Androgen Deprivation Therapy in Advanced Salivary Gland Cancer

**Purpose**

Salivary Gland (SG) Cancers are a rare and heterogeneous group of tumors, usually approached by multidisciplinary teams in high specialized centers. Until today no standard of care exists to treat these cancers. The identification of a target, the androgen receptor, in SG tumors has allowed for new treatment strategies options for this rare group of diseases. As a matter of fact, strong positivity for androgen expression has been found in salivary duct carcinoma and adenocarcinomas. The purpose of this study is therefore to evaluate the efficacy and safety of chemotherapy versus androgen deprivation therapy (ADT) in patients with recurrent and/or metastatic AR expressing SGCs.

The study will include two cohorts of patients: Cohort A, which comprises chemo-naïve patients, and Cohort B, which comprises pretreated patients.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Intervention</th>
<th>Phase</th>
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</thead>
</table>
| Salivary Gland Cancer | Drug: bicalutamide + triptorelin  
Drug: Cisplatin + Doxorubicin  
Drug: Carboplatin + Paclitaxel | Phase 2 |

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

**Official Title:** A Randomized Phase II Study to Evaluate the Efficacy and Safety of Chemotherapy (CT) vs Androgen Deprivation Therapy (ADT) in Patients With Recurrent and/or Metastatic, Androgen Receptor (AR) Expressing, Salivary Gland Cancer (SGCs)

**Resource links provided by NLM:**

- MedlinePlus related topics: Cancer
- Genetic and Rare Diseases Information Center resources: Kennedy Disease, Oral Cancer
- U.S. FDA Resources

**Further study details as provided by European Organisation for Research and Treatment of Cancer - EORTC:**

**Primary Outcome Measures:**

- Progression Free Survival (PFS) [ Time Frame: 37 months after First Patient In ] [ Designated as safety issue: No ]  
  PFS is a primary outcome for cohort A

- Response rate (RR) [ Time Frame: 37 months after First Patient In ] [ Designated as safety issue: No ]  
  RR is a primary outcome for cohort B
Secondary Outcome Measures:

- Response Rate (RR) [ Time Frame: 37 months after First Patient In ] [ Designated as safety issue: No ]
  RR is a secondary outcome for cohort A

- Progression Free Survival (PFS) [ Time Frame: 37 months after First Patient In ] [ Designated as safety issue: No ]
  PFS is a secondary outcome for cohort B

Other Outcome Measures:

- Overall Survival (OS) [ Time Frame: 37 months after First Patient In ] [ Designated as safety issue: No ]
- Adverse Events according to CTCAE v4.0 [ Time Frame: 37 months after First Patient In ] [ Designated as safety issue: No ]
  adverse events will be recorded using International Common Terminology Criteria for Adverse Events (CTCAE), version 4.0, the investigator will assess whether those events are drug related (reasonable possibility, no reasonable possibility) and this assessment will be recorded in the database for all adverse events

Estimated Enrollment: 152
Study Start Date: February 2015
Estimated Study Completion Date: December 2020
Estimated Primary Completion Date: December 2020 (Final data collection date for primary outcome measure)

<table>
<thead>
<tr>
<th>Arms</th>
<th>Assigned Interventions</th>
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</thead>
<tbody>
<tr>
<td>Active Comparator: Chemotherapy</td>
<td></td>
</tr>
<tr>
<td>Chemotherapy = either Cisplatin + Doxorubicin or Carboplatin + Paclitaxel</td>
<td></td>
</tr>
<tr>
<td>Patients from cohort A (chemonaive) may be randomized in this arm to receive chemotherapy</td>
<td></td>
</tr>
<tr>
<td>Drug: Cisplatin + Doxorubicin Drug: Carboplatin + Paclitaxel</td>
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<tr>
<td>Experimental: Androgen Deprivation Therapy (ADT)</td>
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</tr>
<tr>
<td>ADT = bicalutamide + triptorelin</td>
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</tr>
<tr>
<td>Patients from cohort A (chemonaive) may be randomized to receive ADT, and patients from cohort B (pre-treated) will receive ADT without having been randomized.</td>
<td></td>
</tr>
<tr>
<td>Drug: bicalutamide + triptorelin</td>
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</tbody>
</table>

Detailed Description:

Patients in Cohort A will be randomized 1:1 at the study entry to receive ADT (triptorelin + bicalutamide 50 mg) or standard chemotherapy. Patients of Cohort A randomized to the control arm (chemotherapy arm) will be given the option to enter Cohort B at the time of disease progression. As long as Cohort A is open to recruitment, patients who will be treated by chemotherapy will be simultaneously enrolled in Cohort B. Accrual in Cohort B will be stopped when recruitment of 76 eligible patients in Cohort A is reached.

Eligibility

Ages Eligible for Study: 18 Years and older (Adult, Senior)
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- Histologically proven diagnosis of recurrent and/or metastatic salivary duct cancer; adenocarcinoma, NOS; and AR expression in at least 70% of nuclei of neoplastic cells based on central review
- Sufficient tissue must be available either historically or a biopsy must be done as a part of this study and sent to central review for patients enrolled in both cohorts
- Presence of at least one uni-dimensional measurable lesion by CT-scan or MRI according to RECIST criteria version 1.1 (target lesion).
- Patients older than 18 years old;
- Performance Status ECOG 0-1;
- Adequate bone marrow function:
  - WBC ≥ 3.5/10exp9L
  - absolute neutrophil count ≥ 1.5x10exp9/L
  - hemoglobin > 9 g/dL
  - platelet count ≥ 100x10exp9/L
- Adequate liver function:
  - AST < 2.5 times upper limit of normal
  - ALT < 2.5 times upper limit of normal

https://clinicaltrials.gov/ct2/show/NCT01969578?term=eortc+1206&rank=1

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• bilirubin < 1.5 times upper limit of normal

• the concomitant evidence of AST < 2.5 times upper limit of normal, ALT < 2.5 times upper limit of normal and bilirubin > 1.5 times upper limit of normal is not allowed

• Adequate renal function:
  • serum creatinine level (≤ 1.3 mg/dL)
  • calculated creatinine clearance ≥ 60 mL/min based on the standard Cockcroft and Gault formula

• Adequate cardiac function as demonstrated by a clinically normal 12 lead ECG; additionally for patients who will receive Cisplatin and Doxorubicin adequate cardiac function should be demonstrated by a left ventricular ejection fraction (LVEF) ≥ 50% (within 2 weeks prior to treatment start)

Exclusion Criteria:

• Actively bleeding tumor if the patient is intended to be treated with carboplatin

• Patients with bone disease or brain disease as the sole disease site; brain metastases are allowed in case of systemic disease, but must have been treated at least 4 weeks before enrollment and must be stable after that;

• recent history of congestive heart failure, unstable angina within the past 3 months, cardiac arrhythmia, myocardial infarction, congenital long QTc prolongation, stroke, TIA within the past 6 months;

• previous cardiac toxicity induced by another anthracycline or previous exposure to maximum cumulative dose of another anthracycline if the patient is intended to be treated with doxorubicin

• history of allergic reactions attributed to compounds of similar chemical or biological composition to cis/carboplatin, paclitaxel, doxorubicin, bicalutamide or triptorelin;

• concomitant medications with terfenadine, astemizole, cisaprid

• use of phenytoin

• Patients who received vaccine for yellow fever

• active second malignancy during the last five years except non melanomatus skin cancer or carcinoma in situ of the cervix;

• positive serum pregnancy test within 1 week prior to the first dose of study treatment for Women of child bearing potential (WO CBP);

• no adequate birth control measures, as defined by the investigator, during the study treatment period and for at least 6 months after the last study treatment for patients of childbearing / reproductive potential;

• psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow-up schedule; those conditions should be discussed with the patient before registration in the trial;

• written informed consent not given according to ICH/GCP, and national/local regulations, before patient registration

• participation in another interventional clinical trial in the preceding 4 weeks prior to randomization

• for cohort A patients: previous chemotherapy for recurrent/metastatic disease (previous chemotherapy given concomitantly with RT in the past is allowed, including cisplatin but it should be completed at least 6 months before enrollment).

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.

Please refer to this study by its ClinicalTrials.gov identifier: NCT01969578

Contacts

Contact: Céline Demarez, PhD  celine.demarez@eortc.be
Contact: General study e-mail address  1206@eortc.be

Locations

Belgium

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  Principal Investigator: Yassine Lalami

Universitair Ziekenhuis Antwerpen
  Edegem, Belgium, 2650
  Principal Investigator: Pol Specenier

France

CHU de Nantes - Hotel Dieu
  Nantes, France

Germany

Charite - Universitaetsmedizin Berlin - Campus Benjamin Franklin
  Berlin, Germany, 12200

Recruiting

Not yet recruiting
Principal Investigator: Sebastian Ochsenreither

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Budapest, Hungary, 1122
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Principal Investigator: Cecilia Moro
Fondazione IRCCS Istituto Nazionale dei Tumori
Milan, Italy
Principal Investigator: Laura Locati

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Principal Investigator: Spoukje Oosting-Lenstra
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Principal Investigator: Carla van Herpen

Sponsors and Collaborators
European Organisation for Research and Treatment of Cancer - EORTC

Investigators
Principal Investigator: Lisa Licitra Fondazione IRCCS Istituto Nazionale Tumori
Study Chair: Kevin Harrington The Royal Marsden

More Information
Responsible Party: European Organisation for Research and Treatment of Cancer - EORTC
ClinicalTrials.gov Identifier: NCT01969578 History of Changes
Other Study ID Numbers: EORTC-1206 2013-000314-38
Study First Received: September 24, 2013
Last Updated: November 28, 2016
Health Authority: Austria: Agency for Health and Food Safety
Belgium: Federal Agency for Medicinal Products and Health Products
France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis)
Germany: Federal Institute for Drugs and Medical Devices
Netherlands: The Central Committee on Research Involving Human Subjects (CCMO)
United Kingdom: Medicines and Healthcare Products Regulatory Agency

Keywords provided by European Organisation for Research and Treatment of Cancer - EORTC:
salivary duct cancer
adenocarcinoma, NOS
androgen deprivation
androgen receptor

Additional relevant MeSH terms:
Salivary Gland Neoplasms
Mouth Neoplasms
Head and Neck Neoplasms
Neoplasms by Site
Neoplasms
Mouth Diseases
Stomatognathic Diseases
Salivary Gland Diseases
Paclitaxel
Liposomal doxorubicin
Bicalutamide
Cisplatin
Carboplatin
Doxorubicin
Methyltestosterone
Triptorelin Pamoate
Androgens
Ascorbic Acid
Estrogens, Conjugated (USP)
Antineoplastic Agents, Phytogenic
Antineoplastic Agents
Tubulin Modulators
Antimitotic Agents
Mitosis Modulators
Molecular Mechanisms of Pharmacological Action
Antibiotics, Antineoplastic
Topoisomerase II Inhibitors
Topoisomerase Inhibitors
Enzyme Inhibitors
Hormones

ClinicalTrials.gov processed this record on January 11, 2017
