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Systematic review of capecitabine monotherapy for advanced breast cancer

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Introduction

- Increasing numbers of patients with advanced breast cancer are presenting with disease that has failed taxane and anthracycline therapy.[1]
- Capecitabine recently gained licensing approval in the UK and Europe and is the first oral chemotherapy treatment approved for this patient group.
- Capecitabine was selected for appraisal by the UK National Institute for Clinical Excellence (NICE).

Materials and Methods

- A systematic search of 14 electronic databases (inception to May 2002) and additional sources was undertaken.

Inclusion criteria

- Intervention: Oral capecitabine used as monotherapy for patients who had failed treatment with taxanes and anthracycline-containing regimens, or who had failed taxanes and for whom, further anthracycline therapy was not indicated.
- Study design: In the absence of RCTs, uncontrolled phase II and other observational studies.
- Participants: Patients with locally advanced or metastatic breast cancer.
- Outcomes: Overall survival, progression-free survival, tumour response (complete and partial), time to treatment failure, adverse events/toxicity, and quality of life.

Characteristics of the included studies

- Seven uncontrolled Phase II studies were identified, five studies had only been published as conference abstracts.
- The number of participants varied between the included studies.
- All of the studies included patients who had received on average 2-3 chemotherapy treatments and the percentage of patients pre-treated with both a taxane and an anthracycline ranged from 39% to 100%.
- The dosage schedules differed between the seven studies.
- In addition, two studies using other observational designs were identified, both included mixed groups of patients at different stages of treatment.

Table 1. Summary of data from phase II studies

Study	N	Dosage	Median survival	Overall response rate†
Blum et al. 1999	162	2510 mg/m²/day for 14 days out of a 21-day cycle	12.6 months (95% CI: not reported)	20% (95% CI: 14, 26%)
Blum et al. 2001	74	2510 mg/m²/day for 14 days out of a 21-day cycle	12.2 months (95% CI: 8.0 to 15.3)	26% (95% CI: 16, 36%)
Cervantes et al. 2000*	32	2500 mg/m²/day for 14 days out of a 21-day cycle	Not reported	41% (95% CI: 24, 58%)
Fumoleau et al. 2002*	126	2500 mg/m²/day for 14 days out of a 21-day cycle	15.2 months (95% CI: 13.5 to 19.6)	28% (95% CI: 20, 34%)
Reichardt et al. 2001*	136	2500 mg/m²/day for 14 days out of a 21-day cycle	10.4 months (95% CI: 8.2 to 12.7)	15% (95% CI: 9, 22%)
Semiglazov et al. 2002*	31	2510 mg/m²/day for 14 days out of a 21-day cycle	8.1 months (95% CI: not reported)	21% (95% CI: 6, 35%)
Watanabe et al. 2001*	60	1657 mg/m²/day for 21 days out of a 28-day cycle	Not reported	20% (95% CI: 10, 33%)

*only published as conference abstracts
†composite of complete and partial response rate

Results

- Evidence for the effectiveness of capecitabine was limited.
- Capecitabine monotherapy appeared to demonstrate antitumour activity.
- In the absence of a control group it was not possible to determine what 'additional' survival patients had experienced with capecitabine.
- Capecitabine was associated with a particular risk of developing hand-foot syndrome (a condition which may cause blistering and degradation of the skin) and diarrhoea.

Conclusions

- Based on the current evidence, no conclusions could be drawn regarding the therapeutic benefit of capecitabine monotherapy.
- Good quality controlled trials are urgently required to compare the effectiveness of capecitabine with the alternative third- and subsequent line therapies currently available, including standard palliative care.
- Future trials should ensure that data are collected on a range of outcomes, with particular emphasis on quality of life and patient preferences.

References

1. Blum JL. The role of capecitabine, an oral, enzymatically activated fluoropyrimidine, in the treatment of metastatic breast cancer. *Oncologist* 2001;6:56-64