the Applicant's base case, implementation of the ERG-preferred extrapolation generally resulted in more conservative incremental-survival estimates and thus increased incremental cost-effectiveness ratio.

Figure 2: Changes made by the ERG to the Applicant's base case extrapolations for OS where clinical opinion was used (n=17)



Note: OS: Overall Survival, ICER: Incremental Cost Effectiveness Ratio, ERG: Evidence Review Group.
In comparison to the Applicant's base case, changes made by the ERG are considered conservative when the ICER increases.

Figure 3: Changes made by the ERG to the Applicant's base case extrapolations for PFS/DFS where clinical opinion was used (n=15)



Note: DFS: disease-free Survival, PFS: progression-free survival, ERG: Evidence Review Group.
In comparison to the Applicant's base case, changes made by the ERG are considered optimistic when the ICER decreases and conservative when the ICER increases.

DISCUSSION

Immature survival data for OS and/or PFS/DFS were extrapolated in the majority of the STAs reviewed. In these STAs, the Applicants' base case extrapolations were routinely aligned with clinical opinion obtained by the Applicant. However, the ERG-preferred extrapolations often differed to those chosen by the Applicant. Where they differed, the majority of ERG-preferred extrapolations were associated with more conservative estimates of survival.

REFERENCES

(1) Latimer NR. National Institute for Health and Care Excellence (NICE) Decision Support Unit (DSU) Technical Support Document 14: Survival analysis for economic evaluations alongside clinical trials—extrapolation with patient-level data. Report by the NICE DSU, June 2011.