ISRCTN17533723 https://doi.org/10.1186/ISRCTN17533723

Triple combination therapy for recurrent /metastatic head and neck squamous cell carcinoma

Submission date
17/11/2015

Recruitment status
No longer recruiting

Registration date
23/11/2015

Overall study status
Completed

Last Edited
02/09/2020

Condition category
Cancer

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

Plain English summary of protocol

Background and study aims
Head and neck squamous cell carcinomas (HNSCC) are cancers that usually begin in what are called squamous cells that line the moist, mucosal (mucus producing) surfaces inside the head and neck (for example, inside the mouth, nose and throat). HNSCC is the sixth most common cancer in the world and accounts for about 6% of all cancers. If, once treated, the cancer comes back or if it spreads (recurrent/metastatic – or R/M), the prognosis is poor, with patients surviving only about 8 months, on average. Cetuximub with platinum-based therapy plus 5-fluorouracil (5-FU) is considered the first line treatment of choice for R/M HNSCC, but its costs are of concern, particularly for developing countries. Hence, cisplatin combined with 5-FU is still the most common treatment for R/M HNSCC in Taiwan. Research has shown that a drug called tegafur/uracil (UFUR) when used in combination with cisplatin, produces similar results as 5-FU and is well-tolerated by patients. In addition, studies have found that the combination of irinotecan and cisplatin is a treatment that works well. This study is investigating the performance and the safety of a irinotecan/cisplatin/UFUR (IUC) triple combination treatment, by determining the maximum tolerated dose (MTD), how much of the treatment is needed to cause toxic effects (dose-limiting toxicities – or DLTs), how well patients tolerate the therapy and how successful it is at treating R/M HNSCC.

Who can participate?
Adults aged between 20-75 with R/M HNSCC.

What does the study involve?
This study is split into two stages, with different participants involved in each stage. For stage 1, the participants are given different doses of irinotecan, with the dose increasing until they develop DLTs. The MTD is then calculated as the dose below the dose that results in DLTs for one third of the participants in the study. For stage 2, participants are given the MTD of irinotecan combined with cisplatin and UFUR twice a day for 5 days every two weeks per their treatment cycle. Each participant taking part in stage 2 of the study has computed tomography

or magnetic resonance imaging scans of their tumors done before starting their treatment and then every 3 months until their disease progresses or they withdraw from the study for another reason. This is to see how they respond to the treatment.

What are the possible benefits and risks of participating?
It is hoped that the combination of irinotecan to the cisplatin and UFUR, will prolong progression free survival and overall survival. Risks include myelosuppression (decrease in bone marrow activity, leading to fewer red blood cells, white blood cells and platelets). Other possible side effects include nausea, vomiting, diarrhea, mucositis (pain and inflammation of the body tissues that produce mucus) and infection.

Where is the study run from?
Taipei Veteran's General Hospital (Taiwan)

When is the study starting and how long is it expected to run for?
February 2010 to July 2015

Who is funding the study?
TTY Biopharm Company

Who is the main contact?
1. Professor Muh-Hwa Yang (scientific)
2. Dr San-Chi Chen (scientific)

Contact information

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Scientific

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Additional identifiers

Protocol serial number
N/A

Study information

Scientific Title
Cisplatin/UFUR/Irinotecan triple combination therapy for recurrent/metastatic head and neck squamous cell carcinoma: a phase I/II clinical study

Study objectives
The response of treatment and prognosis is poor in recurrent/metastatic head and neck squamous cell carcinoma. Triple combination therapy may increase the tumor response and disease control.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Institutional Review Board of Taipei Veterans General Hospital, 22/01/2010, ref: 2010-01-004 MB.

Study design
Interventional non-randomised study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Recurrent/metastatic head and neck squamous cell carcinoma

Interventions
Phase I:
Irinotecan was supplied with the dose of 40, 50, 60, 70 mg/m2, then escalated with 5 mg/m2 increase in each step. Three participants were enrolled in each dose level until the dose-limiting toxicities (DLTs) developed. The maximum tolerated dose (MTD) was defined as the dose level below the dose that more than one third of the patients experienced DLTs. Irinotecan intravenously (IV) over 90 mins was given on day 1, combined with cisplatin 50mg/m2 IV over 60

mins on day 1, and oral UFUR 200mg twice a day after meal (400 mg/day) for 5 days every 2 weeks. Hence, the recommended dose of irinotecan, combined with cisplatin and UFUR were given in the subsequent phase II study.

Phase II:
In phase II, the maximum tolerated dose of irinotecan intravenously (IV) over 90 mins was given on day 1, cisplatin 50mg/m2 IV over 60 mins on day 1, and oral UFUR 200mg twice a day for 5 days every 2 weeks per treatment cycle.

Intervention Type
Drug

Phase
Phase I/II

Drug/device/biological/vaccine name(s)
1. Irinotecan 2. Cisplatin 3. UFUR (tegafur/uracil)

Primary outcome(s)
Phase I:
The determination of a recommended dose of irinotecan when combined with cisplatin and UFUR in patients with recurrent or metastatic HNSCC, by monitoring the dose-limiting toxicity at each dose level.

Phase II:
Overall objective response rate (ORR) of irinotecan in combination with cisplatin and UFUR. Measurable disease was required, which is defined as a lesion that can be measured in at least 1 dimension as 20 mm with conventional technique or 10 mm with spiral CT scan or MRI. Tumor assessments were made by computed tomography or magnetic resonance imaging scans at enrollment and after every 3 months until disease progression or withdraw. The revised RECIST guideline (version 1.1) was used to evaluate tumor response.

Key secondary outcome(s))
1. Progression-free survival (PFS)
2. Disease control rate (DCR)
3. Overall survival (OS)
4. Quality of life (QoL)
5. Safety profile

Completion date
09/07/2015

Eligibility

Key inclusion criteria
1. Aged between 20 and 75 years
2. Histologically or cytologically confirmed non-nasopharyneal head and neck squamous-cell carcinoma which is locoregional recurrence after curative local treatment and unsuitable for further local treatment, or primary distant metastasis at diagnosis, or metastatic disease after primary local treatment.
3. No prior primary chemotherapy for metastatic disease

4. Previous induction or concurrent chemotherapy with primary radiotherapy or adjuvant therapy after curative surgery is allowed, but the chemotherapy regimen has to have been completed at least 3 months before study entry.
5. At least one measurable disease was required, which is defined as lesion that can be measured in at least 1 dimension as 20 mm with conventional technique or 10 mm with spiral CT scan or MRI.
6. Patients should have life expectancy of at least 12 weeks

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
57

Key exclusion criteria
1. Less than 4 weeks since previous radiotherapy or 2 weeks since previous major surgery
2. Presence of CNS metastasis
3. Bone only metastasis
4. Co-existence with other malignancy with the exception of curative treated non-melanoma skin cancer or cervical carcinoma in situ within 5 years prior to the entry of study
5. Inadequate hematologic function (hemoglobin < 8 mg/dl, white blood cell < 3,000/mm3, absolute neutrophil count < 1,500/mm3, and platelets < 100,000/mm3)
6. Inadequate hepatic function (serum bilirubin > 1.5 times the upper limit (ULN) or alanine aminotransferase or aspartate aminotransferase > 2.5 times ULN if no liver metastasis or greater than 5 times the normal)
7. Inadequate renal function (serum creatinine > 1.5 mg/dl and creatinine clearance less than 60 ml/min); concurrent treatment with other investigational drug

Date of first enrolment
02/06/2010

Date of final enrolment
07/09/2015

Locations

Countries of recruitment
Taiwan

Study participating centre

Taipei Veteran's General Hospital
Taiwan
11217

Sponsor information

Organisation
Taipei Veterans General Hospital

ROR
https://ror.org/03ymy8z76

Funder(s)

Funder type
Industry

Funder Name
TTY Biopharm Company

Results and Publications

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	results	01/05/2016	02/09/2020	Yes	No