

ICECREAM: Cetuximab antibody treatment for colorectal cancer with a G13D gene mutation

The ICECREAM trial has helped researchers answer an important health question. It has provided evidence that cetuximab alone is not an effective treatment for tumours with the G13D mutation.

We appreciate the part played by our volunteer participants. This trial can save future patients with such tumours from a treatment that is not likely to work. Here is a summary of the trial and results.

What was the trial about?

Cetuximab (Erbitux) is an antibody from a biological source used to treat bowel cancers. It appears not to work for tumours with some gene mutations. But several small studies had suggested that it was possible that cetuximab was effective in tumours with one particular mutation (the rare *KRAS* G13D mutation).

The ICECREAM trial is a phase 2 trial, that is, small trial exploring whether a new combination of drugs will be effective, while also being safe. Its first question was whether cetuximab could work in patients with this rare mutation. The investigators also tried to evaluate whether adding standard chemotherapy as well would further improve outcomes.

Eligible patients

53 people with the G13D mutation had cancer of the bowel that had spread. They had already had the available chemotherapy treatments, including irinotecan. About three-quarters were men.

Treatment

All patients had weekly infusions of cetuximab. Half the patients were randomly allocated to also receive the standard chemotherapy, irinotecan. Treatment continued until the disease worsened or patients or their treating doctors decided to stop.

The two treatment groups were similar in terms of age, time on treatment and the number of treatment cycles they had during the trial.

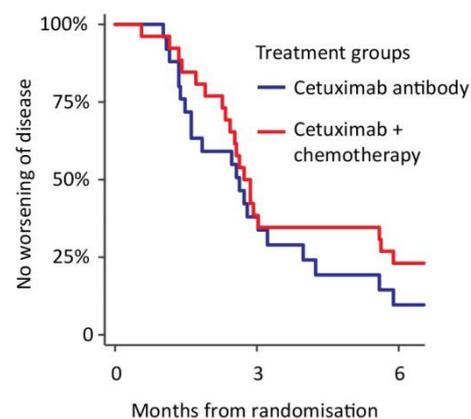
How was the effect of treatment measured?

The effect was assessed at 6 months by the proportion of patients who had their disease controlled by the treatment. This was measured by CT scans every 6 weeks.

The investigators also looked at survival, changes in quality of life, and side-effects of treatment.

Was the treatment effective?

Not really. The investigators concluded that cetuximab alone is not an effective treatment for patients whose tumours have a G13D mutation, and therefore cannot be recommended. After 6 months, only 10% in the cetuximab-alone group and 23% in the cetuximab-chemotherapy group did not have worsening of their disease.



The graph shows that, at 6 months, the disease had not worsened in 10% of patients in the cetuximab group and 23% in the cetuximab-irinotecan group.

The slightly better result in the group receiving chemotherapy was thought to be due to:

- irinotecan enhancing cetuximab

or

- irinotecan adding some direct additional benefit of its own

What were the side-effects of the treatment?

People in the group having chemotherapy had more side-effects than the group having cetuximab alone. The most common problems during chemotherapy treatment were skin rashes, fatigue and diarrhoea. In a few cases, these were severe.

Were there any serious side-effects?

Five patients in the cetuximab-alone group and 10 patients in the cetuximab-chemotherapy group had a serious adverse event, requiring hospital, but not all of these events were clearly due to the treatment.

What does this mean for trial patients?

Contrary to some earlier reports, cetuximab is not a useful treatment for tumours with G13D mutations. Although the combination treatment did show a minor benefit, given the side-effects observed and uncertainty about the need for cetuximab, these results do not justify the routine use of this drug combination for patients with this type of mutation.

What will the researchers do next?

Another group of patients, who have tumours without mutations, have also been enrolled in the ICECREAM trial. It is already known that cetuximab is an effective treatment for these patients, but it is not clear whether these patients get better results when chemotherapy is included. This part of the trial will help to answer whether there is a difference in effectiveness between cetuximab when given alone or when combined with chemotherapy for these patients.

The tumour tissue provided by both groups of ICECREAM patients will be used, with their permission, to look for other potential individual factors that help predict the effects of treatment.

The investigators also intend to analyse the results of the quality-of-life questionnaires.

Where can I find out more about the trial?

Talk with your GP or oncologist.

The results have been published in a scientific journal

Segelov E, and others. Response to cetuximab with or without irinotecan in patients with refractory metastatic colorectal cancer harboring the KRAS G13D mutation. *Journal of Clinical Oncology*. Published online 25 Apr 2016. [link to summary](#)

Trial registration

Australian New Zealand Clinical Trials Registry
www.anzctr.org.au
registration number ACTRN12612000901808

Australasian Gastro-Intestinal Trials Group (AGITG)

agitg.org.au/clinical-trials/trials-open-to-recruitment/icecream

The sponsor was the Australasian Gastro-Intestinal Trials Group, and the trial was coordinated by the Clinical Trials Centre at the University of Sydney. Funding was from Merck Serono Australia Pty Ltd.

Some of the investigators have received research or travel funding or have had advisory roles for Merck Serono or other pharmaceutical companies.

Results of any clinical trial do not represent complete knowledge about treatment. Patients should discuss this information with their treating doctor.