

Randomised controlled trials

Merck Serono

Searches by Merck Serono were performed in the following databases on 5 October 2009 and updated on 2 November 2010:

- Ovid EMBASE
- Ovid MEDLINE
- Ovid MEDLINE In-Process & Other Non-Indexed Citations
- The Cochrane Central Register of Controlled Trials (CENTRAL).

Hand searches were also undertaken on several internet resources to identify relevant conference proceedings:

- American Society of Clinical Oncology (ASCO): www.asco.org
- European Cancer Organisation (ECCO): www.ecco-org.eu
- American Association of Cancer Research (AACR): www.aacr.org.

Separate search strategies were provided by the manufacturer for EMBASE, MEDLINE, MEDLINE In-Process & Other Non-Indexed Citations and CENTRAL. Database searches in EMBASE, MEDLINE and MEDLINE In-Process & Other Non-Indexed Citations were based on a conjunction of terms identifying the metastatic colorectal cancer population with known *KRAS* status and terms identifying cetuximab, panitumumab and bevacizumab as interventions. For each term a combination of thesaurus headings (where possible) and free-text search words was used. No outcomes were specified to limit the searches in any of these databases.

The EMBASE, MEDLINE and MEDLINE In-Process & Other Non-Indexed Citations searches included a study design filter to limit results to clinical trials. No additional filters were applied in any databases.

Within the search strategies the combinations of terms to define the metastatic colorectal cancer population and/or the intervention were appropriate and were replicable. Overall, we found the syntax to be highly focused, which has the potential to impinge on the sensitivity of the search. The choice of RCT filter was good and highly sensitive. The internet searches appear vague in their recording of findings and limited in their depth, and the CENTRAL search was considered poor because of some uncertainty regarding the use of the interface. That said, we found no additional trials.

Amgen

Searches by Amgen were performed in the following databases on 24–29 September 2010 and updated in January 2011:

- EMBASE
- MEDLINE

- MEDLINE In-Process & Other Non-Indexed Citations
- CENTRAL
- Cumulative Index to Nursing and Allied Health Literature (CINAHL)
- Web of Science.

Conference abstracts were also searched:

- Conference Proceedings Citation Index – Science (CPCI-S)
- Conference Proceedings Citation Index – Social Sciences & Humanities (CPCI-SSH).

The following websites were searched to identify recently completed trials:

- National Research Register: www.nihr.ac.uk/Pages/NRRArchiveSearch
- Current Controlled Trials: www.controlled-trials.com/mrct/.

A search strategy was provided only for MEDLINE by the manufacturer, which we considered to be an acceptable bare minimum; it would have been preferable to have records of all of the database searches. The search employed terms identifying the metastatic colorectal cancer population and terms identifying cetuximab, panitumumab and bevacizumab as interventions, although Chemical Abstracts Service (CAS) registry numbers were not included. Free-text terms and medical subject heading (MESH) terms were used in the searches. No outcomes were specified to limit the search; however, a study design filter was in place to limit hits to clinical trials.

The combinations of terms within the search strategies to define the metastatic colorectal cancer population and/or the intervention were appropriate and were replicable. The search was considered satisfactory but not particularly sensitive. We found no additional trials.

Roche

The following databases were searched in January 2011:

- The Cochrane Library
- MEDLINE
- MEDLINE In-Process & Other Non-Indexed Citations
- EMBASE
- EMBASE In-Process
- BIOSIS.

Searches were restricted to English-language publications. Roche reports that the search strategy was modified to account for differences in syntax and thesaurus headings between databases. Searches included terms for free text and the relevant MESH/EMTREE index terms.

Hand searches were also undertaken on the following resources:

- ASCO: www.asco.org
- ESMO: www.esmo.org
- ESMO/ECCO joint meeting 2009 (European Cancer Organisation conference)
- reference lists of previous trials and systematic reviews.

A full search strategy, with terms listed by numerical lines, was not included in the search report. Consequently, it is difficult to comment on the precision of retrieval.

Non-randomised controlled trials

Merck Serono

Manufacturer searches were performed in the following databases on 2 July 2010:

- Ovid EMBASE
- Ovid MEDLINE
- MEDLINE In-Process & Other Non-Indexed Citations.

Separate search strategies were provided by the manufacturer for EMBASE, MEDLINE and MEDLINE In-Process & Other Non-Indexed Citations. EMBASE, MEDLINE and MEDLINE In-Process & Other Non-Indexed Citations database searches were based on a conjunction of terms identifying the metastatic colorectal cancer population and terms identifying cetuximab as an intervention, although the CAS registry numbers were not included. For each term a combination of thesaurus headings (where possible) and free-text search words was used. No study filter was used and no outcomes were specified to limit the searches in any of these databases. The searches were limited to English-language publications and human-only populations.

Amgen

Non-RCTs were not searched for.

Roche

Non-RCTs were included.

Inclusion/exclusion criteria used in study selection

Merck Serono

The submission included RCTs in which the population had advanced or metastatic colorectal cancer after first-line treatment, without specification of outcomes. We consider that these inclusion and exclusion criteria are appropriate.

Amgen

The submission included RCTs in which the population had metastatic colorectal cancer after first-line treatment and which compared panitumumab monotherapy with placebo, best supportive care, cetuximab monotherapy, bevacizumab monotherapy or irinotecan/oxaliplatin-based chemotherapy. Outcomes were specified. Studies not available in English were excluded. We consider these inclusion and exclusion criteria to be appropriate.

Roche

The submission included RCTs in which the population had metastatic colorectal cancer requiring treatment after failure of first-line therapy. All therapies other than bevacizumab with non-oxaliplatin therapy were excluded. We consider these inclusion and exclusion criteria to be appropriate.

Details of relevant studies not included in the manufacturers' submissions

Despite the variability in search strategies between manufacturers we were unable to identify any additional studies.