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A prospective, randomised, double-blind, multicentre, phase III clinical study on transarterial chemoembolisation (TACE) combined with sorafenib versus TACE plus placebo in patients with hepatocellular cancer (HCC) before liver transplantation (LTx) - Heidelberg Liver Cancer Study (HeiLivCa Study)

Submission date 24/04/2008	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 30/05/2008	**Overall study status** Completed	
Last Edited 19/06/2015	**Condition category** Cancer	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)

2008-002269-29

Protocol serial number
N/A

Study information

Scientific Title
A prospective, randomised, double-blind, multicentre, phase III clinical study on transarterial chemoembolisation (TACE) combined with sorafenib versus TACE plus placebo in patients with hepatocellular cancer (HCC) before liver transplantation (LTx) -Heidelberg Liver Cancer Study (HeiLivCa Study)

Acronym
HeiLivCa

Study objectives
To determine whether the combination of transarterial chemoembolisation (TACE) and sorafenib (Arm A) in comparison to TACE plus placebo (Arm B) better controls tumour growth within the liver in patients with hepatocellular cancer (HCC) in terms of time to progression (TTP) before curative liver transplantation.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics Committee at the University of Heidelberggave, 24/10/2008, ref: NCT-2007-11-01-1011

Study design
Prospective randomised double-blind multicentre phase III trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Hepatocellular cancer

Interventions
Arm A: TACE + Sorafenib. Sorafenib will be administered 400 mg twice daily (oral).
Arm B: TACE + placebo

Carboplatin is used for TACE in both arms. Duration of treatment is until LTx or disease progression.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Sorafenib

Primary outcome(s)
Time to progression

Key secondary outcome(s))
1. Rates of patients reaching LTx
2. Disease control rates (DCR) defined as complete response (CR) + partial response (PR) + static disease (SD), overall response rate, complete response rates and partial response rates. These will be measured at imaging after each TACE and during regular imaging during the trial as well as at follow up imaging studies.
3. Frequencies of TACE treatments
4. To compare 1- and 2-year overall survival (OS) after liver transplantation, between treatment arms defined as the time from the date of randomisation to the date of death due to any cause. Additionally, the 1- and 2-year survival rates with a correction for transplantation-related mortality will be compared between both arms.
5. Progression-free survival (PFS)
6. Patient reported outcomes (PROs), defined as health-related quality of life using the self administered European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire for Cancer patients (EORTC QLQ-C30) and the EORTC QLQ-HCC18. These will be carried out at baseline, every visit after TACE and during regular study visits after the TACE period as well as at follow-up
7. Type, severity (graded by the National Cancer Institute, Common Toxicity Criteria for Adverse Events [CTCAE] Version 3.0), seriousness and relatedness of adverse events. These will be assessed at baseline, every visit after TACE and during regular study visits after the TACE period as well as at follow-up
8. Association of tumour marker

Completion date
01/06/2013

Eligibility

Key inclusion criteria
1. Both male and female patients
2. Patients with HCC without extrahepatic disease
3. Patients with HCC without prior systemic therapy, basically eligible for liver transplantation (LTx) at screening
4. HCC diagnosed by histology or per non-invasive European Association for the Study of the Liver (EASL) criteria (only cirrhotic patients):
4.1. Radiological criteria: two coincident imaging techniques: focal lesion greater than 2 cm with arterial hypervascularisation
4.2. Combined criteria: one imaging technique associated with alpha-fetoprotein (AFP): focal lesion greater than 2 cm with arterial hypervascularisation and AFP levels greater than 400 ng/ml
5. Pretreatment computed tomography (CT) or magnetic resonance imaging (MRI) and bone scan without evidence of radiographically definable vascular invasion or extrahepatic disease not older than 28 days

6. Sufficient haematologic, liver and renal function: Hb greater than 9.0 g/%, white blood cell (WBC) count greater than 3,000 cells/mm^3 (absolute neutrophil count [ANC] greater than 1.500 cells/mm^3), platelets greater than 75,000 cells/mm^3, bilirubin less than 3 mg/dl. Patients should have bilateral renal function, as determined by abdominal CT with serum creatinine less than 1.5 mg/dl and creatinine clearance (CrCL) greater than 30 ml/min in 24 h urine or Modification of Diet in Renal Disease Rate (MDRD).
7. Prothrombin time International Normalised Ratio (PT-INR)/activated partial thromboplastin time (PTT) less than 1.5 x upper limit of normal (patients who are being therapeutically anticoagulated with an agent such as coumadin or heparin will be allowed to participate provided that no prior evidence of underlying abnormality in these parameters exists)
8. Performance status: Karnofsky index greater than 70%
9. No acute infections at the time of therapy initiation
10. Staging studies completed within 3 weeks of protocol registration
11. Patients must sign a study specific informed consent form

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Residual radiological definable extrahepatic disease, portal vein involvement or lymph node involvement in CT, MRI or bone scan. Patients who are not potentially eligible for LTx are excluded
2. Patients with prior or concomitant systemic anticancer therapy or local tumour therapy (i.e. laser-induced interstitial thermotherapy [LITT]; percutaneous ethanol injection [PEI], cryotherapy, radiofrequency ablation [RFA]), or with prior TACE or with concomitant biologic-response modifiers, strong CYP3A4 inhibitors
3. Patients with significant cardiovascular disease such as myocardial infarction <6 months previously, chronic heart failure (revised New York Hearth Association [NYHA] grade III-IV) or unstable coronary artery disease
4. Patients with severe pulmonary disease that would be hazardous for LTx
5. Uncontrolled hypertension defined as systolic blood pressure greater than 150 mmHg or diastolic pressure greater than 90 mmHg, despite optimal management
6. Thrombotic or embolic events including transient ischaemic attacks within the past 6 months
7. Haemorrhage/bleeding event greater than or equal to Grade 3 within 4 weeks of first dose of study drug
8. Patients with contraindication to arterial procedure during TACE (portal or liver vein infiltration, allergy against contrast dye, uncontrolled hyperthyroidism)
9. Patients with previous malignancy other than carcinoma in situ of the skin and the cervix within 5 years prior treatment
10. Patients less than 18 years
11. Pregnant or breast-feeding patients. Women of childbearing potential must have a negative pregnancy test performed within seven days prior to the start of study drug. Both men and

women enrolled in this trial must use adequate barrier birth control measures during the course of the trial (and men for at least 3 months after last administration of study medication). Women of childbearing potential must agree to practice adequate contraception and to refrain from breastfeeding, as specified in the informed consent
12. Patients with uncontrolled infections or HIV sero-positive patients
13. Mental conditions rendering the patient incapable to understand the nature, scope, and consequences of the study
14. History of hypersensitivity to the investigational medicinal product or to any drug with similar chemical structure or to any excipient present in the pharmaceutical form of the investigational medicinal product
15. No patient will be allowed to enrol in this study more than once

Date of first enrolment
01/11/2008

Date of final enrolment
10/07/2012

Locations

Countries of recruitment
Germany

Study participating centre
Im Neuenheimer Feld 110
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Sponsor information

Organisation
University of Heidelberg (Germany)

ROR
https://ror.org/038t36y30

Funder(s)

Funder type
Industry

Funder Name
Bayer Vital GmbH (Germany)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	11/05/2015		Yes	No
Protocol article	protocol	26/11/2008		Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes