European Organisation for Research and Treatment of Cancer trial 62024: Imatinib after surgery for gastrointestinal stromal tumours (GIST)

The 'Adjuvant GIST' trial, also known as EORTC 62024, has helped researchers answer an important health question. It has provided evidence that could change the way some stomach and intestine cancers are treated in the future.

We appreciate the part played by our volunteer participants. Without them, this trial would not have been possible. Here is a summary of the trial and results.

What was the trial about?

Imatinib (Glivec or Gleevec) is a biological therapy that blocks tyrosine kinases (chemical messenger proteins between cells) and therefore hinders the growth of cancer cells.

Imatinib changed the lives of many people with advanced gastrointestinal stromal tumours (or GISTs) when it was discovered (about 15 years ago) that imatinib could shrink their cancers, giving patients more time to live.

The 62024 trial took the next step of trialling imatinib for people who had newly diagnosed GISTs. They were patients who had had surgery to remove their tumours but still had a moderate or high risk of a relapse.

The trial enrolled 908 patients from 12 countries. Their average age was 59, and just over half were men.

The patients were randomly allocated to standard treatment—observation and tests by their oncologists—or to imatinib tablets for 2 years.

Patients were then followed up for an average of nearly 5 years.

How was the effect of treatment measured?

The main problem with imatinib in earlier trials was that after a few years, the tumour could mutate and become resistant to the treatment.

Therefore, in the 62024 trial, the main outcome measured was how long the patient could continue before having to change to another treatment. This was assessed at 3 years. The two randomised groups were compared.

The investigators also measured, first, the time until the disease came back (relapse) and, second, the survival time.

Was the new treatment better?

Both groups of patients were similar in the time it took to need a change to a new treatment; that is, there was no significant difference for patients on imatinib and those having no drug.

When the data were assessed at 3 years, 16% of participants in the imatinib group and 34% in the observation-only group had relapsed. This was a significant difference. However, at 5 years, 31% in the imatinib group and 37% in the observation group had relapsed. The imatinib group's relapse rate had caught up. This suggests that imatinib delayed the patient's relapse but did not prevent it eventually.

Even though 282 patients (nearly a third) had a relapse, 93% of the patients on imatinib treatment and 92% of those who were not allocated to the drug were still alive after 5 years.

What were the side-effects of the treatment?

56 (12%) of the participants taking imatinib stopped treatment because of side-effects. Common reasons for stopping were skin rashes or peeling (2%), nausea or vomiting (2%) and diarrhoea (2%).

Were there any serious side-effects?

Some participants had a severe abnormality in blood cells (neutrophils) (3%), a serious disturbance of their liver function (3%), a major change in weight (3%) or a severe infection (3%).

What does this mean for trial patients?

The trial found that patients having imatinib treatment for at least 2 years after their operation were less likely to have a relapse over the first 3 years.

Using imatinib for up to 3 years was safe and effective and did not result in resistance. That is, imatinib did not cause the tumour to change and grow.

However, patients were more likely to relapse if they stopped the treatment, suggesting that imatinib slows the cancer growth, but does not eliminate it.

How will the results help patients and doctors in future?

For people with a diagnosis of a high-risk or moderate-risk GIST, the main treatment is an operation to remove the cancer. The results from the 62024 trial add to available evidence on the benefit of imatinib for GIST.

The information from this trial will help researchers plan the design of trials to improve treatments in the future.

What will the researchers do next?

The main trial is now finished, but trial participants will continue to be followed up to see whether there is a long-term survival difference with imatinib treatment.

Where can I find out more about the trial?

Talk with your GP or oncologist.

The results have been published in a scientific journal

Casali PG, and others. Time to definitive failure to the first tyrosine kinase inhibitor in localized GI stromal tumors treated with imatinib as an adjuvant. *Journal of Clinical Oncology* 2015, volume 33, issue 36, pages 4276–4283. link

Trial registration

The trial was registered in the United States:

clinicaltrials.gov/show/NCT00103168

Australasian Gastro-Intestinal Trials Group

Link to summary of the trial in Australia

The study was funded by the EORTC (European Organisation for Research and Treatment of Cancer) Charitable Trust and Novartis. In Australia, the sponsor was the Australasian Gastro-Intestinal Trials Group. Funding was received from the Cancer Councils of South Australia, Victoria and New South Wales and the Queensland Cancer Fund

Some of the authors have received payments for research or have had advisory roles for pharmaceutical companies. Full disclosures of these are listed with the results in the *Journal of Clinical Oncology* 2015, volume 33, issue 36, pages 4276–4283.

Results of any clinical trial do not represent complete knowledge about treatment. Patients should not change their therapy on their understanding of the results.