Docetaxel versus Docetaxel and Lapatinib in recurrent or metastatic squamous cell carcinoma of the head and neck (SCCHN)
An open label multicenter randomized phase II study.
A study of the Dutch Head and Neck Cancer Group (DHNCG)
(NWHHT 08-02)

Published: 19-01-2009
Last updated: 05-05-2024

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Ethical review	Approved WMO
Status	Pending
Health condition type	Metastases
Study type	Interventional

Summary

ID

NL-OMON32481

Source
ToetsingOnline

Brief title
TyvTax

Condition

- Metastases

Synonym
SCCHN

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: GlaxoSmithKline,Industrie,Sanofi-aventis

Intervention

Keyword: Docetaxel, Head and neck cancer, Lapatinib

Outcome measures

Primary outcome

The primary objective of this study is to select the candidate treatment with the highest level of activity for subsequent phase III testing. Activity is defined as clinical benefit (CR,PR or stable disease) in patients with recurrent SCCHN not amendable for local therapy or metastatic SCCHN. Clinical benefit will be assessed in week 8, i.e. after two courses of docetaxel.

Secondary outcome

To evaluate the two treatment groups with respect to the following: progression free survival (PFS), overall survival (OS), efficacy (defined as CR + PR) and quality of life.

Study description

Background summary

Squamous cell carcinoma of the head and neck (SCCHN) represents 5% of newly diagnosed cancers in adult patients. Worldwide more than 500.000 new cases are diagnosed annually. It is a potentially curable malignancy when diagnosed at an early stage. Unfortunately, 60% of the patients present with advanced irresectable locoregional disease. In this group of patients the prognosis is quite poor. Only 30% to 50% will be alive after 3 years following standard therapy. Sixty to 70% will develop locoregional recurrences within 2 years and 30% will develop distant metastases. Patients with recurrent and/or metastatic SCCHN have a dismal prognosis with a medium survival time around 5-9 months and a poor quality of life. In the Netherlands according to the national treatment guidelines treatment with methotrexate (with a RR 15%) is often advocated in patients with recurrent and/or metastatic SCCHN. Recently, Vermorken et al. have demonstrated that addition of cetuximab to platinum based chemotherapy resulted in a prolongation of the median overall survival from 7.4 months to 10.1 months (HR 0.8, p=0.04) in patients with recurrent and/or metastatic SCCHN. This study has demonstrated prolongation of the overall survival in this patient group for the first time in twenty five years. This observation emphasizes that modulation of EGFR in combination with chemotherapy could be a valuable treatment modality in patients with recurrent and/or metastatic SCCHN. However cisplatin containing regimens cannot be administered in an outpatient clinic approach and result in considerable toxicity, i.e. renal impairment, peripheral neuropathy and ototoxicity. Single agent docetaxel induces a response in 21-42% in patients with recurrent squamous cell cancer of the head and neck, but thus far no survival benefit has been demonstrated. Lapatinib is a small molecule inhibitor of the tyrosine kinase activity of both EGFR1 and EGFR2. A phase II study results presented at ESMO 2008 demonstrated clear clinical activity with monotherapy lapatinib in patients with squamous cell carcinoma of the head and neck. (ESMO 2008 abstract #688O Del Campo). In preclinical studies enhancement of docetaxel induced cytotoxity was observed in six human cell lines of SCCHN by gefitinib, another small-molecule tyrosine kinase inhibitor with activity against EGFR, and celecoxib, a cyclooxygenase-2 inhibitor. Thus, combination of doxetaxel and lapatinib in treatment of recurrent and/or metastatic SCCHN may result in better outcome, may reduce treatment related toxicity and can be administered in a non-clinical setting.

Study objective

The primary objective of this study is to select the candidate treatment with the highest level of activity for subsequent phase III testing. Activity is defined as clinical benefit (CR,PR or stable disease) in patients with recurrent SCCHN not amendable for local therapy or metastatic SCCHN. Clinical benefit will be assessed in week 8, i.e. after two courses of docetaxel.
Secondary objectives are:
• To evaluate the two treatment groups with respect to the following: progression free survival (PFS), overall survival (OS), efficacy (defined as CR + PR).
• To determine the qualitative and quantitative toxicities associated with

docetaxel and lapatinib or docetaxel in subjects
with local or locoregional recurrence not amendable for local therapy or metastatic disease.
• To evaluate volumetric tumor responses and to correlate those with tumor responses based on RECIST criteria.
• To evaluate and compare quality of live in the two treatment groups using Quality of life questionnaire (QLQ)-C30
(Version 3.0) and the head and neck cancer-specific QLQ-H&N35.

Study design

An open label multicenter randomized phase II study.

Intervention

Arm A:
Docetaxel at a dose of 75 mg/m² as 1 hour i.v. infusion on day 1 every 3 weeks until disease progression
Arm B:
Docetaxel at a dose of 75 mg/m² as 1 hour i.v. infusion on day 1 every 3 weeks and Lapatinib 1250 mg o.d. day 1 and every day thereafter continuously until disease progression

Prophylactic G-CSF therapy
All patients must receive prophylactic pegfilgrastim (Neulasta®) in order to prevent docetaxel related neutropenia and/or its complications (fever and infection). These injections have a fixed dose of 6 mg and can be given once per chemotherapy cycle on day 2, independent of body weight and should be given 1 day after the chemotherapy administration

Study burden and risks

In comparison to similar patients treated outside this study patients could suffer from the known toxicity of docetaxel, i.e. acute hypersensitivity reaction, nausea, hematologic toxicity (including neutropenic fever), impaired hepatic function, gastro-intestinal toxicity, peripheral neuropathy and nail changes and known toxicity of lapatinib, i.e. diarrhea, rash, fatigue and nausea. Rare toxicities of lapatinib are interstitial pneumonitis and a decrease in LVEF. In order to reduce these potential burdens all patients will be treated with pegfilgastrim and specific stopping rules, treatment advices and follow-up are included in the protocol. In order to evaluate treatment response and quality of live more frequent imaging (i.e. CT or MRI scans) will be performed and quality of life questionnaire will be performed.

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

•>=18 years of age
•Histologically or cytologically confirmed diagnosis of SCCHN
•Local or locoregional recurrence not amendable for local therapy or metastatic disease
•Tumor tissue available for immunohistochemical evaluation of EGFR 1 and 2 expression
•Measurable or evaluable disease (RECIST)
•WHO performance 0-2
•Effective contraception for both male and female subjects if risk of conception exists
•Neutrophils >=1.5 x 109 cells/L, platelet count >= 100 x 109 cells/L and hemoglobin >= 6 mmol/L
•Total bilirubin within normal institutional limits (ULN)
•Aspartate-aminotransferase (AST) and alanine-aminotransferase (ALT) <=2.5 × ULN
•Creatinin within normal institutional limits or Creatinine clearance > 60 mL/min

•Cardiac ejection fraction >= 50% as measured by echocardiogram or MUGA scan
•Signed written informed consent before any study related activities are carried out
•Expected adequacy of follow-up

Exclusion criteria

•Patients previously treated with EGFR inhibitor
•Patients previously treated with Docetaxel or Paclitaxel
•Nasopharyngeal carcinoma
•Active infection (infection requiring IV antibiotics), including active tuberculosis, and known and declared HIV.
•Pregnancy (absence confirmed by serum or urine β-HCG test) or lactation period
•Concurrent treatment with any other anti-cancer therapy.
•Class 3-4 cardiac morbidity, as defined by the new York Heart association Criteria (e.g. uncontrolled or symptomatic congestive heart failure, myocardial infarction within six months prior to the start of study, uncontrolled or symptomatic angina) and any cardiac condition, which in the opinion of the treating physician, would make this protocol unreasonably hazardous for the patient.
•Current active hepatic or biliary disease (with exception of Gilbert*s syndrome, asymptomatic gallstones, liver metastases or stable chronic liver disease per investigator assessment)
•Renal function as measured by creatinine clearance <30 ml/min
•Presence of severe and/or uncontrolled concurrent medical disease (e.g. uncontrolled diabetes mellitus, uncontrolled liver disease, including chronic viral hepatitis judged at risk of reactivation, uncontrolled active infection such as HIV infection, etc.)
•Concomitant (or within 4 weeks before randomisation) administration of any other experimental drug under investigation; Chemotherapy or other anti-cancer therapy for the recurrence or metastatic disease; chemotherapy for initial treatment, i.e. chemoradiotherapy, is allowed, unless it has been stopped 3 weeks before inclusion

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-12-2008
Enrollment:	74
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

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
CCMO	NL25440.031.08