MATWIN
MATURATION & ACCELERATING TRANSLATION **WITH INDUSTRY**

TECHNOLOGY OFFER

SUPPORTING INNOVATION AND TECHNOLOGY TRANSFER IN ONCOLOGY

AGP
ANTI-GLIOBLASTOMA PEPTIDE (AGP)

CONTEXT & BACKGROUND

Glioma are the most frequent primary cerebral tumours, classified into 4 grades: I – II: low grades (20-25%), III – IV: malignant glioma (70-75%). Glioblastoma are the grade IV glioma, with a very bad prognostic. Despite the standard referential treatment (Stupp treatment), which involves surgery, radiotherapy and chimiotherapy, the median survival rate is approximately 12 months, and the survival rate after 3 years is lower than 5%.
In France glioblastoma caused 3.000 deaths in 2011, with 4.560 new cases in 2010 (INCa: www.e-cancer.fr). In the States it caused 14.080 deaths in 2012, with 23.130 new cases in 2012 (NCI: www.cancer.gov). In the world 175.000 deaths in 2008 are estimated, with 238.000 new cases in 2008 (IARC: www.iarc.fr).
The classical chimiotherapy is Temodal (Temozolomide a DNA alkylation product). The market in 2009 represented approximately 1 billion $/year. New therapies are under test, in particular using immune-therapies targeting the different pathways that are affected in glioblastoma (VEGFR, VEGF, EGFR, PDGFR, ...etc). Most of these treatments failed to be used following clinical trials because of their low efficiency and poor specificity, due to the abnormally high number of mutations in glioblastoma patients. Therefore, they present too many side effects.
Most of these new treatments, as well as the "old" treatments (immunotherapies, gene therapy, 5FU microspheres) were first tested locally (following the surgery), because following the surgery a 4-6 weeks period is necessary for patients to recover from surgery.
There is an urgent need to find a product to inhibit glioblastoma proliferation following the surgery.

INNOVATIVE COMPONENT & TECHNOLOGY

- The Anti-Glioblastoma-Peptide is capable:
1- to penetrate specifically in all the glioblastoma cells lines and primary cultures that were tested (rat, mouse and human),
2- to block microtubule polymerisation,
3- to inhibit glioblastoma cell division in vitro (cell culture models) and in vivo (stereotaxic implantation of glioblastoma cells in the striatum of rats or mice).
- The peptide has no similar effect on the other cells of the nervous system, and shows no detectable toxicity following intra-cranial or intra-venous administration
.- This peptide can be used locally following the resection of the glioblastoma tumour, or injected by stereotaxy into glioblastoma tumours that cannot be operated. (See figure at the end of this document)

SCOPE

A new anti-glioblastoma treatment

KEYWORDS

Glioblastoma, peptide, microtubule, cancer from the nervous system.

OBJECTIVES

The objective of is to bring the peptide from our laboratory to the bedside of the glioblastoma patients.
Therefore, we need to find an industrial partner for the clinical transfer of this promising anti-glioblastoma peptide, because our academic laboratories do not have the capacity to ensure a fast and GLP/GCP compliant project.
The main tasks will be to:
1- Synthesize and characterize cGMP batches of the AGP peptide.
2- determine the optimal in vivo (rodents) dose/effect use of the cGMP peptide, and characterize the biodistribution, pharmacokinetic properties and possible toxic effects of the peptide,
3- write and submit the Investigational New Drug Application
4- Conduct a Phase I/II clinical trial in order to assess the safety of the peptide and to determine its optimal active dose in patients

DEVELOPMENT & MATURATION STAGE

The AGP project is strongly supported by the TTO Ouest Valorisation through a R&D maturation program of 150 K€ that will end by march 2017. Ouest Valorisation also agreed to license the peptide to GlioCure SAS a spin-off company of Angers University dedicated to the treatment of glioblastoma.
GlioCure's founders are Louis-Marie Bachelot, a biotech entrepreneur with more than 15 years of experience in the Biotech sector who holds a Master Degree in Finance & Economics from Sciences-Po Paris and a Master of Biochemistry & Molecular Biology from King's College London, Dr. Joël Eyer, an INSERM Fellow and a world-renowned expert of the neuronal cytoskeleton, and Claire Lepinoux-Chambaud, PhD and neuroscientist.
GlioCure's Scientific and Medical board will also include Professor Philippe Menei, head of the neurosurgery department at Angers University Hospital.
GlioCure's main objective is to obtain an IND for the peptide and to secure a co-development deal within 30 months.

INTELLECTUAL PROPERTY & PATIENT CO-OWNER(S)

- Patent 1: Bocquet A., Peterson A., Eyer J. (2005) Peptide capable d'inhiber la polymérisation de la tubuline et son utilisation pour inhiber la prolifération cellulaire. N° WO/2005/121172.
- Patent 2: Eyer J., Peterson A., Balzeau J., Berges R. (2011) Use of a neurofilament peptide for the treatment of glioma. Patent WO/2011/073207

TARGET POPULATION

Patients affected by a glioblastoma tumour.

TARGET PROFILE

The end product will be the peptide in solution that will be administrated directly following the removal of the glioma tumour by neurosurgery. Alternatively, if the tumour cannot be removed because it is located in a critical or profound place into the brain, then the peptide can be administrated in the tumour using classical stereotaxy.
Following the removal of the tumour a minimum of time (generally at least 6 weeks) is necessary for the patient to recover from surgery, and before radiotherapy and chimiotherapy can be started. In this interval of time it is absolutely necessary to stop glioblastoma cell proliferation and migration. In this circumstance, the presence of the AGP peptide will be particularly efficient. The peptide will be produced at a cGMP level, and will be solubilised extemporaneously by the pharmacy of the hospital. The exact amount to deliver to each patient as well as the exact concentration will be done by healthcare professionals. It is important to note that the end product does not need a complex and risky biological purification with several toxic impurities. The peptide is a purely synthetic peptide that can be produced by grams or kilograms at a cGMP grade at higher than 99.9% purity. Thus, all the pre-clinical investigations will focus only on the peptide itself and not on possible contaminants.
Note that other peptides are presently tested in clinical phases, and this peptide does not present synthesis problem.
Therefore, the cGMP production should not represent a major technological bottleneck.

STRENGHTS & COMPETITIVE ADVANTAGES

The current state of the art shows that glioblastoma is a fatal tumour of the nervous system.
- This product is a new therapeutic approach for the treatment of glioblastoma as a drug delivered by stereotactic surgery within the glioblastoma tumour or following the tumour removal by surgery. This will be the preferred administration.
- This product acts specifically by penetrating selectively in glioblastoma cells, and blocking cell division only in glioblastoma cells (by aggregation of tubulin in an un-polymerizable state).
- This peptide appears as an attractive alternative in the current context where glioblastoma affected patients have not real effective therapeutic solutions and lead to rapid death.

INDUSTRIAL APPLICATIONS & OPPORTUNITIES

GlioCure is looking for:
- a seed funding of 2 M€ including 300 to 400 K€ in order to achieve the non-regulatory preclinical development of AGP within the 12-15 coming months.
- an industrial partner that can bring significant capacities and expertise regarding the GMP manufacturing and regulatory submissions of anticancer drugs, to accelerate the preclinical development.

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