

Glioblastoma

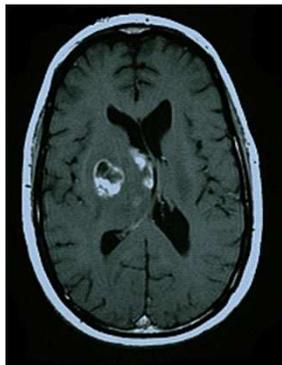
Glioblastoma is the **most aggressive and most prevalent** of the primary brain tumours.

It is invariably fatal with most patients **dying within 12 months of diagnosis**

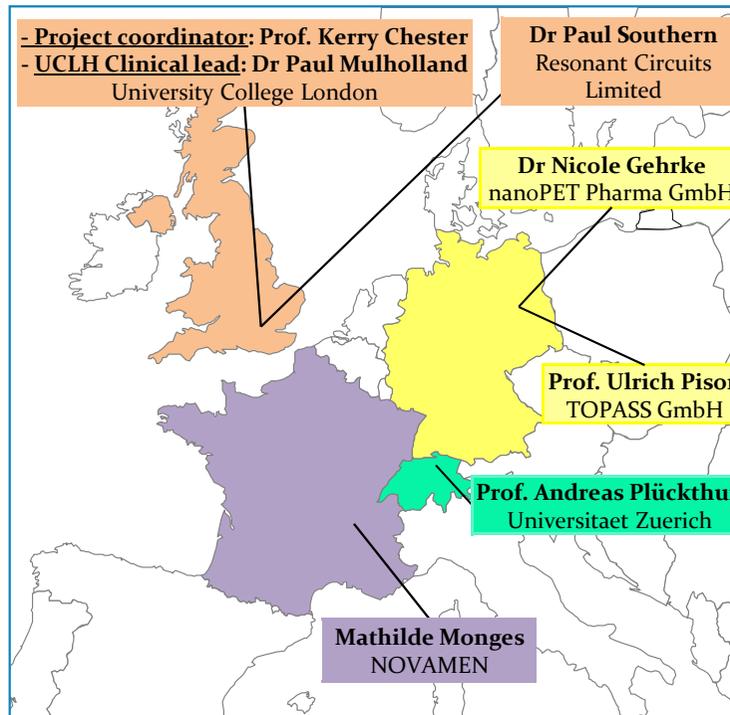
37,400 people were diagnosed with brain and other central nervous system tumours in Europe in 2001.

Current treatment can involve **chemotherapy, radiation and surgery.**

No standard treatment exists for the management of **patients with recurrent/relapsed glioblastoma.**



Consortium

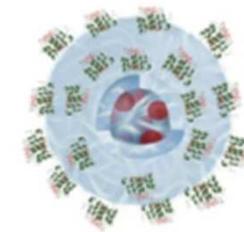


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Dartrix

DARPin Targeted Magnetic Hyperthermic Therapy for Glioblastoma



www.dartrix.eu



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DARTRIX, DARPIn Targeted RX (therapy) is a multidisciplinary collaborative project that will develop high-affinity protein scaffolds to create a new generation of targeted therapeutics for the treatment of glioblastoma. There is great need; glioblastoma is virtually incurable and most patients die within 12 months of diagnosis. DARPins are small, non-immunoglobulin human protein scaffolds that can be engineered to incorporate additional favourable properties to target glioblastoma cells with exceptionally high affinity.

The new DARPins will be coupled to Ferucarbotran, a form of Super Paramagnetic Iron Oxide

Nanoparticles (SPION) more usually employed for Magnetic Resonance Imaging (MRI). When stimulated by an appropriate alternating magnetic current, SPION generate heat that can kill cancer cells very effectively. The conjugation of DARPins with SPION (**DARTRIX** particle) leads to a potent therapeutic for thermal ablation of glioblastoma.

The consortium has all the skills and knowledge to develop DARPins from bench-to bedside for glioblastoma treatment. This **DARTRIX** particle will pioneer targeted hyperthermic cancer treatment of glioblastoma in an innovative adaptive first-in-human trial.

DARTRIX specific objectives

1. To develop new efficient and safe therapy against glioblastoma and improve life expectancy of patients
2. To generate new affinity heat-stable DARPins specifically to target cell surface markers/subsets of glioblastoma cells
3. To engineer the new DARPins to avoid non-specific uptake (e.g. by macrophages)
4. To create a range of **DARTRIX** particles based on the new DARPins and designed to optimize treatment
5. To develop efficient GMP-compatible systems for scale up and manufacture of DARTRIX particles with stable formulation
6. To evaluate the safety, toxicity, dose and therapeutic potential of the **DARTRIX** particle *in vitro* using a range of human brain cells
7. To test the safety; immunogenicity, toxicity, dose and efficacy of the **DARTRIX** particles *in vivo* using a mouse xenograft model of human glioblastoma
8. To Evaluate the **DARTRIX** particles in a first-in-human trial in glioblastoma, using MRI to confirm delivery of the particles followed by therapeutic hyperthermia for treatment

Targeted hyperthermic cancer treatment of glioblastoma

Drug engineering

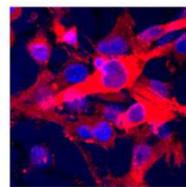
DARPIn: Specific cancer cell targeting



DARTRIX particle: New glioblastoma treatment

Ferucarbotran: killing cells by heat

In vitro evaluation of DARTRIX particle



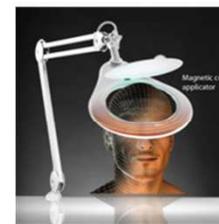
Test on human brain cells

Pre-clinical trial



Test on mouse xenograft model of human glioblastoma

First-in-man clinical trial on glioblastoma



Kill cancer cells using targeted heat and DARTRIX particle

01/03/2012 to 28/02/2017