

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

<b>Submission date</b> 17/11/2015	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 23/11/2015	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 02/09/2020	<b>Condition category</b> Cancer	<input type="checkbox"/> 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. Cetuximab 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

### Type(s)

Scientific

### Contact name

Prof Muh-Hwa Yang

### ORCID ID

<http://orcid.org/0000-0002-9436-5400>

### Contact details

No. 201 Shipai Road, Sec. 2  
Taipei  
Taiwan  
11217

### Type(s)

Scientific

### Contact name

Dr San-Chi Chen

### Contact details

No. 201 Shipai Road, Sec. 2  
Taipei  
Taiwan  
11217

## **Additional identifiers**

**EudraCT/CTIS number**

**IRAS number**

**ClinicalTrials.gov number**

**Secondary identifying numbers**

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

### **Secondary study design**

Non randomised study

### **Study setting(s)**

Hospital

### **Study type(s)**

Treatment

## **Participant information sheet**

Not available in web format, please use contact details to request a participant information sheet

## **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/m<sup>2</sup>, then escalated with 5 mg/m<sup>2</sup> 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/m<sup>2</sup> 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/m<sup>2</sup> 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 measure**

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.

## **Secondary outcome measures**

1. Progression-free survival (PFS)
2. Disease control rate (DCR)

3. Overall survival (OS)
4. Quality of life (QoL)
5. Safety profile

**Overall study start date**

19/02/2010

**Completion date**

09/07/2015

## Eligibility

**Key inclusion criteria**

1. Aged between 20 and 75 years
2. Histologically or cytologically confirmed non-nasopharyngeal 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

**Age group**

Adult

**Sex**

Both

**Target number of participants**

A total of 14 patients were enrolled into phase I study and 43 patients into phase II study.

**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/mm<sup>3</sup>, absolute neutrophil count < 1,500/mm<sup>3</sup>, and platelets < 100,000/mm<sup>3</sup>)

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

**Sponsor details**

No. 201 Shipai Road, Sec. 2

Taipei

Taiwan

11217

**Sponsor type**

Industry

**ROR**

<https://ror.org/03ymy8z76>

## **Funder(s)**

**Funder type**

Industry

**Funder Name**

TTY Biopharm Company

## Results and Publications

**Publication and dissemination plan****Intention to publish date****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?
<a href="#">Results article</a>	results	01/05/2016	02/09/2020	Yes	No