

Immune-Based Treatments for Brain Cancer Post Impressive Early-Stage Results



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According to NCI/NIH statistics, approximately 19,000 individuals in the US are diagnosed with primary brain cancers each year (with a similar number estimated to occur in Europe) with Temodar (temozolomide or TMZ) given to nearly every patient with a diagnosis of GBM, which is the most common and aggressive form of primary brain cancer. Newly diagnosed individuals with GBM typically undergo surgery to remove the tumor, followed by radiation (RT) and chemotherapy (TMZ).

In May 2009, Roche (OTC:RHHBY) announced that the FDA granted accelerated approval (based on Phase 2 data, including OS of 9.2 months for recurrent GBM) of Avastin (bevacizumab) for the treatment of patients with GBM that have progressive disease following prior therapy. In March 2010, **Health Canada also approved Avastin** for use as a single agent for the treatment of patients with GBM after relapse or disease progression following prior therapy. Avastin is not yet approved in Europe for GBM and Roche is currently conducting a Phase 3 AVAGLIO study for this indication.

In addition, Eisai (OTC:ESALY) markets the Gliadel Wafer (polifeprosan 20 with carmustine implant), which is indicated in patients with newly diagnosed high-grade malignant glioma as an adjunct to surgery and radiation, as well as in patients with recurrent GBM as an adjunct to surgery.

Below is a summary analysis of published data for the treatment of GBM, with the following abbreviations used throughout: RT=radiation therapy, TMZ=Temodar (chemotherapy), n=number of patients evaluated, PFS=progression free survival (listed in months), OS=overall survival (listed in months), 1Y=one-year, 2Y=two-year.

1.) **Stupp et al. New England Journal of Medicine (NEJM), March 2005** (historical control)

a.) RT+TMZ

n=287 PFS=6.9 OS=14.6 1Y-OS=61.1% 2Y-OS=26.5%

2.) **Grossman et al. ASCO 2009.** Summary data presented below for three novel agents + RT + TMZ evaluated in single-arm Phase 2 studies with the same eligibility criteria.

a.) Talampanel (no PFS data)

n=60 OS=20.3 1Y-OS=78% 2Y-OS=42%

b.) Poly ICLC (no PFS data)

n=85 OS=18.3 1Y-OS=79%

c.) Celingitide (no PFS data) (Merck KGaA, OTC:MKGAY)

n=102 OS=21.9 1Y-OS=82%

3.) **Sampson et al. ASCO 2009 Poster Presentation** (CDX-110, Celldex/Pfizer)

a.) ACTIVATE study: RT+TMZ+CDX-110

n=18 PFS=14.2 OS=26 1Y-OS=94% 2Y-OS=53%

b.) ACT II study: RT+TMZ+CDX-110

n=22 PFS=15.2 OS=23.6 1Y-OS=100% 2Y-OS=50%

c.) Matched historical control: RT+TMZ

n=17 PFS=6.3 OS=15 1Y-OS=70% 2Y-OS=6%

4.) **Yu et al. 2009.** A phase I trial of tumor associated antigen-pulsed dendritic cell immunotherapy for patients with glioblastoma.

Presented at the Congress of Neurological Surgeons Annual Meeting on October 26, 2009. (ICT-107, IMUC)

a.) RT+TMZ+ICT-107 (median OS data not yet reached, estimated at 36 months)

n=16 PFS=17.7 1Y-OS=100% 2Y-OS=75%

ImmunoCellular Therapeutics Ltd. (OTCBB:IMUC) - \$1.10, market cap = \$18 million

ICT-107 autologous (patient-derived) dendritic cell (DC) therapeutic cancer vaccine candidate

IMUC expects to apply for Orphan Drug status 2Q10 and expects to begin a Phase 2 study during 4Q10. As previously reported, a Phase I study showed median progression-free survival (PFS) of 19 months in GBM patients. ICT-107 targets six cancer-specific peptide antigens (a multi-epitope cancer vaccine targeting the following: HER2, TRP-2, gp100, MAGE-1, IL13R alpha, and AIM-3), including targets that are highly expressed on cancer stem cells.

ICT-121 (off-the-shelf + adjuvant therapeutic cancer stem cell or CSC vaccine candidate)

IMUC has identified novel peptides to broaden the potential use and has filed for a provisional US patent. IMUC expects an IND filing for GBM during 2H10 and may begin a Phase I study for this indication by year-end 2010 while also exploring the possibility of a licensing / development agreement as it focuses its resources on the Phase 2 development of ICT-107 as a priority for in-house development.

Peregrine Pharma (NASDAQ:PPHM) - \$3.15, market cap = \$162 million

Cotara (a targeted, anti-cancer monoclonal antibody, radio-isotope combo)

PPHM has expanded its Phase 2 brain cancer program into the US and expects to complete patient enrollment in the 40-patient study during 2010. In addition, PPHM previously announced published long-term data from prior studies with 25% (7 of 28) GBM patients surviving over 1 year and 3 of 28 (10.7%) patients surviving after five years of treatment

Exelixis (NASDAQ:EXEL) - \$6.66, market cap = \$719 million

XL765 (anti-cancer agent that inhibits PI3K and mTOR or mammalian target of rapamycin)

Phase 1b/2 study with Temodar for GBM

XL184 (anti-cancer agent that inhibits MET, VEGFR2, and RET)

Phase 2 study for GBM

Curis Inc. (NASDAQ:CRIS) - \$3.04, market cap = \$230 million

GDC-0449 (Hedgehog pathway inhibitor, anti-cancer agent)

The National Cancer Institute (NCI) is currently sponsoring a Phase I study in young patients (age 3-21) with medulloblastoma that is recurrent or did not respond to previous treatment, a Phase 2 study in adult patients with recurrent or refractory medulloblastoma, and a Phase 2 study in patients with recurrent GBM that can be removed by surgery.

Celldex Therapeutics (NASDAQ:CLDX) - \$6.17, market cap = \$196 million

CDX-110 (EGFRvIII therapeutic cancer vaccine) (variant of epidermal growth factor receptor, EGFR)

Co-developed with Pfizer (NYSE:PFE) with an ongoing Phase 2 study (ACT III) in patients with newly diagnosed GBM (brain cancer) that is fully enrolled (60 patients).

YM BioSciences (AMEX:YMI) - \$1.19, market cap = \$78 million

Nimotuzumab (nimo) (a humanized epidermal growth factor or EGFR-targeting monoclonal antibody, mAb)

The following are brain cancer related studies for nimo that have expected data in 2010: Phase 3 adult glioma (2Q10), Phase 2 pediatric glioma (3Q10), and Phase 2 brain mets (spread) from lung cancer (4Q10)

In addition, YMI has acquired CYT997 (a small molecule vascular disrupting agent or VDA) with results expected 2Q10 for a Phase I/II study in patients with GBM.

Northwest Biotherapeutics (OTCBB:NWBO) - \$0.83, market cap = \$48 million

NWBO is developing DCVax-Brain as a personalized, active immunotherapy for brain cancer that utilizes a patient's own dendritic cells loaded with their tumor-associated antigens with the goal of achieving a targeted immune response against the tumor with a low incidence of side effects. Last October, NWBO **announced long-term follow-up data** for DCVax-Brain from previously conducted studies and NCT00045968 is the ClinicalTrials.gov identifier for a Phase 2 study in patients with GBM that is not yet recruiting patients.