



PRESS RELEASE

NH TherAguix and the CHU Grenoble-Alpes announce the publication of the results of the First-In-Human phase 1 clinical trial on the combination of AGuIX with radiotherapy on multiple brain metastases patients.

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NH TherAguix (“NHT”), a clinical stage company developing innovative nanomedicines for the treatment of cancer, and the CHU Grenoble Alpes announce the publication of the results of the First-In-Human phase 1 clinical trial on the combination of AGuIX, its candidate drug, with radiotherapy on multiple brain metastases patients, by **Verry Camille et al.**, in ***Radiotherapy & Oncology medical journal***.¹

This First-In-Man NANORAD trial led by the Grenoble Alpes University Hospital (principal investigator Dr. Camille Verry, Radiotherapy Department), allowed to assess favourably AGuIX in terms of tolerance after intravenous administration in combination with whole brain radiation therapy in patients with multiple brain metastases not suitable for stereotactic radiotherapy. Five dose levels (15, 30, 50, 75 and 100 mg/kg) have been successfully tested on 15 patients with a total of 354 brain metastases from 4 types of primary cancers (melanoma (n=6), lung cancer (n=6), colon cancer (n=1) and breast cancer (n=2)). All patients have received one intravenous injection of AGuIX associated with a conventional whole brain radiation therapy (10 x 3 Gy).

This trial has demonstrated that the combination of AGuIX with radiotherapy for these patients is safe and feasible. Thus, the dose of 100 mg/kg, reached without occurrence of dose limiting toxicities, was selected for the phase II trial that is currently ongoing. The pharmacokinetic study has confirmed the distribution of AGuIX and its renal elimination. AGuIX specifically targets brain metastases and is retained within tumors for up to 1 week, allowing radiosensitization during the fractionation of the treatment. Finally, a clinical benefit according RECIST v1.1 (partial response or stable disease) was proven for 13 over 14 evaluable patients. MRI analysis also showed a significant correlation between contrast enhancement and tumor response, thus supporting a radiosensitizing effect.

¹ [Theranostic AGuIX nanoparticles as radiosensitizer: A phase I, dose-escalation study in patients with multiple brain metastases \(NANO-RAD trial\)](#). Verry C, Dufort S, Villa J, Gavard M, Iriart C, Grand S, Charles J, Chovelon B, Cracowski JL, Quesada JL, Mendoza C, Sancey L, Lehmann A, Jover F, Giraud JY, Lux F, Crémillieux Y, McMahon S, Pauwels PJ, Cagney D, Berbeco R, Aizer A, Deutsch E, Loeffler M, Le Duc G, Tillement O, Balosso J. *Radiother Oncol.* 2021 May 4:S0167-8140 (21)..

A first scientific publication on the same trial and already published² explains in more details the targeting of brain metastases by accumulation of AGuIX. Beyond the qualitative aspect, it was possible to quantify the concentration of nanoparticles revealing the potential of AGuIX to be used as a theranostic drug allowing to quantify the radiosensitization prior to radiotherapy.

For patients with multiple brain metastases, despite advances in stereotactic radiosurgery and new systemic treatments (immunotherapy and targeted therapy for example), estimates of overall survival at 2 years and at 5 years for all types of primary tumors are approximately 8% and 2% respectively. Consequently, there is still a huge unmet medical need for these patients.

Dr. Camille Verry, principal investigator of this clinical trial and national coordinator of the ongoing NANORAD 2 multicenter trial reports:

“The results of this phase 1 study are very encouraging, with the demonstration of a favorable tolerance of AGuIX as a candidate drug in humans and a remarkable distribution in brain metastases. The simplicity of the intravenous use of these nanoparticles combined with first elements in favor of a radiosensitizing effect allow to think that AGuIX could be a drug of choice in the future for neuro-oncology, if results are confirmed”.

Markus Loeffler, Chief Medical Officer of NHT, comments:

“Following this trial, the company entered phase 2 with 2 clinical trials focusing on radiotherapy of brain metastases, either by whole brain radiation therapy (NANORAD 2), or in a complementary manner by stereotactic radiosurgery/radiotherapy (NANOBRAINMETS). NANORAD 2 is a French multicenter randomized trial (100 patients) piloted by the CHU Grenoble Alpes (p.i. Dr Camille Verry). It combines whole brain radiation therapy with 3 intravenous injections of AGuIX at 100 mg/kg. NANOBRAINMETS is a trial (134 patients) led by the Dana Farber Cancer Institute - Harvard (p.i. Dr Ayal Aizer). In this trial, stereotactic radiation is combined with 2 intravenous injections of AGuIX at 100 mg/kg, to have better tumor control and increase patient survival”.

About AguiX

The drug candidate AGuIX, whose potential efficacy is based on nanoscale structuring, is administered by intravenous injection. It combines three essential assets to fight tumors and accessible from the same injection: target, image and treat. AGuIX technology is therefore part of the theranostic concept which corresponds to a combination of therapy (radiosensitizing effect) and diagnosis (visible in MRI), and more broadly in the personalized medicine of tomorrow, without changing the patient's care path. Due to its biodistribution and mode of action, the nanomedicine AGuIX has a broad spectrum of action against solid tumors, 60% of which are treated by radiotherapy.

²[Targeting brain metastases with ultrasmall theranostic nanoparticles, a first-in-human trial from an MRI perspective.](#) Verry C, Dufort S, Lemasson B, Grand S, Pietras J, Troprès I, Crémillieux Y, Lux F, Mériaux S, Larrat B, Balosso J, Le Duc G, Barbier EL, Tillement O. **Sci Adv.** 2020 Jul 15; 6(29).

About the company NH TherAguix (www.nhtheraguix.com)

NH TherAguix is a French biotech start-up based in Grenoble and created in 2015 by two co-founding scientists, Prof Olivier Tillement (Scientific advisor of NH TherAguix and Director of the Fennec team, Institute Lumière Matière, University of Lyon 1) and Géraldine Le Duc (CEO of NH TherAguix), after 10 years of preclinical research. The technology of the drug candidate AGuIX is supported by 14 patent families and more than 70 scientific publications. The production of AGuIX is handled by partners such as Sanofi and Carbogen. The team currently consists of 19 people and its board of directors is chaired by Hervé Brailly (Co-founder and current chairman of the supervisory board of Innate Pharma). The company is pursuing its strategy ambitiously as it is currently focused on its clinical development in the USA and on the preclinical development of a second-generation drug.

About CHU Grenoble Alpes (www.chu-grenoble.fr)

In the Top 10 of the best hospitals in France, CHU Grenoble Alpes (CHUGA) is the benchmark and referral institution for hospitals in the Alpine Arc. With more than 10,000 professionals, the CHUGA welcomes 900,000 patients each year. Efficient in all medical specialties and with state-of-the-art equipment, the CHUGA has many areas of excellence, both in medical care and in research. It is the first French university hospital to be certified at level A in its entirety and in first intention by the college of the High Authority of Health (HAS). The CHU Grenoble Alpes has great potential in many research fields on which its scientific notoriety is based. With more than 1,400 clinical research protocols in active file, more than 1,000 new publications and 5,000 healthy patients and volunteers included each year, the Delegation for Clinical Research and Innovation at CHU Grenoble Alpes ranks 12th nationally.

Contacts :

Géraldine Le Duc
CEO & Co-founder
leduc@nhtheraguix.com

Isabelle Dray
Press Relations
idray@actifin.fr