



## Lay Summary of Clinical Study Results

TACE-2: A randomized placebo-controlled, double-blinded, phase III trial of sorafenib in combination with transarterial chemoembolization in patients with unresectable advanced hepatocellular carcinoma

Version 1.0 01-Mar-2022

Sponsor:	University College London (UCL)
Sponsor reference number:	07130
CRCTU reference number:	HE3005
EudraCT number:	2008-005073-36
IRAS number:	7162



CANCER  
RESEARCH  
UK

BIRMINGHAM  
CANCER RESEARCH UK  
CLINICAL TRIALS UNIT



UNIVERSITY OF  
BIRMINGHAM

## INTRODUCTION

Deciding which treatments work best for patients almost always takes results from several studies. This summary shows only the main results from the TACE-2 study, which was sponsored by University College London and supported by the NIHR, Bayer Schering Pharma AG, and Biocompatibles UK Ltd. Other studies may provide new information or different results.

We want to thank all the participants of this study and their caregivers who helped the researchers learn more about combining sorafenib with chemoembolisation to treat cancers that started in the liver. We hope this summary will help them understand and feel proud of their important role in medical research.

This summary is for informational purposes only. If you need medical advice, please contact your doctor. If you participated in this study and have questions about the results, please speak with a doctor or other staff member at the study site.

## WHY WAS THIS RESEARCH NEEDED?

Before a treatment is available to all patients, researchers do clinical studies to get information about how well the treatment works and about how safe it is.

There are different treatments for liver cancer. One is blocking the supply of oxygen and food that the cancer needs to grow (embolisation). Doctors can do this by injecting small beads into the blood vessels near the cancer. The beads can also deliver chemotherapy directly to the tumour. This is called chemoembolisation. Transarterial chemoembolisation (TACE) is a type of chemoembolisation used for liver cancer.

The researchers in this study wanted to see if combining sorafenib with TACE using beads loaded with the chemotherapy drug doxorubicin could be better than TACE alone for treating liver cancers that couldn't be removed by surgery.

Sorafenib is a targeted cancer drug called a tyrosine kinase inhibitor. A tyrosine kinase is a chemical messenger (an enzyme) that signals cancer cells to grow. Sorafenib blocks these signals. Sorafenib can also work by blocking the growth of new blood vessels that supply the cancer with food and oxygen.

## WHAT WERE THE MAIN QUESTIONS STUDIED?

The main questions the researchers wanted to answer in this study were:

- If combining sorafenib with TACE can be better than TACE alone for treating a liver cancer that couldn't be removed by surgery.

- What are the side effects of combining sorafenib with TACE
- How combining sorafenib with TACE affects patients quality of life

## WHO PARTICIPATED IN THE STUDY?

Patients at least 18 years with advanced liver cancer that couldn't be removed by surgery.

All the participants in the study:

- Had a diagnosis of liver cancer confirmed with a biopsy or imaging tests
- Could not receive a liver transplant
- Were well enough to complete their daily activities (performance status 0 or 1)
- Were expected to live 3 months or more
- Had satisfactory blood test results
- Had satisfactory heart function
- Were able to swallow tablets
- Were willing to use reliable contraception during treatment and for 3 months afterwards if there was any chance they or their partners could become pregnant

Patients could not participate in this trial if:

- Their cancer had spread to other organs
- They previously had another cancer apart from successfully treated non melanoma skin cancer or in situ carcinoma of the cervix
- They had already had an embolization or radiation therapy to treat their liver cancer
- They had other condition or disease that advised against receiving the trial treatment
- They had major surgery or bleeding in the past 4 weeks
- They had had an experimental drug in the past 4 weeks
- They had an active infection or were HIV positive
- They had any other medical condition that could affect their participation
- They were pregnant or breastfeeding

## WHAT TREATMENTS DID THE PARTICIPANTS TAKE?

In this trial some people had sorafenib and some people had an identical dummy drug (placebo) as swallowed tablets. All recruited participants were expected to have at least one TACE procedure using beads loaded with doxorubicin.

TACE-2 was a randomised trial. The people taking part were put into one of two treatment groups randomly chosen by a computer. This helped make sure the treatments were chosen fairly and that comparing the results of the treatments was as accurate as possible. Neither the patients nor their doctors decided or knew what treatment each participant was taking. Studies are done this way

because knowing what treatment the participants are taking can affect the results of the study. This is called a double-blind trial.

The groups were:

- People receiving sorafenib tablets combined with TACE
- People receiving placebo tablets combined with TACE

If the cancer came back, doctors asked the patient to stop taking the sorafenib or dummy drug, and their doctors offered them other treatment options.

If the patients had very bad side effects, their doctor could choose to reduce the number of tablets they took or stop the treatment completely after discussing with them.

## WHAT HAPPENED DURING THE STUDY?

Before deciding to take part in the study, all the participants were provided with detailed information. They could also discuss it with their families and clinical team. This is called “informed consent.” Then the doctors and nurses asked the participants about their medical history and checked their health to make sure they could join the study.

Patients had to have some tests done before taking part in the trial. These tests included:

- A physical examination
- Blood tests
- CT or MRI scans of the chest and abdomen
- Heart tests

During treatment, patients saw their doctor at least every 6 weeks for a physical exam and blood tests, plus heart tests if required. Participants also had a scan every three months to check the size of the tumour.

The doctors had to record how the cancer was responding to the treatment and the side effects reported by the patients.

Participants were also asked to fill out questionnaires before starting treatment, and at each clinic visit during treatment. The questionnaires asked about side effects and how patients were feeling. This is called a quality of life (QoL) study. Patients could still take part in the trial if they did not agree to complete these questionnaires.

The researchers also asked patients to give 6 extra blood samples during the trial and, if available, a sample of their cancer and normal liver tissue removed during a biopsy. Patients could still take part in the trial if they did not agree to these extra samples.

## WHAT WERE THE RESULTS OF THE STUDY?

This is a summary of the main results from this study. These are the results from all the participants combined. The individual results of each participant might be different and are not in this summary.

The study started in November 2010, recruitment stopped in November 2015, and the study was formally closed in March 2021.

The trial aimed to recruit 206 patients in each arm (412 patients in total). However, the study closed early after an analysis of the results obtained up to that point did not show a significant benefit for the study drug, sorafenib.

The study included 313 participants recruited in hospitals throughout the UK:

- 156 people had dummy drug (placebo) with TACE
- 157 people had sorafenib with TACE

After an average follow up of 620 days, the trial team looked at the average time it took before the cancer got worse. They found that it was not significantly different between the two groups.

The team also looked at the average length of time people in each group lived. Again, they found that there were no differences between placebo and sorafenib.

The trial team also analysed the adverse effects on each group. The most common problems reported by patients taking sorafenib were feeling tired, abdominal pain, diarrhoea, feeling or being sick, and changes in the skin on the palms and soles of the feet.

Out of 313 recruited, 108 patients stopped treatment early (68 taking sorafenib, 40 taking placebo). Sixty-six patients reported that toxicities or adverse events were the main reason to stop taking the trial treatment (30 taking sorafenib, 47 taking placebo).

A medical problem reported during a clinical trial that puts the participant's life at risk, requires hospitalization, causes disability, causes a baby being born with medical problems, or may have turned into one of these problems if not treated, is called a serious adverse event. These may be related to the patient's disease, trial treatment or other causes.

Serious adverse events were reported for 65 patients taking sorafenib and 50 patients taking placebo. In total, there were 95 events in the sorafenib group and 86 in the placebo group. As illustrated by these numbers, some participants had more than 1 serious event. However, only 44 of these were considered to be likely related to the study treatments.

Patient reported outcomes from the QoL questionnaires showed worse social and role functioning scales and worse diarrhoea and loss of appetite symptoms in patients treated with sorafenib. No differences were seen in other questionnaire scales.

## HOW HAS THIS STUDY HELPED PATIENTS AND RESEARCHERS?

The results of this study have helped researchers learn more about using sorafenib in combination with TACE for patients with advanced liver cancer. The results might be used when designing other studies using sorafenib or planning to find new treatments for people who have a similar condition.

## WHERE CAN I LEARN MORE ABOUT THIS STUDY?

You can find more information about this study at the websites listed below:

- <https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-combining-two-treatments-for-cancer-liver-TACE-2>
- <https://www.isrctn.com/ISRCTN93375053>

If you have questions about this study, you can also contact the trial team by e-mail at [TACE2@trials.bham.ac.uk](mailto:TACE2@trials.bham.ac.uk).

## STUDY INFORMATION

Acronym:	TACE-2
Title:	A randomized placebo-controlled, double-blinded, phase III trial of sorafenib in combination with transarterial chemoembolization in patients with unresectable advanced hepatocellular carcinoma
Sponsor:	University College London
Sponsor Reference Number:	07130
EudraCT Number:	2008-005073-36
REC Reference Number:	09/H1102/114
Start Date:	November 2010
End of Trial:	March 2021