The results of the ERG's additional sensitivity analyses indicate that alternative choices of parametric functions to model OS may reduce the ICER for regorafenib (ICER range = £72,642 to £81,081 per QALY gained). The use of alternative parametric functions to model time to treatment discontinuation leads to ICERs in the range £74,122 to £81,703 per QALY gained. The use of the utilities from the SHARP trial increase the ICER for regorafenib versus BSC to £92,719 per QALY gained. Increasing the disutility associated with progressed disease (relative to the progression-free utility score) does not have a substantial impact on the ICER for regorafenib. The exploratory analysis in which the number of hospitalisations per month estimated in the survey was applied to the entire population has only a minor impact on the ICER for regorafenib compared with assuming that the percentage requiring hospitalisation was correct and that patients were hospitalised once per month. The inclusion of dose reductions to [redacted] for all patients from the start of treatment reduces the ICER to [redacted] per QALY gained; the ERG notes that this represents a highly optimistic scenario and that the ICER for regorafenib is likely to be higher than this estimate.

5.6 Discussion

The CS includes a systematic review of published economic evaluations of treatments for HCC together with a *de novo* health economic evaluation of regorafenib (plus BSC) versus BSC alone in patients with HCC. The company's review did not identify any economic evaluations of regorafenib within this indication. Additional searches undertaken by the ERG identified one economic evaluation study which assessed regorafenib versus BSC in patients (Parikh *et al*[35]); this study was published after the company's searches had been carried out. The company and the ERG both agreed that this study is not relevant to the current appraisal due to the use of a short time horizon, the absence of any form of extrapolation of time-to-event outcomes and the use of a US health care system perspective.

Owing to the absence of any relevant existing studies, the company developed a *de novo* partitioned survival model to assess the cost-effectiveness of regorafenib (plus BSC) versus BSC alone in adult patients with unresectable HCC who have been previously treated with sorafenib. Incremental health gains, costs and cost-effectiveness of regorafenib are evaluated over a 15-year time horizon from the perspective of the NHS and PSS. The company's model includes three health states: (1) progression-free; (2) progressed disease, and (3) dead. The model parameters were mostly informed by analyses of time-to-event data (PFS, OS and time on treatment) collected within the RESORCE trial[6] (January 29th 2016 DCO). PFS was modelled using the observed PFS estimates, OS was modelled using a log normal distribution with a treatment effect covariate (an HR) and time to treatment discontinuation was modelled using a "cycle-cohort simulation" approach. Resource use was informed by a survey of three clinical experts undertaken in 2015. The model assumes that a small proportion of patients treated with regorafenib will discontinue prior to disease progression and that a proportion of patients continue regorafenib treatment following progression. The model includes a mean daily dose of

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