Platinum-Cetuximab Combined With Docetaxel or With 5FU in Patients With Recurrent/Metastatic HNSCC (TPExtreme)

Purpose

This study evaluates the efficacy of the new docetaxel-cisplatin-cetuximab regimen (TPEx) versus the standard platinum-5FU-cetuximab EXTREME regimen as a first-line treatment in recurrent and/or metastatic HNSCC. Half of patients will be treated by TPEx regimen, while the other half will be treated by EXTREME regimen.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Intervention</th>
<th>Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head and Neck Squamous Cell Carcinoma</td>
<td>Drug: Cisplatin Drug: 5-Fluorouracil Drug: Docetaxel Drug: Cetuximab Drug: granulocyte colony-stimulating factor (G-CSF)</td>
<td>Phase 2</td>
</tr>
</tbody>
</table>

Study Type: Interventional
Study Design:
Allocation: Randomized
Endpoint Classification: Safety/Efficacy Study
 Intervention Model: Parallel Assignment
Masking: Open Label
Primary Purpose: Treatment

Official Title: **TPExtreme**: Randomized, Controlled Trial of Platinum-Cetuximab Combined Either With Docetaxel (TPEx) or With 5FU (Extreme) in Patients With Recurrent/Metastatic Squamous Cell Cancer of the Head and Neck

Resource links provided by NLM:
- Genetics Home Reference related topics: head and neck squamous cell carcinoma
- Drug Information available for: Cisplatin Docetaxel Granulocyte colony-stimulating factor Cetuximab
- Genetic and Rare Diseases Information Center resources: Squamous Cell Carcinoma of the Head and Neck
- U.S. FDA Resources

Further study details as provided by Groupe Oncologie Radiotherapie Tete et Cou:
Primary Outcome Measures:

- **Overall survival** [Time Frame: Until patient death or at least one year after the end of the treatment] [Designated as safety issue: No]
  
  Overall survival is defined as the time to death from any cause measured from randomization. Patients with disease progression may be treated with off protocol therapy but will be followed for overall survival evaluation.

Secondary Outcome Measures:

- **Objective response rate** [Time Frame: At 12 weeks] [Designated as safety issue: No]
  
  Objective response rate (complete response (CR) or partial response (PR) according to RECIST 1.1 criteria and assessed by central imaging review) at 12 weeks. For the statistical analysis patients not evaluable (whatever the reason, including death) will be considered as failure (i.e. no CR, no PR).

- **Best overall tumor response rate** [Time Frame: until progression or at least one year after the end of the treatment]
  
  Best overall tumor response rate (RECIST 1.1 criteria) during chemotherapy and maintenance: CR or PR or SD confirmed for CR or PR by a second assessment 6 weeks later.

- **Progression free survival** [Time Frame: until progression or death or at least one year after the end of the treatment] [Designated as safety issue: No]
  
  Progression free survival (PFS): minimum time from randomization to progression as defined by RECIST 1.1 criteria or to death from any cause. Patients who don't have any of these events are censored at the date of last follow-up.

- **Time to Progression** [Time Frame: until progression or death or at least one year after the end of the treatment] [Designated as safety issue: No]
  
  Time to Progression (TTP): minimum time from randomization to progression as defined by RECIST 1.1 criteria. In case of death from other cause than cancer and no prior progression, the patient will be censored at the time of death. In case of death related to cancer without an accurate date of progression before death, the patient will be considered in progression at the time of death. In the event of no progression and no death, the patient will be censored at the date of last follow-up.

- **Toxicity** [Time Frame: until the end of the maintenance, an expected average of 4 months of maintenance] [Designated as safety issue: Yes]
  
  Toxicity (according to CTC-NCI V4): all grades.

- **Compliance** [Time Frame: until the end of the maintenance, an expected average of 4 months of maintenance] [Designated as safety issue: No]
  
  Compliance: Insufficient compliance for cetuximab is defined as a patient missing more than 2 consecutive infusions of cetuximab, even if the missed infusions are due to toxicity. Insufficient compliance for chemotherapy is defined as a patient missing more than 2 consecutive infusions of chemotherapy, even if the missed infusions are due to toxicity.

- **EORTC QLQ-C30** [Time Frame: At baseline before treatment, at Week 12, Week 18 and at Week 26] [Designated as safety issue: No]
  
  Health related quality of life (QoL) assessed by EORTC QLQ-C30. The primary endpoint of the QoL study is the global health status/quality of-life scale of the QLQ-C30 questionnaire.

- **EuroQol-5D** [Time Frame: At baseline before treatment, at Week 12, at Week 26 and then every 2 months until death or at least one year after the end of the treatment] [Designated as safety issue: No]
  
  Quality-adjusted life-years (QALYs) based on Euroqol EQ-5D measurements.

- **Net monetary benefit** [Time Frame: until death or at least one year after the end of the treatment] [Designated as safety issue: No]

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**Estimated Enrollment:** 416  
**Study Start Date:** October 2014  
**Estimated Study Completion Date:** December 2017  
**Estimated Primary Completion Date:** December 2017 (Final data collection date for primary outcome measure)
Active Comparator: EXTREME: Cisplatin, 5-FU and Cetuximab
Chemotherapy: 6 cycles (every 3 weeks) of Cisplatin (100 mg/m² iv on Day1), 5FU (4000 mg/m² total dose starting on day 1 and during 96h in continuous infusion), and Cetuximab (loading dose of 400 mg/m² iv on Day1, then 250 mg/m² iv weekly).

If cisplatin is not tolerated and/or when the total cumulative dose of cisplatin (including prior administration) reaches 600 mg/m², cisplatin has to be replaced by carboplatin, AUC 5 (but not exceeding 750 mg), except in the case of bleeding tumor.

Cetuximab maintenance: cetuximab continuation (250 mg/m² iv weekly) will begin only if at least disease stabilization is observed at the end of chemotherapy, and will be continued until PD or unacceptable toxicity.

Experimental: TPEx: Cisplatin, Docetaxel and Cetuximab
Chemotherapy: 4 cycles (every 3 weeks) of Cisplatin (75 mg/m² iv on Day1), Docetaxel (75 mg/m² iv on Day1), and Cetuximab (loading dose of 400 mg/m² iv on Day1, then 250 mg/m² iv weekly).

If Cisplatin is not tolerated, cisplatin is replaced by carboplatin, AUC 5 (but not exceeding 750 mg), except in the case of bleeding tumor.

Primary prophylactic administration of GCSF must be administered systematically after each cycle of chemotherapy.

Cetuximab maintenance: cetuximab continuation (500 mg/m² iv every two weeks) will begin only if at least disease stabilization is observed at the end of chemotherapy, and will be continued until PD or unacceptable toxicity.

Detailed Description:
The EXTREME regimen, i.e. cetuximab added to platinum (100 mg/m² every 3 weeks) and 5FU (96h continuous infusion at 1000 mg/m²/day every 3 weeks) during 6 cycles of treatment and continued as maintenance in patients with stable disease, is currently the standard of care in first line recurrent metastatic HNSCC.

From our previous experience (phase II GORTEC “TPEx” study), the TPEx regimen of 4 cycles of docetaxel-cisplatin-cetuximab followed by maintenance with cetuximab every 2 weeks seems more efficient (overall survival) compared to EXTREME regimen. Docetaxel combined with cisplatin (each administered at 75mg/m² every 3 weeks) also appeared more convenient than the standard Cisplatin-5FU-Cetuximab EXTREME regimen (4 cycles of chemotherapy instead of 6 cycles and no i.v. continuous infusion). Toxicity was manageable with G-CSF support. In addition the toxicity / efficacy profile also seems favourable as suggested by the excellent dose intensity achieved and the high rate of patients (78%) who were able to start maintenance therapy.

Taking together all these considerations, the TPEx regimen might be a good substitute for EXTREME as first-line treatment in patients with recurrent metastatic HNSCC, and it is justified and necessary to perform a direct comparison in a randomized trial to further test this hypothesis.

Eligibility

Ages Eligible for Study: 18 Years to 71 Years
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria
Inclusion Criteria:
- Histologically confirmed diagnosis squamous cell carcinoma of head and neck: oral cavity, oropharynx, hypopharynx, larynx (histological confirmation is mandatory at least for initial diagnosis)
- Recurrence and/or metastatic disease not suitable for local therapy
- At least one measurable lesion (RECIST) by CT or MRI
- PS < 2
- Age ≥ 18 years and < 71 years
- Clearance of creatinine > 60ml/mn (MDRD)
- Haematological function as follows: absolute neutrophil count > 1.5 x 109/l, platelet > 100 x 109/l, hemoglobin ≥ 9.5 g/dl
- Hepatic function as follows: bilirubin ≤ Upper limit of normal (ULN); SGOT/SGPT < 1.5 ULN; AP < 2.5 ULN
- Estimated life expectancy > 12 weeks
- Informed Consent Form signed
- Affiliation to a health insurance
- Negative pregnancy test in women of childbearing potential within 14 days prior to treatment initiation (premenopausal or less than 12 months of amenorrhea post-menopause, and who have not undergone surgical sterilization). Both men and women (of childbearing potential) who are sexually active must use adequate contraception, during and for at least 6 months post-treatment.

**Exclusion Criteria:**

- Patients with nasopharyngeal cancer, paranasal sinus cancer or unknown primary
- Prior systemic chemotherapy for the head and neck carcinoma, except if given as part of a multimodal treatment for locally advanced disease which was completed more than 6 months prior to study entry
- Surgery (excluding diagnostic biopsy) or radiotherapy within 6 weeks before study entry
- Contra-indication to receive cisplatin
- Known dihydropyrimidine dehydrogenase (DPD) deficiency
- Administration of prophylactic phenytoin
- Recent or planned yellow fever vaccination
- Prior dose of cisplatin > 300 mg/m² (a patient who received prior RT + 3 cycles of cisplatin or 3 cycles induction TPF, i.e. total dose of cisplatin ≤ 300 mg/m², for locally advanced primary HN cancer can be included)
- Prior anti-EGFR treatment received less than 12 months before enrolment in the trial
- Known hypersensitivity reaction to 5FU, cisplatin, carboplatin, docetaxel or cetuximab
- Documented or symptomatic brain or leptomeningeal metastasis
- Clinically significant cardiovascular disease, e.g. cardiac failure of New York Heart Association classes III-IV, uncontrolled coronary artery disease, cardiomyopathy, uncontrolled arrhythmia, uncontrolled hypertension, or history of myocardial infarction in the last 12 months
- Malignancies within 5 years prior to randomization, with the exception of adequately treated basal or squamous cell skin cancer and carcinoma in situ of the cervix
- Active infection (infection requiring IV antibiotics), including active tuberculosis and known and declared human immunodeficiency virus (HIV).
- Significant disease which, in the judgment of the investigator, would make the patient inappropriate for entry into the trial.
- Any social, personal, medical and/or psychologic factor(s) that could interfere with the observance of the patient to the protocol and/or the follow-up and/or the signature of the informed consent.
- Pregnant or breast feeding women

**Contacts and Locations**

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see [Learn About Clinical Studies](Learn About Clinical Studies).

Please refer to this study by its ClinicalTrials.gov identifier: NCT02268695

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Centre Médical de Forcilles  Not yet recruiting
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More Information
No publications provided

Responsible Party: Groupe Oncologie Radiotherapie Tete et Cou
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Other Study ID Numbers: GORTEC 2014-01
Study First Received: October 13, 2014
Last Updated: March 23, 2015
Health Authority:
  France: Agence Nationale de Sécurité du Médicament et des produits de santé
  Germany: Federal Institute for Drugs and Medical Devices
  Germany: Ethics Commission
  Spain: Agencia Española de Medicamentos y Productos Sanitarios
  Spain: Comité Ético de Investigación Clínica

Keyw ords provided by Groupe Oncologie Radiotherapie Tete et Cou:
Recurrent/Metastatic HNSCC
Taxanes

Additional relevant MeSH terms:
  Carcinoma, Squamous Cell
  Head and Neck Neoplasms
  Carcinoma
  Neoplasms
  Neoplasms by Histologic Type
  Neoplasms by Site
  Neoplasms, Glandular and Epithelial
  Neoplasms, Squamous Cell
  Cetuximab
  Cisplatin
  Docetaxel
  Lenograstim

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