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Effectiveness of incorporating cetuximab into both docetaxel/cisplatin/fluorouracil induction chemotherapy and chemoradiotherapy in inoperable squamous cell carcinoma of the oral cavity

Submission date
05/10/2015

Recruitment status
No longer recruiting

Registration date
26/10/2015

Overall study status
Completed

Last Edited
12/05/2021

Condition category
Cancer

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol

Background and study aims
Mouth cancer is the most common type of cancer that affects the head and neck area. About 90% of all mouth cancers start in the thin, flat cells which line the lips and the inside of the mouth (squamous cells) and are known as oral squamous cell carcinoma (OSCC). If OSCC is found early, then in most cases a complete cure is possible using a combination of chemotherapy, radiotherapy and surgery. If it is left untreated however, then it can spread very quickly to other areas of the mouth, head and neck. If the tumour is small enough, then it can be completely removed in an operation. If the tumour is inoperable however, patients tend to have a worse outlook, and more aggressive chemotherapy is often needed. Cetuximab is a medication which is used to treat advanced cancer of the head and neck. It belongs to a group of drugs called monoclonal antibodies, which work by “locking onto” specific proteins (receptors) on the surface of the cancer cells, preventing them from multiplying. The first-line drug treatment (induction chemotherapy) for head and neck cancers is usually TPF treatment, which is the name of a combination of chemotherapy medications (docetaxel, cisplatin and fluorouracil). Although cetuximab is usually only used in the late stages of head and neck cancer, it could potentially be incorporated into the TPF treatment (C-TPF) in induction chemotherapy. If this proves successful, then later radiotherapy (treatment to destroy cancer cells with radiation) could be more successful. The aim of this study is to find out whether C-TPF is an effective induction treatment for inoperable oral squamous cell carcinoma.

Who can participate?
Adults with inoperable oral squamous cell carcinoma where the cancerous cells have spread.

What does the study involve?
All participants are given two complete cycles of C-TPF treatment. This involves weekly treatment with cetuximab, docetaxel, cisplatin and fluorouracil administered intravenously

(through a drip). After completing the treatment, participants have an MRI scan in order to find out whether the treatment has had any effect on the tumour size. Any participants who have responded to the C-TPF treatment are then given bio-chemoradiotherapy (bio-CRT), which involves radiotherapy and weekly treatment with cetuximab and cisplatin for a further 7 weeks. At the end of the bio-CRT treatment, participants attend monthly follow-up clinic visits. Participants are given another MRI scan two months after the bio-CRT treatment has ended, which is repeated every three months until the disease gets worse (disease progression) or the patient dies.

What are the possible benefits and risks of participating?
A benefit of participating is that patients can receive the new combinational treatment (C-TPF), which may prove to be a more effective treatment. The risks include the side effects from both cetuximab and TPF, which should be manageable.

Where is the study run from?
Taipei Veterans General Hospital (Taiwan)

When is the study starting and how long is it expected to run for?
April 2011 to May 2015

Who is funding the study?
1. Taiwan Clinical Oncology Research Foundation (Taiwan)
2. Taipei Veterans General Hospital (Taiwan)
3. Ministry of Health and Welfare (Taiwan)

Who is the main contact?
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Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
C-TPF (cetuximab, cisplatin, docetaxel, 5-FU) induction chemotherapy in inoperable squamous cell carcinoma of oral cavity: a phase II study

Study objectives
C-TPF will be an effective induction treatment for inoperable oral squamous cell carcinoma.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Institutional Review Board of Taipei Veterans General Hospital, 05/11/2015, ref: 2010-08-028 MB

Study design
Single-arm prospective open label phase II study

Primary study design
Interventional

Secondary study design
Non-comparative open labelled phase II study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Oral Squamous Cell Carcinoma

Interventions
All participants receive two cycles of C-TPF induction treatment. After completing the induction, MRI will be examined for the response of the treatment. Only complete or partial response participants will enter following bio-CRT. At the end of the bio-CRT, all participants will attend a follow-up visit every month at physicians' clinics. The first MRI image will be taken 2 months after completing the bio-CRT then every 3 months until disease progression or patient death.

Induction chemotherapy (C-TPF):
IC consisted of weekly cetuximab plus tri-weekly TPF twice for a total of seven weeks. Cetuximab was administered at a loading dose of 400 mg/m2 over a period of 120 minutes

during the first week, followed by weekly 60-minute infusions of 250 mg/m2 for six weeks. A total of 7 courses of cetuximab were given during the induction phase. The tri-weekly TPF regimen was docetaxel 60 mg/m2 as a 3-hour intravenous infusion, followed by intravenous cisplatin 75 mg/m2 for a period of 3 hours and a 96-hour continuous infusion of fluorouracil at 850 mg/m2 per 24 hours. A total of 2 courses of TPF were given during the induction phase.

Bio-chemoradiotherapy (bio-CRT)
The definitive curative radiation dose administered to the primary tumor was 70 Gy, which was administered as fractions of 2 Gy per day, 5 days per week. The dose administered to uninvolved lymph nodes was between 44-60 Gy. Involved lymph nodes received 60-66 Gy. Radiotherapy must have been given with either three-dimensional conformal radiotherapy (3D-CRT) or intensity-modulated RT (IMRT) techniques. Bio-chemotherapy was administered by a 60-minute infusion of 250 mg/m2 cetuximab weekly plus 60-minute infusions of 30 mg/m2 cisplatin weekly for a total of 7 weeks.

Intervention Type
Drug

Phase
Phase II

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

Primary outcome measure
Objective response rate (ORR) of induction chemotherapy is measured by MRI according to RECIST criteria in week 7, after two cycles of C-TPF treatment.

Secondary outcome measures
1. Progression free survival will be measured by MRI first 2 months after bio-CRT and then every 3 months, until disease progression or patient death
2. Overall survival will be followed up until patient death at physicians' clinic visits every month
3. Efficacy of bio-CRT will be measure by comparing the first MRI 2 months after bio-CRT to the MRI taken after induction chemotherapy
4. Acute side effects are recorded during the treatment of induction and bio-CRT. Late side effects are recorded by physicians during the follow-up clinic visits.

Overall study start date
05/07/2015

Completion date
05/07/2018

Eligibility

Key inclusion criteria
1. Aged between 18-70 years
2. Histologically proven locally advanced inoperable stage IV oral squamous cell carcinoma (OSCC)
3. At least one measurable lesion

4. An ECOG performance status < 2
5. Adequate hematological profile (WBC > 3 x 109/L, neutrophils > 1.5 x109/L, hemoglobin > 9 g /dl, platelets > 100 x 109/L)
6. Adequate liver and renal function panel (serum bilirubin < 1.5 x ULN, AST/ALT < 5 x ULN, creatinine < 1.25 x ULN and/or creatinine clearance > 50 ml/min)
7. Life expectancy of more than 12 weeks
8. Effective contraception for both male and female subjects if the risk of conception exists

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
70 Years

Sex
Both

Target number of participants
43

Total final enrolment
43

Key exclusion criteria
1. Distant metastasis or locally recurrent tumors
2. Prior chemotherapy, radiotherapy or surgery for HNC
3. Simultaneous double cancers except for cervical carcinoma in situ
4. Localized skin squamous cell cancer, or basal cell carcinoma of the skin
5. Use of an investigational agent within the past 28 days prior to enrollment
6. Known grade 3/4 allergic reactions to any components of the treatment
7. Pregnancy or breast-feeding
8. Clinically active disease unrelated to cancer itself
9. History of severe pulmonary or cardiac disease in the past 12 months
10. Uncontrolled chronic neuropathy
11. Participation in another clinical trial within the past 30 days
12. Legal incapacity or limited legal capacity

Date of first enrolment
30/09/2015

Date of final enrolment
05/06/2018

Locations

Countries of recruitment
Taiwan

Study participating centre
Taipei Veterans General Hospital
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Sponsor information

Organisation
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Sponsor type
Industry

ROR
https://ror.org/03ymy8z76

Funder(s)

Funder type
Research organisation

Funder Name
Taiwan Clinical Oncology Research Foundation

Funder Name
Taipei Veterans General Hospital

Funder Name
Ministry of Health and Welfare

Results and Publications

Publication and dissemination plan
The initial result has been e-published on ASCO2015 poster (No. e17016). The final results will be submitted to a peer reviewed journal for publication.

Intention to publish date
31/12/2018

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/07/2017	12/05/2021	Yes	No