LUX-Head & Neck 2;A randomised, double-blind, placebo-controlled, phase III study to evaluate the efficacy and safety of afatinib (BIBW 2992) as adjuvant therapy after chemoradiotherapy in primary unresected patients with stage III, IVa, or IVb loco-regionally advanced head and neck squamous cell carcinoma

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Soft tissue neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON39253

Source
ToetsingOnline

Brief title
LUX-Head & Neck 2

Condition

- Soft tissue neoplasms malignant and unspecified

Synonym
head and neck cancer, squamous cell carcinoma of the head and neck

Research involving
Human

Sponsors and support

Primary sponsor: Boehringer Ingelheim
Source(s) of monetary or material Support: Boehringer Ingelheim bv

Intervention

Keyword: adjuvant, afatinib, squamous cell carcinoma

Outcome measures

Primary outcome

The primary endpoint of this trial is Disease Free Survival (DFS), defined as

the time from

randomisation until recurrence of tumour or death of any cause, whichever

occurs first.

Secondary outcome

The secondary endpoints

DFS rate at 2 years

Overall survival (OS), defined as the time from randomisation until death

(irrespective of reason)

Health related quality of life (HRQOL)

Study description

Background summary

Head and neck cancers constitutes a group of biologically similar cancers originating in the upper aerodigestive tract. Most head and neck cancers (>90%) are squamous cell carcinomas (SCC). Head and neck squamous cell carcinoma (HNSCC) is the 6th most common type of cancer with an incidence of approximately 650,000 new cases worldwide each year, and its incidence is rising rapidly in developing countries. Over expression of the epidermal growth factor receptor (EGFR) is seen in the overwhelming majority of HNSCC. The EGFR is a member of the human epidermal receptor (HER)/Erb-B family of receptor tyrosine kinases that are responsible for signal transduction (R10-5898). EGFR activation plays an important role in malignant cell proliferation, angiogenesis, metastasis, and inhibition of apoptosis. Both EGFR over expression and EGFR gene amplification are prognostic factors for shorter progression free survival (PFS) and overall survival (OS).

About 50% of patients with HNSCC are diagnosed with loco-regionally advanced (LA) disease (stages III-IVb) and have a 5-year survival rate varying from 10 to 75% depending on stage, site of primary tumour, HPV association, and other known risk factors. Patients, who present with LA disease, stage III-IVb, are treated with a combination of chemotherapy, surgery, or radiotherapy (RT).

After completion of CRT, the standard of care is no treatment. However, more than 50% of patients with LA HNSCC will relapse. There is thus a pressing need for the study of novel approaches and agents for this group of patients.

EGFR has been implicated in supporting oncogenesis and progression of human solid tumours and is a promising target for anti-cancer therapy. Afatinib is a second generation irreversible EGFR inhibitor. Possibly afatinib is a promising agent for the maintenance of remission in patients with HNSCC following CRT.

Study objective

The objective is to investigate the efficacy and safety of afatinib over placebo when given as adjuvant therapy for patients with no evidence of disease after CRT in primary unresected patients with LA SCC stage III or IVa/b of the oral cavity, oropharynx, or hypopharynx, or larynx stage IVa/b. The main objective of the trial is to test the superiority of afatinib as adjuvant therapy vs. placebo in terms of disease free survival (DFS) for this trial patient population.

Study design

After completion of CRT, the patients will have a Magnetic Resonance Imaging (MRI) or
Computed Tomography (CT) scan and patients must have no evidence of disease (NED) before randomisation.

Eligible patients will be randomised (2:1) to receive either afatinib or placebo based on
stratification factors: Prior use of EGFR-targeted antibody therapy and nodal status.

Patients will receive continuous daily treatment with oral afatinib or placebo for one and a halve year or
until tumour recurrence, unacceptable AEs, or other reason necessitating treatment withdrawal. The study medication will be dispensed every 4 weeks. The starting dose of afatinib will be 40 mg once daily. In the event of no or minimal drug-related AEs after four weeks of treatment or later, the dose should be increased to 50 mg. As detailed in Section 4.1.4, dose reduction will occur in the event of certain drug-related AEs.

Intervention

During the treatment period, patients will visit the investigational site in weeks one, two, and four, and then every four weeks for assessment of safety parameters and AEs as outlined in the Flow Chart. Tumour recurrence will be assessed regularly by MRI/CT scan until tumour recurrence or lost to follow-up. Health related quality of life (HRQOL) will be assessed until tumour recurrence. The end of treatment (EOT) information is obtained when the study medication is discontinued. After the EOT visit, patients will continue in the follow-up period. During the follow up period, data on vital status (survival), ECOG performance status drug-related, HRQOL, AEs, and concomitant anti-cancer therapy will be collected.

Study burden and risks

Patients come regularly for visits. In case a scan needs to be made the time necessary is longer. Average estimation is 1-3 hours per visit.

Afatinib is not yet registered. Therefore unexpected side effects can occur. Also, known side effects can occur. The scans will involve radiation. From blooddrawing side effects can occur.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

*Histologically or cytologically confirmed loco-regionally advanced squamous cell carcinoma, stage III, IVa, or IVb, of the oral cavity, oropharynx, or hypopharynx, or larynx stage IVa or IVb ;*Unresected tumour prior to chemo-radiotherapy due to:;o Technical unresectability (e.g. tumour fixation/invasion to either base of the skull, cervical vertebrae, nasopharynx, or fixed lymph nodes); and/or;
o Low surgical curability (T3-T4, N2-N3 excluding T1N2); and/or;
o Organ preservation;
*Concomitant platinum-based chemo-radiotherapy (for minimum requirements see the protocol) completed no longer than 24 weeks prior to randomisation. At randomisation, chemo-radiotherapy induced side effects CTCAE grade * 2;
*No evidence of disease (NED), defined as no measurable or palpable tumour on clinical and radiographic (e.g. CT scan or MRI) examinations as judged by the investigator in either of the following:
a) No residual tumour after CRT;
b) No residual tumour after CRT followed by R0 tumour resection;
c) No evidence of nodal disease after CRT followed by neck dissection;

In case of palpable mass, NED must be confirmed by biopsy;
*ECOG performance status 0 or 1 at the time of randomisation

Exclusion criteria

-Exclusion 1 is deleted with amendment 2 (protocol revision 03)
-Patients with smoking history of * 10 pack years and with primary tumour site base of tongue
-Patients with smoking history of * 10 pack years and with primary tumour site tonsil
-Primary cancer of nasopharynx, sinuses, or salivary glands
-Prior treatment with EGFR-targeted small molecules, EGFR-targeted antibodies, and/or any investigational agents for treatment of HNSCC

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	04-09-2012
Enrollment:	21
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	afatinib
Generic name:	-

Ethics review

Approved WMO Date:	05-07-2011
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-11-2011
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-01-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-02-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-02-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	04-04-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-07-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	

Date:	07-08-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-09-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-10-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-11-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-01-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	14-04-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-04-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-08-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

	(Rotterdam)
Approved WMO Date:	22-09-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-09-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-09-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2011-000392-14-NL
CCMO	NL36686.078.11