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UCLA Department of Neurology

# Partners *in* Discovery



UCLA NEURO-ONCOLOGY PROGRAM:

# MEETING THE CHALLENGE OF GLIOBLASTOMA

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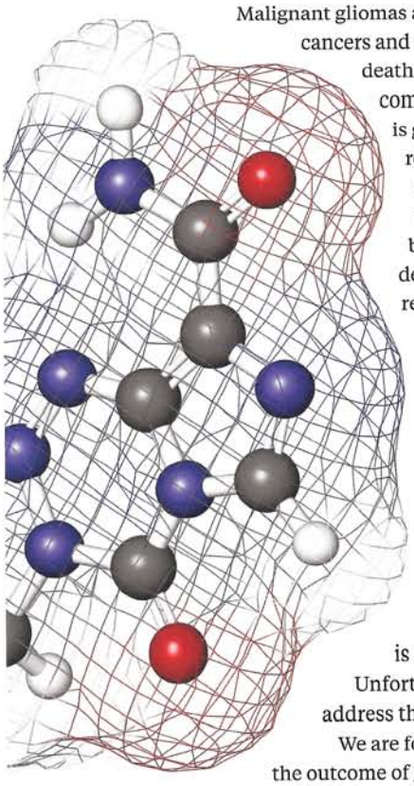

Malignant gliomas are among the most lethal of human cancers and the second leading cause of cancer deaths among young adults. The most common of the malignant gliomas is glioblastoma. Although this is a relatively rare tumor, compared to lung, breast and prostate cancer, its ability to infiltrate and damage the surrounding brain makes it a particularly devastating tumor. Complete surgical removal is impossible.

Glioblastoma also is one of the most resistant tumors to radiation and chemotherapy, which accounts, in part, for the poor survivorship rates. What's more, while the best way to treat any cancer is either to prevent it or catch it early, this approach is unavailable to glioblastoma patients at present. We do not know how or what causes this tumor to form and the tumor is only detectable when fully formed. Unfortunately, this means that we can only address the tumor once it is identified.

We are focusing all of our efforts on changing the outcome of glioblastoma. The UCLA Neuro-Oncology program has committed to evaluating numerous well designed and cutting-edge clinical trials that approach killing the tumor or controlling it through a variety of mechanisms. These include: molecularly guided small-molecule and antibody-targeted therapy, gene transfer therapy with viruses, and immune- based therapies utilizing antibodies to release the native inhibitory effects of the immune system preventing tumor cell kill and control. We offer these trials to any and all patients with glioblastoma with the goal of rapidly defining which populations will achieve the best possible results. We work to refine and improve these results toward a cure.

## UCLA CLINICAL TRIALS

### UCLA MOLECULARLY GUIDED TRIALS

Our goal is to identify a molecular target in the brain tumor that is responsible for the growth and progression of the tumor and then to treat it with a specific inhibitor.

**Target:**

- EGFR: This is the most common molecular abnormality in glioblastoma, present in more than 50 percent of patients. Currently, the following molecularly guided trials are being offered to patients with EGFR-mutated tumors:
- Neratinib: Small molecule targeting amplified EGFR-recurrent malignant glioma
- AMG595: Antibody drug conjugate against EGFR vIII-recurrent malignant glioma
- IDH1 and IDH2: These molecular abnormalities are common in lower grade gliomas, seen predominantly in young adults. Currently the following molecularly guided trials are being offered to patients with IDH-mutated tumors:
- AG120 and AG221: Small molecule targeting IDH mutated recurrent malignant glioma
- FGFR: This is a rare but very targetable mutated receptor in glioblastoma.
- BGJ398: Small molecule targeting FGFR mutated recurrent malignant gliomas
- Other Targets: Many tumors have commonly activated molecular pathways leading to growth and progression. Although not directly mutated, these pathways can be targeted to slow or stop tumor progression. The following agents are used either alone or in combination to treat glioblastoma:
- GDC0084: Small molecule targeting PI3k/TOR Kinase in recurrent malignant gliomas
- MLN0128: Small molecule targeting TOR Kinsase in surgically accessible recurrent malignant gliomas
- AMG386: Antibody against Tie2 and used with bevacizumab in recurrent malignant gliomas.

### UCLA GENE TRANSFER THERAPY

This form of clinical trial utilizes genetically engineered viruses to infect and deliver a gene of choice to the tumor that will cause it to die or become susceptible to death from another treatment.

**Gene-transferred Cytosine deaminase:**

- Toca 511: replication competent retrovirus transferring cytosine deaminase to recurrent malignant glioma cells to create susceptibility to orally administered 5FC

### UCLA IMMUNE-BASED THERAPIES

These trials use therapies that allow the immune system to kill tumor cells by releasing factors , called Immune Check-Point Inhibitors, which inhibit the immune system from successful tumor control. UCLA offers the following immune-based therapies:

- Nivolumab and Ipilimumab: These are antibodies against PD-1 and CTLA-4 that release the inhibitory effects of the immune system to attack malignant glioma.