ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: June 3, 2021

ClinicalTrials.gov ID: NCT04094077

Study Identification

Unique Protocol ID:	ET18-270 NANOSTEREO
Brief Title:	Evaluating AGuIX® Nanoparticles in Combination With Stereotactic Radiation for Brain Metastases (NANOSTEREO)
Official Title:	A Phase II Study Evaluating AGuIX® Nanoparticles in Combination With Stereotactic Radiation for Oligo Brain Metastases.
Secondary IDs:	

Study Status

Record Verification:	June 2021
Overall Status:	Terminated [Study stopped after a negative result delivred by the CPP for a substancial modification of the protocol]
Study Start:	January 17, 2020 [Actual]
Primary Completion:	February 24, 2021 [Actual]
Study Completion:	February 24, 2021 [Actual]

Sponsor/Collaborators

Sponsor:	Centre Leon Berard
Responsible Party:	Sponsor
Collaborators:	

Oversight

U.S. FDA-regulated Drug:	No
U.S. FDA-regulated Device:	No
U.S. FDA IND/IDE:	No
Human Subjects Review:	Board Status: Approved Approval Number: 19.09.01 Board Name: Comité de Protection des Personnes Est III Board Affiliation: French Ministry of Health Phone: 03.83.15.43.24 Email: cppest3@chru-nancy.fr Address: Hôpital de Brabois Rue du Morvan

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Data Monitoring: Yes

FDA Regulated Intervention: No

Study Description

Brief Summary: This study evaluates the clinical impact of AGuIX® nanoparticles in combination with Fractionated Stereotactic Radiation in oligo brain metastases.

Detailed Description: AGuIX® (Activation and Guidance of Irradiation by X-ray, NH TherAguix) are Gadolinium chelated polysiloxane based nanoparticles with Magnetic Resonance contrast properties, able to accumulate in the tumor through the enhanced permeability and retention effect and sufficiently small (sub-5 nm diameter) to allow for renal clearance.

AGuIX® nanomedicine can be used as:

- Positive contrast agent for Magnetic Resonance Imaging (MRI). It displays higher efficacy than commercial contrast agents and so it can be used to delineate precisely the tumors.
- A booster of Radiotherapy during the radiotherapy protocol, after the localization of the tumor.

This is permitted by the high radiosensitizing potential of AGuIX® that allows a local increase of efficacy of X-ray damages. French and international groups have demonstrated the radiosensitizer effect of AGuIX® to improve the efficacy of radiotherapy.

Thanks to a difference in porosity between the vascular networks, AGuIX® penetrates and resides in tumor tissues, but not in healthy tissues.

Conditions

Conditions: Brain Metastases

Keywords: Stereotactic Radiation
Nanoparticles

Study Design

Study Type: Interventional

Primary Purpose: Treatment

Study Phase: Phase 2

Interventional Study Model: Single Group Assignment
This study is a paucicentric, single arm Phase II trial conducted according to a single stage Fleming-A'Hern design and aiming to evaluate the efficacy of AGuIX® during FSRT of brain metastasis.

Number of Arms: 1

Masking: None (Open Label)

Allocation: N/A

Enrollment: 1 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Aguix + Stereotactic Radiation	Drug: AGuIX 2 IV injections (100 mg/Kg/injection) at day 4 and day 8 + Strereotactic Radiation from day 8 to day 15 as per standard practice.

Outcome Measures

Primary Outcome Measure:

1. Rate of local control
   The primary endpoint is the rate of local control defined as the proportion of patients with a complete response, a partial response or a stable disease. Response of Brain lesion will be evaluated using the RECIST classifications with partial response (PR, > 30% decrease in longest diameter), stable disease (SD <30% decrease and <20% increase in longest diameter), progressive disease (PD > 20% increase in longest diameter) and Complete response (CR) (complete disappearance of the brain lesion).

   [Time Frame: 1 year]

Secondary Outcome Measure:

2. Distant Brain failure
   Distant Brain failure is defined as the presence of new brain metastases or leptomeningeal enhancement outside the irradiated volume.

   [Time Frame: 6 month and at 1 year]
3. Time to brain relapse
   The event of interest will be the local progression on any irradiated lesion.

   [Time Frame: 6 month and 1 year]
4. Tumor target volume
   The Tumor target volume agreement is the comparison between both the MRI images with AGuIX® and Gd-chelates. It is defined as the correlation between the irradiation volume calculated based on the MRI before nanoparticles injection and the volume calculated after nanoparticles injection.

   [Time Frame: 4 days]
5. Brain lesion 3-D volume variation
   Brain lesion 3-D volume variation will be analysed using volumetric T1 post-gadolinium MRI.

   [Time Frame: 45 days and 3 month]
6. Adverse events
   The assessment of safety will be based mainly on the frequency of adverse events based on the common toxicity criteria (CTCAE-V5.0) grade.

   [Time Frame: From Day 1 to Day 45]
7. FACT-Br
   The FACT-Br consists of a general version (FACT-G) and a brain subscale (BRCS). The FACT-G consist of 27 questions with 4 domains assessing physical well-being (score range: 0-28), social/family well-being (score range: 0-28), emotional well-being (score range: 0-24) and functional well-being (score range: 0-28). The BRCs is a 23-item questionnaire related to neurological concerns that provides an additional set of disease-specific questions pertaining to brain neoplasms (score range: 0-92). The FACT-Br total score is the sum of the FACT-G total score and the BrCS score. Positive change scores indicate improved quality of life.

   [Time Frame: 45 days, 3 month, 6 month, 9 month and 12 month]
8. MMSE

The MMSE is an 11-item measure that tests five areas of cognitive function: orientation, registration, attention and calculation, recall and language. The minimum score is 0 and the maximum score is 30 with higher MMSE scores indicating better cognition.

[Time Frame: 45 days, 3 month, 6 month, 9 month and 12 month]

Eligibility

Minimum Age:	18 Years
Maximum Age:	
Sex:	All
Gender Based:	No
Accepts Healthy Volunteers:	No

Criteria: Inclusion Criteria:

- Male or female patients aged of at least 18 years on day of signing informed consent.
- Histologically-confirmed diagnosis of any histological type of solid tumors, excluding primary central nervous system (CNS) tumors.
- Radiological evidence by MRI : At least one and a maximum of 5 brain metastases, and at least one brain lesion with a longest diameter ≥ 2 cm and eligible for FSRT.
- Patient without progression on extracranial disease documented by radiological assessment as per RECIST v1.1 within 4 weeks before inclusion.
- For patients treated with a systemic anti-cancer therapy: a minimal 2-week washout period is required from the date of last systemic treatment administration to Day 1, except for hormonal agents.
- ECOG Performance Status (PS) ≤2.
- Absolute neutrophil count (ANC) ≥ 1.0 G/L, Platelets ≥ 75 G/L, Hemoglobin ≥ 8 g/dL, Serum creatinine OR Creatinine clearance according to CKD-EPI ≤ 1.5 x Upper Limit of Normal (ULN) OR ≥ 50 mL/min/1.73m2, ASAT and ALAT ≤ 3 x ULN (or ≤ 5.0 ULN in case of liver metastasis or hepatic infiltration),INR and Activated Partial Thromboplastin Time (aPTT) ≤1.5 x ULN.
- Women of child-bearing potential must have a negative serum pregnancy test at screening and must agree to use 2 effective forms of contraception from the time of the negative pregnancy test up to 3 months after the last dose of the study drug.
- Fertile men must agree to use contraceptive measures up to 3 months after the last dose of study drug.
- Patients who understand, sign, and date the written voluntary informed consent form at the screening visit prior to any protocol-specific procedures. Patient should be able and willing to comply with study visits and procedures as per protocol.
- Patients must be covered by a medical insurance.

Exclusion Criteria:

- Prior local treatment with radiotherapy (whole / partial brain or stereotactic radiosurgery) or surgical resection of brain lesions.
- Patient participating to another clinical trial with an investigational agent.
- Patients who have not recovered from significant adverse events (i.e. Grade > 2 AE according to NCI CTCAE v5.0) due to prior treatment with anti-cancer agents with exception of any Grade alopecia or lab values presented in inclusion criteria.

- Contra-indication for MRI enhanced with gadolinium (e.g. cardiac pacemaker, implanted defibrillator, certain cardiac valve replacements, certain metal implants).
- Patients who are pregnant or breastfeeding.

Contacts/Locations

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References

Citations:

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