MATWIN
MATURATION & ACCELERATING TRANSLATION **WITH INDUSTRY**

TECHNOLOGY OFFER

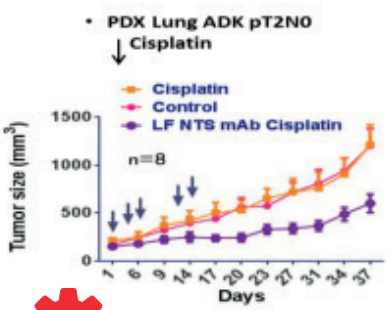
SUPPORTING INNOVATION AND TECHNOLOGY TRANSFER IN ONCOLOGY

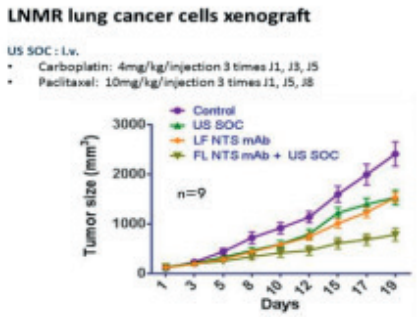
NEUROTENSIN ANTIBODIES

THERAPY

CONTEXT & BACKGROUND

Lung cancer is the leading cause of cancer-related deaths in western countries. Two-thirds of patients have reached a metastatic and inoperable state when they meet the oncologist. Treatment options are mainly platinum-based chemotherapy combined with pemetrexed, or targeted therapy.
We propose to restore the response to platinum-based chemotherapy in lung adenocarcinoma resistant tumors with a monoclonal antibody directed against neurotensin. Our goal is to develop this immunotherapy for clinical use.
Recent drug development in targeted and immunotherapy improved the overall survival of eligible patients. Nevertheless, all patients with advanced NSCLC suffer from progression of their disease and will finally be treated by the platinum based standard of care treatment (SOC). Consequently, 95 % of all lung cancer patients will receive a platinum based treatment for their lung cancer cure. Unfortunately, only 30% of patients are responsive to SOC. Therefore, a clear need exists for new therapies to improve the platinum salt based SOC. Neurotensin (NTS) and its high affinity receptor (NTSR1) are up regulated in 20% of lung cancers. In a clinical study, NTSR1 overexpression was shown to predict a poor prognosis for 5 year overall survival in 389 patients in stage I to stage III lung adenocarcinoma. Interactions between NTS and NTSR1 induce pro-oncogenic biological effects associated with neoplastic processes and tumor progression. Sustained activation of NTSR1 results in concomitant chronic activation of EGFR, HER2 and HER3 resulting in a higher degree of aggressiveness of tumor expressing NTS and NSTR1. Two NTS monoclonal antibodies were developed and successfully tested for their ability to neutralize NTS oncogenic effects.
NTS mAb directed against the mature peptide and LF NTS mAb directed against the uncleaved peptide. The antitumoral activities of the monoclonal antibodies were tested in a very aggressive lung cancer model (LNM-R) and in a triple negative breast cancer model (MD1-MB 231). In both cases, a strong decrease of tumor size was observed in tumors expressing NTS and NTSR1, and not in tumors deleted for NTSR1. In several experimental tumor models (cells, PDX) the presence of NTS antibodies restored or improved the response to cisplatin or SOC (see figure below). Our main objective is to develop NTS targeted therapy as a clinical antitumoral agent and anti drug resistance agent. We wish to reinforce the data already acquired in the preclinical context performed with experimental tumors and by patient derived xenografts (PDX). We will also study the cellular and molecular antitumoral mechanism of NTS antibodies on oncogenic targets and platinum resistant pathways.
The future end products will be an immunotherapy directed against NTS and/or NTS long fragment that could be used in combination with platinum-based cancer treatments in patients having lung adenocarcinomas expressing NTSR1.





INNOVATIVE COMPONENT & TECHNOLOGY

Two anti-neurotensin monoclonal antibodies

OBJECTIVES

Our main objective is to develop NTS based immunotherapy as a clinical antitumoral agent. We wish to reinforce the data already acquired in a preclinical context performed with experimental tumors generated by lung cancer cell lines and their derivatives, and by patient derived xenografts (PDX).

SCOPE

Neurotensin targeted therapy using mAb improves the therapeutic index of platinum salts for patients with lung adenocarcinomas

KEYWORDS

Neurotensin, mAb, lung adenocarcinoma, platinum salts

DEVELOPMENT & MATURATION STAGE

NTS antibodies have been validated in vivo on aggressive lung cancer lines
NTS antibodies improve cisplatin response in vivo

TARGET POPULATION

Patients with lung adenocarcinoma treated with standard of care containing platinum salts (20-30% with adenocarcinoma have high NTS/NTSR1)

TARGET PROFILE

NTS/NTSR1 complex is involved in many oncogenic pathways. NTS targeting allows decreasing over-activity of NTSR1

STRENGHTS & COMPETITIVE ADVANTAGES

- First in-class agent
  - Targets the neurotensin ligand (not the receptor)- should increase probability of success
  - No competition for this target
- Characteristics of the NTS mAb
  - Two antibodies developed for the same target
  - Strong antigen homology sequence between species
  - Good tolerance in toxicity test
  - No toxicity expected

INDUSTRIAL APPLICATIONS & OPPORTUNITIES

- NTS mAb development is possible for many cancer types and in combination with radiotherapy
  - Further extension to ovarian, breast, endometrial, hepatocellular carcinomas, pancreas, prostate, colon,...neuroendocrine tumors...
  - NTS mAb performance can benefit in the selection of patients with a biomarker
  - IHC assay of intracytoplasmic neurotensin receptor expression could be set up for the clinical development in lung cancer and other cancers.

INTELLECTUAL PROPERTY & PATIENT CO-OWNER(S)

- WO2009127619
Methods for the treatment, the prognostic assessment and the staging of **non-small cell lung cancer.**
- WO2010069929
Methods for the treatment and the prognostic assessment of **malignant pleural mesothelioma**
- WO2010079158
Methods for the treatment, the prognostic assessment and the detection of **breast cancer**
- EP14305825
Anti-neurotensin antibodies and uses thereof
Pending EP - EP14305826
Anti-neurotensin long fragment antibodies and uses thereof

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