Title **Systematic Review of the Clinical Effectiveness and Cost Effectiveness of Capecitabine (Xeloda®) for Locally Advanced and/or Metastatic Breast Cancer**

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Aim

To examine the clinical effectiveness and cost effectiveness of oral capecitabine for locally advanced and metastatic breast cancer in relation to its licensed indications.

Conclusions and results

For capecitabine monotherapy, 12 uncontrolled observational studies were identified. The methodological quality of the studies was low. Capecitabine demonstrated antitumor activity, but was associated with a risk of hand–foot syndrome and diarrhea. Economic evaluation was hampered by the poor quality of published studies. Compared indirectly with vinorelbine, capecitabine showed lower costs and improved patient outcomes. For capecitabine combined with docetaxel, one randomized controlled trial (RCT) was identified. Combination therapy was superior to single-agent docetaxel in terms of survival, time to disease progression, and overall response. Adverse events were more frequent with combination therapy. Economic evaluation showed an improved QALY score for combination therapy with slightly reduced costs.

Recommendations

No conclusions could be drawn on the therapeutic benefit of capecitabine monotherapy; RCTs are required. Capecitabine was cost effective compared with vinorelbine, but the poor quality of the trials may invalidate this conclusion. Based on limited evidence, combined therapy was more effective than single-agent docetaxel and likely to be cost effective, but was associated with higher incidences of hand–foot syndrome, nausea, diarrhea, and stomatitis.

Methods

Two reviewers independently screened and assessed all titles and/or abstracts including economic evaluations. RCTs and observational studies that investigated capecitabine monotherapy, in patients pretreated with an anthracycline-containing regimen or a taxane, or capecitabine in combined with docetaxel, in patients pretreated with an anthracycline-containing regimen, were included. Economic evaluation was based on data reported by the manufacturer.

Further research/reviews required

There is an urgent need for basic research into the effectiveness of new second-, third-, and subsequent-line chemotherapy agents for treating advanced breast cancer. Good quality RCTs are needed to compare the effectiveness of capecitabine monotherapy with the alternative third- and subsequent-line therapies now available, and with best supportive care. Future trials should collect data on a range of outcomes, with particular emphasis on QoL and patient preferences. These data should facilitate cost-effectiveness analysis. Further RCTs investigating capecitabine in combination with docetaxel and alternative second-line therapies are required. Future trials should avoid selection bias. It is particularly important to analyze the data on an intention-to-treat basis, and that those assessing the outcome measure are blinded. With respect to time to event data, it is important to present the data in Kaplan–Meier survival curves and compare data using an HR with 95% CI. The presentation of dichotomous data in terms of RR with 95% CI, and absolute event rates, is also preferable.

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