De-ESCALaTE HPV: Determination of Epidermal growth factor receptor-inhibitor (cetuximab) versus Standard Chemotherapy (cisplatin) early And Late Toxicity Events in Human Papillomavirus-positive oropharyngeal squamous cell carcinoma.

Published: 27-03-2014
Last updated: 20-04-2024

Primary objective: To compare the severe (acute and late) toxicity (Grade 3-5), as assessed by CTCAE Version 4, caused by cetuximab and RT to that caused by cisplatin and RT in patients with HPV+OPSCC.Secondary objectives:- Compare overall number of...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Miscellaneous and site unspecified neoplasms benign
Study type	Interventional

Summary

ID

NL-OMON44755

Source
ToetsingOnline

Brief title
De-ESCALaTE HPV

Condition

- Miscellaneous and site unspecified neoplasms benign

Synonym
Cancer of the troat, squamous cell carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Cancer Research UK

Intervention

Keyword: HPV positive oropharyngeal squamous cell carcinoma.

Outcome measures

Primary outcome

The primary outcome measure will be the total number of acute and late severe or life-threatening (Grade 3-5) toxicity events occurring up to two years after treatment, and will be compared between both arms.

Secondary outcome

The secondary end points are as follows:

* The number of acute severe (Grade 3-5) toxicities in cetuximab arm compared to cisplatin arm.

* The number of late severe (Grade 3-5) toxicities in cetuximab arm compared to cisplatin arm.

* Similar or better global QoL of the Arm B (cetuximab) group

* Similar or better late (2 year) swallowing by overall MDADI score in cetuximab arm

* Compare EORTC swallowing quality of life domain at 2 years and PEG utilisation rates at 1 year and 2 years between treatment arms.

* Comparison of incremental cost per quality-adjusted life year gained within trial and extrapolated over lifetime.

* Report overall survival in two arms.

* Report loco-regional recurrence rates for both arms.

Study description

Background summary

Oropharyngeal squamous cell carcinoma (OPSCC) incidence is increasing rapidly in the developed world. This has been attributed to a rise in Human Papillomavirus (HPV) infection. HPV+OPSCC is considered a distinct disease entity, affecting younger patients and has a good prognosis following treatment. Subsequently, patients can live with the considerable side effects for several decades.

Radiotherapy and cetuximab (Epidermal Growth Factor Receptor-inhibitor) have demonstrated similar efficacy to *platin* chemoradiotherapy (current standard treatment containing platinum-based compounds) in head and neck cancer, but is potentially less toxic.

Results of this trial will be used to determine the optimum treatment of this debilitating cancer, with the primary aim of decreasing toxicity and improving quality of life for HPV+OPSCC patients.

Study objective

Primary objective:
To compare the severe (acute and late) toxicity (Grade 3-5), as assessed by CTCAE Version 4, caused by cetuximab and RT to that caused by cisplatin and RT in patients with HPV+OPSCC.

Secondary objectives:
- Compare overall number of events of acute severe toxicity between treatment arms.
- Compare overall number of events of late severe toxicity between treatment arms.
- Compare the quality of life outcomes assessed by EORTC QLQ C30 and HN35 between the two treatment arms.
- Compare the effect on swallowing of the two treatment arms (assessed by MDADI and by PEG or RIG utilisation rate at 1 and 2 years).
- Compare the cost-effectiveness of the two treatment arms (assessed by EuroQoL-5D).
- Compare overall survival, recurrence and metastasis between the two arms.

Study design

Randomised, international, multi-centre, open label, phase III clinical trial determining the optimum treatment for patients with HPV+OPSCC.

Intervention

Experimental arm:
Cetuximab: IV 400mg/m2 dose 1 week before start of radiotherapy followed by a weekly IV infusion of 250mg/m2 X 7 during radiotherapy

Control Arm:
Cisplatin: 3 doses of 100mg/m2 given at days 1, 22 and 43 from start of radiotherapy

Study burden and risks

The most common side effects of radiotherapy are: pain and soreness of mouth and throat, redness and sometimes ulcers in the skin of the area being treated, loss of sense of taste, tiredness, hoarseness if the voice box is being treated, noisy or difficult breathing, dryness of the mouth, difficulty swallowing, ulcers in the mouth and dental problems.

The most common side effects of cisplatin chemotherapy are: nausea and vomiting, hearing loss, tiredness, infection, some loss of hair, constipation, soreness of mouth, very small risk of death, long-term effects including dry mouth and swallowing problems.

The most common side effects of cetuximab chemotherapy are: skin rash, nausea and vomiting, tiredness, infection, difficulty swallowing,
soreness of mouth, very small risk of death, long-term effects including dry mouth and swallowing problems.

Contacts

Public
Vrije Universiteit Medisch Centrum

Research Support Services, University House, Kirby Corner Road n.a.
Coventry CV4 8UW
NL
Scientific
Vrije Universiteit Medisch Centrum

Research Support Services, University House, Kirby Corner Road n.a.
Coventry CV4 8UW
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. AJCC TNM Stage III-IVa [T3N0-T4N0, and T1N1-T4N3] oropharyngeal SCC tumours
2. Clinical multidisciplinary team decision to treat with primary curative chemoradiotherapy.
3. No previous treatment for the primary tumour, including surgery, neck dissection or tracheostomy [except node biopsies or diagnostic tonsillectomy].
4. Medically fit (ECOG 0, 1 or 2).
5. Adequate cardiovascular, haematological, renal and hepatic function.
6. Age 18 years or over.
7. Written informed consent given.
8. Using adequate contraception [male and female participants]. Must take contraceptive measures during, and for at least six months after treatment.

Exclusion criteria

1. Distant metastasis (i.e. stage IVc disease).
2. TNM Stage T1-2N0 disease.
3. Treated with primary radical surgery to the primary site e.g. resection.
4. Concurrent use of CYP3A4 inducers or inhibitors. [A standard course of dexamethasone or aprepitant for the prevention of cisplatin-induced nausea and vomiting is permitted]
5. Serious cardiac illness or other medical conditions precluding the use of cisplatin or cetuximab [no history of clinically significant cardiac disease, serious arrhythmias, or significant conduction abnormalities; no uncontrolled seizure disorder; no active neurologic disease; no neuropathy greater than grade 1; hypersensitivity to cisplatin or severe

hypersensitivity to cetuximab; receiving live vaccines; receiving phenytoin in prophylactic use; in dehydrated condition]
6. HPV+ patients who have p16+ tumours who also have N2b, N2c or N3 nodal disease and whose lifetime smoking history is also more than 10 pack years (i.e. have both risk factors).
7. Pregnant or lactating.
8. Previous treatment for any other cancer with cytotoxics, radiotherapy or anti-EGFR therapies.
9. Inadequate renal, haematological or liver functions.
10. Patients with clinically significant hearing impairment.
11. Life expectancy less than three months.
12. Other malignancy within the past three years except basal cell skin cancer or pre-invasive carcinoma of the cervix.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-01-2015
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Cisplatin
Generic name:	Cisplatin
Registration:	Yes - NL intended use

Product type:	Medicine
Brand name:	Erbitux
Generic name:	Cetuximab
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	27-03-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-11-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-07-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-07-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-03-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-04-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2011-005165-21-NL
ISRCTN	ISRCTN33522080
CCMO	NL40537.029.14