

# Brain Tumour treatment.

## Priority Number

n. 102015000086815 \_ 22.12.2015.

## Patent Type

Patent for invention.

## Ownership

Sapienza University of Rome 100%.

## Inventors

Flavia Trettel, Cristina Limatola, Stefano Garofalo.

## Industrial & Commercial Reference

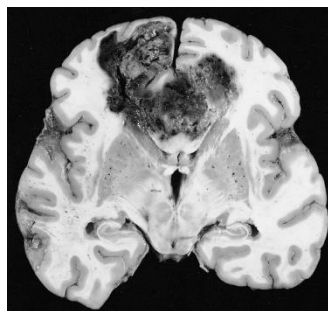
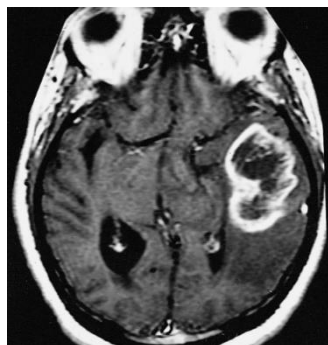
Drug to counteract the progression and development of glioma.

## Time to Market

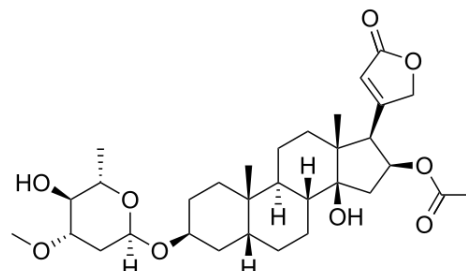
The practical applications in the medium term might concern the development of preclinical studies, in order to obtain information regarding the mechanism of action and the pharmacokinetics of oleandrin. In the long term, in case of a proven efficacy of the molecule, it will be possible to proceed to the determination of the safety, tolerability, pharmacokinetics and pharmacodynamics of the oleandrin in human subjects suffering from glioblastoma.

## Availability

Cession, Licensing, Research, Development, Experimentation and Collaboration.



Glioblastoma multiforme.



Oleandrin structure formula.

## Abstract

We propose the use of Oleandrin, a botanic drug derived from Nerium oleander, to counteract glioma tumor development inducing selective tumor cell death, but also modifying tumor microenvironment hindering tumor progression.

Glioma is the most diffuse and aggressive neoplasm of the nervous system, characterized by high invasion and proliferation, diffuse apoptosis and necrosis, astrogliosis, and microglia/macrophage infiltration, with a poor prognosis.

Standard therapy consists of surgery, radio- and chemotherapy with temozolomide but in spite of these treatments, glioma invariably recurs with limited increase of patient survival.

Available treatments at relapse are largely ineffective and median overall survival of GBM patients is about 15 months, thus there is an urgent need to find adjuvant or alternative treatments to contrast glioma progression.

## Publications

- ❖ Trettel F., Limatola C. et al. (2017) The glycoside oleandrin reduces glioma growth with direct and indirect effects on tumor cells. J. Neurosci. 37:3926 –3939.

## KEYWORDS

- ❑ ONCOLOGY
- ❑ BRAIN TUMOR
- ❑ GLIOBLASTOMA (GMB)
- ❑ OLEANDRIN
- ❑ ANTICANCER TREATMENT

## AREA

- ❑ PHARMACEUTICAL

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# Brain Tumour treatment.

## Technical Description

For the first time, transplanting murine glioma cells in the brain of wt mice, or human glioblastoma cells (both glioblastoma cell lines or primary glioma cells) in the brain of SCID mice, we found that upon daily intraperitoneal injection of oleandrin, in mice bearing tumor cells, there is a significant reduction in tumor volume and increase in the survival of these mice compared to mice not treated with oleandrin.

Moreover in animals treated with oleandrin together with Temozolamide, there is significant increase in mice survival compare to animals treated with Temozolamide alone.

With in vivo and in vitro experiments we characterized the mechanism of action of oleandrin and found that:

- oleandrin impaired glioma development by inhibiting tumor cell proliferation, inducing selective tumor cell death, and reducing tumor cell migration and invasion;
- oleandrin, acting on the brain parenchyma, induces the release of a soluble factor from neurons with

consequent reduction in microglia/macrophage infiltration and phagocytic activity in the tumor mass, a reduction of peritumoral astrogliosis, thus favoring an anti-tumoral microenvironment.

All together these results encourage the use of oleandrin as new co-adjuvant agent in clinical trials for glioma treatment.

## Technologies & Advantages

With this invention we paved the road for a new therapeutic approach for the treatment and prevention of brain tumors, such as glioma, and in particular glioblastoma, demonstrating the efficacy of using the cardioactive glycoside oleandrin as co-adjuvant drug to standard chemotherapeutics such as temozolomide.

The innovative aspect of this invention is that with this molecule we can limit tumor development acting both on tumor cells but also on tumor microenvironment inducing the release of brain endogenous molecules that counteract tumor development and propagation..

## Applications

The present invention relates to a pharmaceutical composition comprising the oleandrin for the treatment and / or prevention of a brain tumor.

In particular, oleandrin is used for the treatment and / or prevention of glioma, preferably in combination with another anti-tumor and therapeutic treatment.



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