European Journal of Cancer 75 (2017) 204–212

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Original Research

Cost-effectiveness of capecitabine and bevacizumab maintenance treatment after first-line induction treatment in metastatic colorectal cancer

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Received 14 October 2016; received in revised form 8 January 2017; accepted 14 January 2017
Available online 24 February 2017

KEYWORDS
Colorectal;
Cancer;
Cost-effectiveness;
Capecitabine;

Abstract ***Aim:*** Capecitabine and bevacizumab (CAP-B) maintenance therapy has shown to be more effective compared with observation in metastatic colorectal cancer patients achieving stable disease or better after six cycles of first-line capecitabine, oxaliplatin, bevacizumab treatment in terms of progression-free survival. We evaluated the cost-effectiveness of CAP-B maintenance treatment.

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http://dx.doi.org/10.1016/j.ejca.2017.01.019

Bevacizumab

Methods: Decision analysis with Markov modelling to evaluate the cost-effectiveness of CAP-B maintenance compared with observation was performed based on CAIRO3 study results (n = 558). An additional analysis was performed in patients with complete or partial response. The primary outcomes were the incremental cost-effectiveness ratio (ICER) defined as the additional cost per life year (LY) and quality-adjusted life years (QALY) gained, calculated from EQ-5D questionnaires and literature and LYs gained. Univariable sensitivity analysis was performed to assess the influence of input parameters on the ICER, and a probabilistic sensitivity analysis represents uncertainty in model parameters.

Results: CAP-B maintenance compared with observation resulted in 0.21 QALYs (0.18LYs) gained at a mean cost increase of €36,845, yielding an ICER of €175,452 per QALY (€204,694 per LY). Varying the difference in health-related quality of life between CAP-B maintenance and observation influenced the ICER most. For patients achieving complete or partial response on capecitabine, oxaliplatin, bevacizumab induction treatment, an ICER of €149,300 per QALY was calculated.

Conclusion: CAP-B maintenance results in improved health outcomes measured in QALYs and LYs compared with observation, but also in a relevant increase in costs. Despite the fact that there is no consensus on cost-effectiveness thresholds in cancer treatment, CAP-B maintenance may not be considered cost-effective.

1. Introduction

Recently, the results of the phase 3 CAIRO3 study showed that metastatic colorectal cancer (mCRC) patients with stable disease or better after 6 cycles of treatment with capecitabine, oxaliplatin and bevacizumab (CAPOX-B) had a significant benefit from capecitabine and bevacizumab (CAP-B) maintenance treatment compared with observation [1]. In this trial, reintroduction of CAPOX-B treatment was planned in all patients who had progressive disease following either CAP-B maintenance or observation. A statistically significant improvement in the primary endpoint of second progression-free survival (PFS-2), defined as the time from randomisation until progression of disease after CAPOX-B reintroduction, was shown for maintenance treatment versus observation, 11.7 months and 8.5 months, respectively (hazard ratio [HR] 0.67, 95% confidence interval [CI] 0.56–0.81). Although the study was not designed to detect a difference in overall survival (OS), an absolute median OS benefit of 3.5 months was observed, which was not statistically significant (HR 0.89, 95% CI 0.73–1.07). Median OS from the time of randomisation was 21.6 months for patients receiving maintenance treatment and 18.1 months for observation [1]. A statistically significant OS benefit in favour of CAP-B maintenance treatment was demonstrated in patients achieving complete response (CR) or partial response (PR) during induction treatment (24.1 months and 18.8 months, respectively [log-rank p = 0.0002]) [1]. However, results for this subgroup analysis require further validation. Maintenance treatment did not impair quality of life (mean change in global quality of life 0.03, 95% CI: 0.35–0.41) [1]. Our findings are supported by the results of the AIO 0207 study, which had a comparable study design [2].

Despite these results, economic concerns may hamper the implementation of CAP-B maintenance therapy in daily practice. Multiple cost-effectiveness analyses of bevacizumab-containing first-line regimens for mCRC treatment have been published with different results: some analyses did [3–6], but others did not show that the addition of bevacizumab to chemotherapy was cost-effective [7–12]. This diversity in results arises due to differences in methodology applied for these cost-effectiveness studies, such as therapy of comparison and country of origin [13]. In addition, as recently described, a cost-effectiveness study can be fully designed and calculated based on assumptions, such as duration of bevacizumab treatment continuation, which might importantly influence cost and effect outcomes [3,14].

Cost-effectiveness of CAP-B maintenance treatment has not been previously evaluated. Therefore, we evaluated the cost-effectiveness of CAP-B maintenance compared with the observational strategy following first-line CAPOX-B induction treatment for mCRC patients based on the CAIRO3 study.

2. Methods

2.1. Patient population

Results of the CAIRO3 study (NCT00442637) [1] were used for this post hoc cost-effectiveness model. The CAIRO3 study was a Dutch multicenter randomised clinical study in which mCRC patients (n = 558) with