CNS Disease Update: Glioblastoma (GBM)

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Objectives

- Review presenting symptoms and diagnosis of Glioblastoma
- Describe current treatment options of Glioblastoma
- Explain the role of bevacizumab in treatment of Glioblastoma
- Discuss novel pathways and future targets for treatment of Glioblastoma

Overview of GBM

- Brain cancers account for 1.4% of all new cancer cases
- GBM account for 80% of malignant gliomas
- Survival rates
  - 1-year: 35%
  - 5-year: 5%
- Most common in 6th to 8th decades of life
  - Males > Females
  - Caucasian > African American

SEER Database: http://seer.cancer.gov/
Omuro A., et. al. JAMA 2013;310(17):1842-1850

Overview of GBM

- Risk Factors
  - Ionizing radiation
    - Only established environmental risk factor
  - Cell phone use, head trauma, foods containing N-nitroso compounds, aspartame, electromagnetic fields, pesticides
    - Inconclusive results
- Hereditary syndromes → increased risk of glioma
  - Li-Fraumeni
  - Neurofibromatosis (I, II)
  - Cowden
  - Turcot
  - Tuberous sclerosis
  - Familial schwannomatosis

Chandana SR, et. al. Am Fam Physician. 2008;77(10):1423-1430
Omuro A., et. al. JAMA 2013;310(17):1842-1850

Presenting Symptoms of GBM

Symptom	Incidence
Headache - often unilateral, throbbing	50%
Seizures	15-25%
Hemiparesis	30-50%
Cognitive changes	40-60%
Nausea/vomiting, gait abnormalities, urinary incontinence, aphasia, visual field defects	Variable

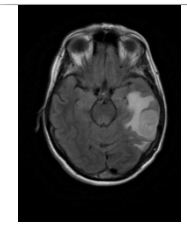
DeAngelis LM. N Engl J Med 2001;344(2):114-123

Diagnosis of GBM

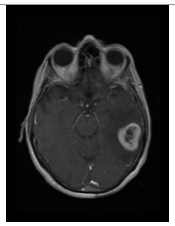
- Imaging is an important initial step in diagnosis
  - CT with contrast
    - Used in acute setting
    - May miss small tumors, brainstem tumors, non-enhancing tumors
  - MRI with gadolinium
    - Preferred study for anatomical evaluation
    - GBM: presents with a central area of T1 hypointensity, representing necrosis, surrounded by a ring-enhancing lesion, representing active tumor

Tonn J-C, et. al. Oncology of CNS Tumors. 2010:147-160

Brain Imaging: MRI with Gadolinium



FLAIR



T1 + Contrast

Diagnosis of GBM

- While radiographic imaging is useful, pathology = gold standard for diagnosis (biopsy or resection)
  - GBM pathology characterized by:
    - Increased cellularity and pleomorphism
    - Higher mitotic rate
    - Presence of vascular proliferation
    - Necrosis

Tonn J-C, et. al. Oncology of CNS Tumors. 2010:147-160

Diagnosis of GBM

- WHO classifies primary brain tumors based on cellular origin and histologic appearance
  - Low grade tumors – Grade I, Grade II
  - High grade tumors – Grade III, Grade IV
  - Grading is critical, determines prognosis and treatment
- Staging not routinely used
  - Gliomas rarely metastasize beyond the CNS; therefore tumor size (T), nodal status (N), and metastasis (M); not applicable

Tonn J-C, et. al. Oncology of CNS Tumors. 2010:147-160

Question

Patient LR is a 68 y/o F in excellent health who runs 2 miles/day. When patient is preparing for her afternoon run, she has a generalized tonic-clonic seizure. Patient is seen in the ER for management. She undergoes imaging of her brain with an MRI and is found to have a 3 cm mass in her frontotemporal region. The MRI shows a ring-enhancing lesion. What is the next step for LR?

A. Initiate treatment with chemotherapy
B. Undergo biopsy/resection
C. Refer to radiation oncologist for treatment
D. Discuss hospice with patient due to GBM diagnosis

Treatment Modalities for GBM

- Local control
  - Surgery
    - Biopsy, gross total resection, local antineoplastic agents
  - Radiation
    - External beam
- Systemic control
  - Chemotherapy
  - Targeted therapy
  - Immunotherapy

Chandana SR, et. al. Am Fam Physician. 2008;77(10):1423-1430

Surgery

- Resection is the initial intervention
  - Gross total excision – associated with longer survival and improved neurologic function
  - Biopsy only – in non-surgical candidates; due to tumor location (basal ganglia, thalamus, brain stem or corpus callosum)
  - May implant Gliadel® wafers (carmustine) into tumor bed after resection
    - Modest survival benefit shown in phase III study in 2003
    - Toxicities: brain edema, infection, seizures
- Goals: relieve mass effect, achieve cytoreduction, provide adequate tissue for histologic evaluation

DeAngelis LM. N Engl J Med 2001;344(2):114-123 Omuro A., et. al. JAMA 2013;310(17):1842-1850
Westphal M., et al. Neuro Oncol. 2003;5(2):79-88

Radiation

- After surgery, adjuvant radiotherapy should be considered in all patients
  - Typical radiotherapy dose: 60 Gy in 30 divided fractions
  - Meta-analysis demonstrated improved PFS for surgery followed by radiotherapy ($p<0.00001$)
    - Resection alone → 14 to 18 weeks
    - Resection, subsequent radiotherapy → 34 to 38 weeks

Omuro A., et. al. JAMA 2013;310(17):1842-1850
Laperriere N., et. al. Radiother Oncol 2002;64(3):259-73

Radiation

- Types
  - Intensity modulated radiation therapy (IMRT)
  - Stereotactic radiosurgery (SRS)
  - Brachytherapy
- IMRT preferred due to better targeting capability
  - IMRT > SRS > brachytherapy

Omuro A., et. al. JAMA 2013;310(17):1842-1850
Laperriere N., et. al. Radiother Oncol 2002;64(3):259-73

Radiochemotherapy

- Newly diagnosed patients (histologically confirmed GBM)
- n = 573 patients from 85 centers
- Primary end point is overall survival (OS)

↓

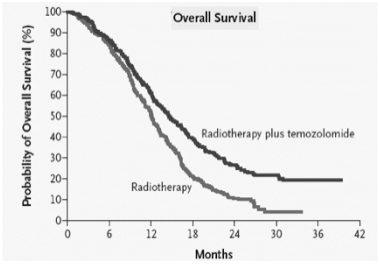
RANDOMIZE

Radiotherapy alone (total of 60 Gy)

Radiotherapy + Continuous daily temozolomide (75 mg/m2)

Stupp R., et. al. N Engl J Med. 2005;352(10):987-96

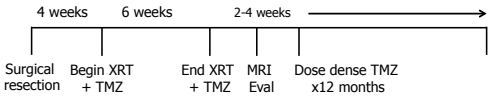
Radiotherapy plus Concomitant and Adjuvant Temozolomide for Glioblastoma



- Median OS: XRT only → 12.1 mos, XRT+Temo → 14.6 mos
- 2 year survival: XRT only → 10%, XRT+Temo → 26%

Stupp R., et. al. N Engl J Med. 2005;352(10):987-96

Standard of Care: Newly Diagnosed GBM



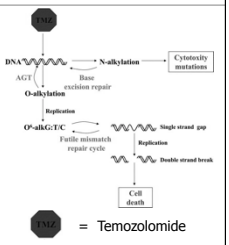
- TMZ dosing during radiation therapy
  - 75 mg/m2 po daily x42 days
- Goal: To complete 12 cycles (28-day) with dose-dense TMZ (150 – 200 mg/m2 on days 1 through 5, off 23 days)
- MRI evaluation every 2 months for assessment; if progressive, therapy is changed

XRT: radiation therapy
TMZ: temozolomide

Stupp R., et. al. N Engl J Med. 2005;352(10):987-96

Temozolomide

- Alkylating agent
  - Delivers a methyl group to purine bases of DNA
  - Interrupts DNA synthesis → cell death
- Dosing schedules
  - Dose dense: 150 – 200 mg/m2 po daily x5 days, off 23 days
  - Metronomic: 50 mg/m2 po daily x28 days



Zhang M., et. al. Semin Radiat Oncol. 2006;16(1):29-37
Kong DS., et al. Neuro Oncol 2010;12(3):289-96

Question

LR undergoes a gross total resection of her mass and per pathology report, patient is diagnosed with a left frontotemporal GBM (WHO Grade IV). She is referred to a radiation oncologist for adjuvant chemoradiation. What dose of temozolomide (TMZ) should she receive with radiation (XRT)? After completion of radiation, what should be the next step in treatment?

A. TMZ 50 mg/m2; continue TMZ 50 mg/m2 daily
B. TMZ 75 mg/m2; change TMZ dosing to 50 mg/m2 daily
C. TMZ 50 mg/m2; change TMZ dosing to 5-day (175 mg/m2)
D. TMZ 75 mg/m2; change TMZ dosing to 5-day (150 mg/m2)
E. Pt should not receive TMZ/XRT; initiate 5-day TMZ (200 mg/m2)

Temozolomide: Adverse Effects

- Common AE
  - GI: nausea/vomiting, constipation
  - Hematologic: lymphopenia, thrombocytopenia, anemia, leukopenia
  - Non-hematologic: increased LFTs
  - Constitutional: fever, myalgia
  - Allergic reaction
- Clinical pearls
  - Monitor ANC, platelet count at baseline and during treatment
  - PCP risk – prophylaxis required for all patients receiving concomitant temozolomide and radiotherapy

Temozolomide [package insert]. New Jersey: Merck; 2008

Temozolomide: MGMT

- O (6)-methylguanine-DNA-methyltransferase (MGMT) demethylates alkyl groups that are placed by temozolomide
- Low MGMT levels associated with better response to temozolomide
- Methylation of the promoter of the MGMT gene is associated with a better prognosis

Heigi ME., et. al. N Engl J Med 2005;352:997-1003

Temozolomide: MGMT

- n = 206 newly diagnosed GBM patients (in conjunction from study comparing XRT versus XRT + TMZ)
- Study question: Is MGMT promoter methylation associated with a benefit from temozolomide treatment?

→ **Determine methylation status of MGMT promoter** → **OUTCOME**

Heigi ME., et. al. N Engl J Med 2005;352:997-1003
Stupp R., et. al. N Engl J Med. 2005;352(10):987-96

TMZ = Temozolomide

Temozolomide: MGMT

- Is MGMT promoter methylation associated with a benefit from temozolomide treatment?
  - MGMT promoter was methylated in 45 percent of 206 assessable cases
  - Methylated MGMT Promoter: median OS 21.7 months
  - Unmethylated MGMT Promoter: median OS 15.3 months
  - $P < 0.001$
- Irrespective of treatment, MGMT promoter methylation was an independent favorable prognostic factor

Heigi ME., et. al. N Engl J Med 2005;352:997-1003

Recurrent GBM Treatment

- In spite of optimal treatment, malignant gliomas will recur
  - Median time to progression from first line treatment of GBM → 7 to 10 months
- Focus of most clinical trials
- Treatment options
  - Re-resection
  - Radiotherapy
  - Low-intensity alternating electric fields (device)
  - Chemotherapy/Targeted Agents

Omuro A., et. al. JAMA 2013;310(17):1842-1850
DeAngelis LM. N Engl J Med 2001;344(2):114-123

Recurrent GBM Treatment

- Re-resection: prolong survival for 6 months
  - Gliadel® wafer implantation: median overall survival increased from 11.6 to 13.9 months
- Radiation therapy: SRS, if possible based on location
- Low-intensity alternating electric fields applied to the brain through a portable device
  - Novocure or NovoTTF-100A
  - Phase III non-inferiority study, showed equivalent efficacy
  - Role in GBM remains unclear

Omuro A., et. al. JAMA 2013;310(17):1842-1850
DeAngelis LM. N Engl J Med 2001;344(2):114-123
Westphal M., et al. Neuro Oncol. 2003;5(2):79-88
Stupp R., et. al. Eur J Cancer. 2012;48(14):2192-2202

Recurrent GBM Treatment

- Standard chemotherapy and targeted agents
  - Temozolomide rechallenge
    - Change the dosing schedule from 5-day to metronomic
  - Irinotecan
    - Dose: 125 mg/m2 IV q2weeks (non-enzyme inducing)
    - Dose: 340 mg/m2 IV q2weeks (enzyme inducing)
  - Lomustine
    - Dose: 110 mg/m2 po q6weeks
    - Dose: 82.5 mg/m2 po q6weeks (in heavily pre-treated patients)
  - Carboplatin
    - Dose: AUC 4 in combination
    - Dose: AUC 5 single agent
    - Often used with irinotecan
  - Etoposide
    - Dose: 50 mg/m2 po 14 days on and 14 days off q28days
    - Dose: 50 mg/m2 po 21 days on 7 days off q28days
  - Targeted biologic agents
    - Bevacizumab
    - Numerous others

DeAngelis LM. N Engl J Med 2001;344(2):114-123
Stupp R., et. al. Eur J Cancer. 2012;48(14):2192-2202

GBM Over-expresses Vascular Endothelial Growth Factor (VEGF)

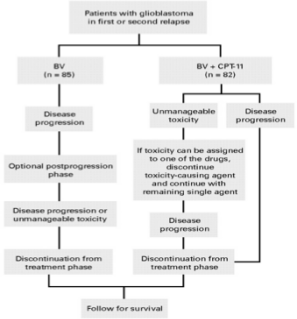
- GBM
  - Highly vascularized tumors
  - High levels of VEGF expression
- VEGF
  - Is the primary growth factor responsible for tumor angiogenesis
- Targeting VEGF could lead to tumor cell death and new treatment options in GBM

Tsai JC., et. al. J Neurosurg. 1995;82(5):864-73

Bevacizumab

- Mechanism
  - Monoclonal antibody to VEGF
- Dosing
  - 10 mg/kg IV q2weeks
- Common AE
  - Hypertension, fatigue, delayed wound healing, proteinuria, DVT/PE, stroke, heart attack, joint pain, GI perforation
- Clinical Pearl
  - Cannot have invasive procedures (including dental work) for 4 to 6 weeks after discontinuation due to delayed wound healing
  - Monitor CBC with dif, UA, and CMP routinely

BRAIN Study: Bevacizumab vs Bevacizumab/Irinotecan in Recurrent GBM

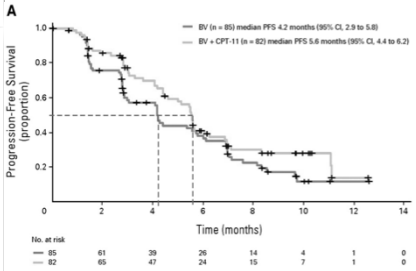


- Phase II, multicenter, open-label, non-comparative trial
- Primary end points
  - 6-month PFS
  - Objective response rate
- Secondary end points
  - Safety
  - Overall survival

- BV: bevacizumab
  Dose: 10 mg/kg IV q2weeks
- CPT-11: irinotecan
  Dose: 125 mg/m2 IV q2weeks (non-enzyme inducing)
  Dose: 340 mg/m2 IV q2weeks (enzyme inducing)

Friedman HS, et al. JCO 2009;27:4733-4740

BRAIN Study



Friedman HS, et al. JCO 2009;27:4733-4740

BRAIN Study

- Estimated 6-month PFS rates were 42.6% (97.5% CI, 29.6% to 55.5%) in the BV group and 50.3% (97.5% CI, 36.8% to 63.9%) in the BV + CPT-11 group
- Exceeded 15% assumed rate for salvage chemotherapy and CPT-11 alone ($p < 0.0001$)
- Led to FDA approval of bevacizumab
  - Treatment of recurrent GBM

Friedman HS, et al. JCO 2009;27:4733-4740

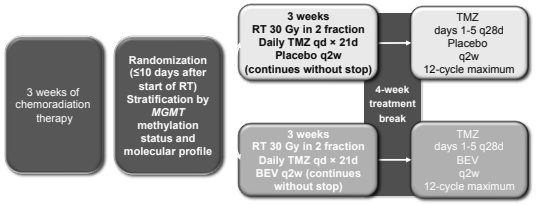
Role of Bevacizumab in the Newly Diagnosed Setting?

- Two large randomized controlled phase III trials (RTOG 0825, AVAglio)
- RTOG 0825
  - Designed to evaluate first-line or early use of bevacizumab
  - Primary Endpoints: OS and PFS
  - Patients stratified based on *MGMT* promoter methylation and a 9-gene signature at baseline (independent predictors of outcomes)
  - Prior to being randomly assigned, all patients received 3 weeks of CRT
  - Patients with newly diagnosed glioblastoma were assigned to
    - CRT with TMZ and placebo (standard of care) n = 317 pts
    - CRT with TMZ and bevacizumab 10 mg/kg IV q2weeks n = 320 pts
  - Following study treatment, patients continued to receive temozolomide for 12 cycles and placebo or bevacizumab q2weeks
  - At disease progression, treatment was un-blinded and cross-over allowed

Gilbert MR, et al. Am Soc Clin Oncol. 2013. Abst 01

CRT: chemoradiotherapy

RTOG 0825 Study Design



BEV = bevacizumab; TMZ = temozolomide; RT = radiotherapy; RTOG = Radiation Therapy Oncology Group

http://www.rtog.org/ClinicalTrials/ProtocolTable/StudyDetails.aspx?study=0825

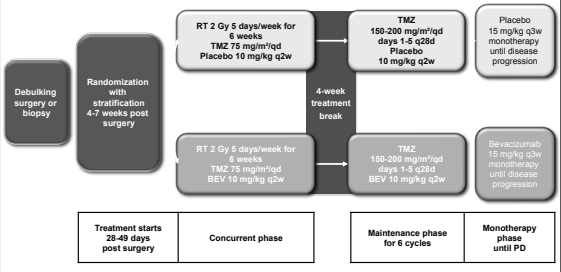
Role of Bevacizumab in the Newly Diagnosed Setting?

- Two large randomized controlled phase III trials (RTOG 0825, AVAglio)
- AVAglio
  - Designed to evaluate efficacy/safety of combining bevacizumab with standard of care
  - Primary Endpoints: OS and PFS
  - Patients with newly diagnosed glioblastoma were randomly assigned to 6 weeks of therapy
    - CRT with temozolomide and placebo (standard of care) n = 463 pts
    - CRT with temozolomide and bevacizumab 10 mg/kg IV q2weeks n = 458 pts
  - Following study treatment, patients continued to receive temozolomide for 6 cycles either with placebo or bevacizumab 10 mg/kg IV q2weeks
  - Continued on to receive placebo or bevacizumab 15 mg/kg IV q3weeks
  - At disease progression, treatment was un-blinded and cross-over allowed

Chinot OL, et. al. Adv Ther. 2011;28(4):334-340
Gilbert MR, et al. Am Soc Clin Oncol. 2013. Abst 01

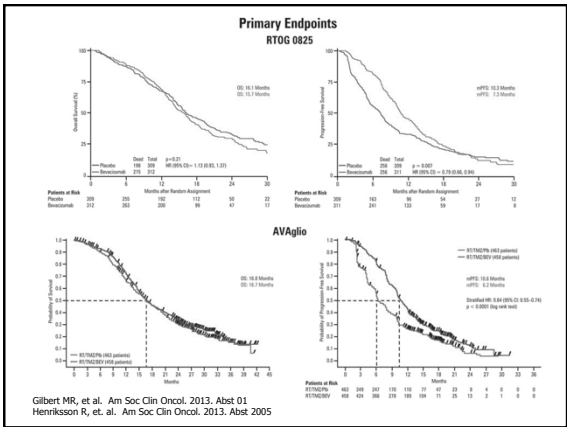
CRT: chemoradiotherapy

AVAglio Study Design



Chinot OL, et. al. Adv Ther. 2011;28(4):334-340

TMZ = Temozolomide; BEV = bevacizumab; PD = progressive disease



Gilbert MR, et al. Am Soc Clin Oncol. 2013. Abst 01
Henriksson R, et al. Am Soc Clin Oncol. 2013. Abst 2005

Question

LR is tolerating the 5-day temozolomide well with no AE and is now cycle 4, day 12 of treatment. She begins to experience the following symptoms: headaches, mainly in the morning when she wakes, and word-finding difficulties. Pt has an MRI and returns to the neuro-oncologists office for evaluation. Pts husband also notes that she has become more agitated recently. Brain imaging as well as clinical presentation both signify disease progression. Which of the following is **not** an appropriate treatment recommendation?

A. Consider a clinical trial
B. Initiate irinotecan with bevacizumab
C. Continue 5-day temozolomide and add bevacizumab
D. Change to metronomic temozolomide and bevacizumab
E. Consider re-resection or additional XRT

Current Thoughts: Bevacizumab and Use in GBM

- Bevacizumab active against recurrent GBM
- Bevacizumab does not have a clear role in newly diagnosed GBM
- Bevacizumab resistance is critical to be evaluated in GBM and new treatment paradigms needed

Nagane M, et. al. Cancers 2013;5:1456-1468

Future Directions

- Pathways
  - IDH1/IDH2 mutations
  - TERT mutations
- Immunologic Therapies
  - Vaccine therapy
    - Dendritic Cell Vaccines
    - EGFR-vIII Vaccines
  - Targeted viruses
    - PVS-RIPO

IDH: isocitrate dehydrogenase
TERT: telomere reverse transcriptase
PVS-RIPO: attenuated poliovirus vaccine

IDH1/IDH2 Mutations

- IDH = isocitrate dehydrogenase
  - IDH1: cytoplasmic, IDH2: mitochondrial
- Colon Cancer, Acute Myeloid Leukemias
  - Incidence: 12-18%
  - IDH2 > IDH1 mutations
- Secondary GBM
  - Incidence: 60-90%
  - IDH1> IDH2
    - Associated with a better prognosis

Presner JR, et. al. Nat Med. 2011 Mar;17(3):291-3

TERT Mutations

- TERT = Telomere reverse transcriptase
  - Telomerase is encoded by the TERT gene
  - Normal Cells
    - Telomeres shortened with each cell division
  - Tumor Cells
    - Telomeres continuously elongated by telomerase
- GBM with TERT promoter mutations
  - Shorter survival

Nonoguchi N, et. al. Acta Neuropathol. 2013 Dec;126(6):931-7

Immunologic Therapies

- Vaccine therapy
  - Dendritic Cell Vaccines
  - EGFR-vIII Vaccines
- Oncolytic viruses
  - PVS-RIPO

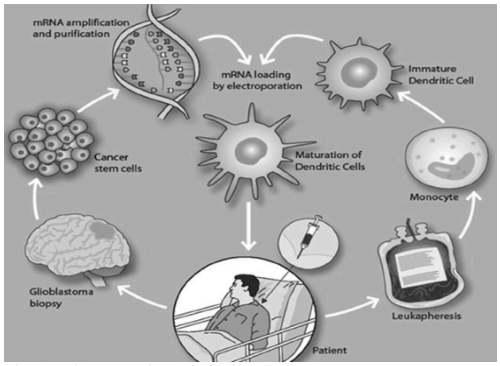
PVS-RIPO: attenuated poliovirus vaccine

Dendritic Cell Vaccines

- Autologous dendritic cells (DCs)
  - Commonly used as antigen presenting cells
  - Shown to activate Natural Killer (NK) cells, NK T cells
- Tumor antigen-loaded DCs
  - Injected into patient (intradermally)
  - Migrate to lymph nodes to activate tumor antigen specific cytotoxic T lymphocytes
  - Induce sustained anti-tumor response by forming immunological memory

Hedge M, et. al. Discov Med. 2014 Mar;17(93):145-54

Dendritic Cell Vaccine Process



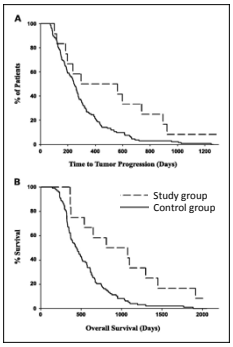
Vik-Mo EO, et. al. Cancer Immunol Immunother (2013) 62:1499–1509

Dendritic Cell Vaccine Trial

- Phase I trial to evaluate feasibility, safety, and induction of systemic and intracranial T-cell responses in GBM patients
- Study design
  - n = 12 patients in a multi-cohort dose-escalation study, treated with tumor antigen-loaded DCs
  - Three biweekly intradermal vaccinations
  - All patients had histologically proven GBM

Liau LM, et. al. Clin Cancer Res 2005;11:5515-5525

Dendritic Cell Vaccine Results



Efficacy

- Time to Tumor Progression
  - Study group 15.5 mo
  - Control group 8.2 mo
  - P = 0.028
- Overall Survival
  - Study group 23.4 mo
  - Control group 18.3 mo
  - P = 0.006

Liau LM, et. al. Clin Cancer Res 2005;11:5515-5525

Dendritic Cell Vaccine Safety

- Safety assessments
  - Evaluation for autoimmune symptoms
  - Neurologic exams done before and 30 min after each vaccination and at all follow-up visits
- Toxicities
  - Well tolerated with no grade 3 or 4 AE
  - No clinical/radiographic signs of autoimmune reactions
  - Grade 1 to 2 AE
    - Low-grade fevers, fatigue, malaise, nausea/vomiting, injection site reactions, transient lymph node swelling, diarrhea, constipation

Liau LM, et. al. Clin Cancer Res 2005;11:5515-5525

EGFR-vIII Target for Treatment

- EGFR gene mutations are frequent in GBM
  - A deletion mutation EGFR-variant III (EGFR-vIII) is the most common
    - Expressed in 20 – 30% of GBM
    - Plays a role in tumorigenesis and development of chemoresistance
    - Correlated with worse prognosis, decreased OS
    - Not expressed in normal brain tissue

Hedge M, et. al. Discov Med. 2014 Mar;17(93):145-54
Babu R, et. al. Core Evid. 2012;7:93-103

EGFR-vIII Vaccine Therapy

- Rindopepimut (CDX-110)
  - An injectable peptide vaccine against GBM tumors that express EGFR-vIII
  - Phase I, II clinical trials in GBM demonstrated significantly increased median time to progression, overall survival comparing rindopepimut to matched historical controls
    - Serious AE are rare, patients typically only experiencing hypersensitivity reactions at injection site
  - Phase III placebo-controlled multi-center studies currently under investigation

Babu R, et. al. Core Evid. 2012;7:93-103

EGFR-vIII Vaccine Therapy

- Study
  - Placebo-controlled, randomized, phase III study
  - To investigate efficacy and safety of addition of rindopepimut to current standard of care (TMZ) in patients with recently diagnosed GBM
- Intervention
  - Two intradermal injections 2 weeks apart, followed by monthly injections until tumor progression or intolerance

Celldex Therapeutics. In ClinicalTrials.gov: NCT01480479 TMZ: temozolomide

EGFR-vIII Vaccine Therapy

- Study
  - Primary Outcome
    - Overall Survival
      - During treatment q3months
      - From end of treatment through end of study (up to 5 yrs)
  - Secondary Outcome Measures
    - PFS: from day 1 through progression or initiation of other therapy
    - Safety and Tolerability: until follow-up

Celldex Therapeutics. In ClinicalTrials.gov: NCT01480479 TMZ: temozolomide

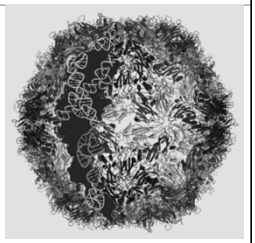
EGFR-vIII Vaccine Therapy

- Study Timeline
  - Start: November 2011
  - Estimated completion: November 2016
- Estimated Enrollment
  - N = 700 patients

Celldex Therapeutics. In ClinicalTrials.gov: NCT01480479

Polio Virus Vaccine

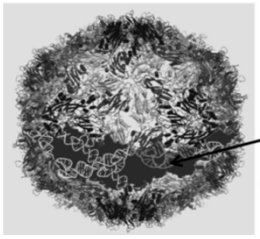
- Polio Virus Receptor
  - Present on many cancer cells
    - GBM
    - Prostate
    - Pancreas
    - Lung
    - Melanoma
    - Breast



PVS-RIPO: attenuated poliovirus vaccine

Bigner DD. In ClinicalTrials.gov: NCT01491893
Image: http://www.cancer.duke.edu/btc/modules/Research3

Safe Tumor-Killing Modified Poliovirus



"Common Cold" Virus Insert Makes Poliomyelitis Impossible, but Tumor-Killing Possible

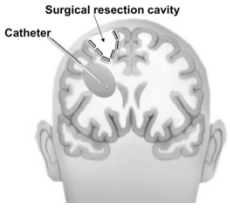
- Protein shell (blue, red and green) arranged in a symmetric structure
- Virus genome (yellow, pink)
  - Sabin vaccine (yellow)
  - Rhinovirus (pink)

Image: http://www.cancer.duke.edu/btc/modules/Research3

DukeMedicine

Polio Virus Vaccine (PVS-RIPO)

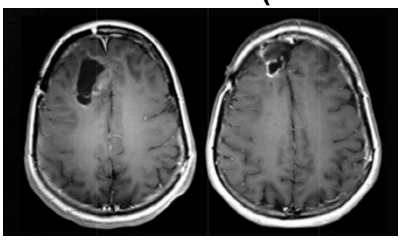
How does it work?



- Infused directly into tumor through convection-enhanced delivery via catheter
- Once inside the tumor, PVS-RIPO infects and kills tumor cells
- Immune system is trained to recognize viral infections → responds against infected tumor

Image: http://www.cancer.duke.edu/btc/modules/Research3

Polio Virus Vaccine (PVS-RIPO)



- Before treatment (04.26.12)
- 27 x 12 mm tumor
- After treatment (01.31.14)
- Only scar tissue remains

Boudin M, et. al. *People Magazine* 05 May 2014; 81(18): 174-8

Future Directions of PVS-RIPO

- Still in early stages of study (Phase I)
- Determine mechanisms of immune response against the tumor
- Phase II/III trials
  - In adults and children with GBM
  - In other cancer types (pancreas, prostate, lung, colon, etc)
  - In brain metastasis

Summary

- Even with currently approved therapies survival rates for GBM remain poor
- Mainstays in treatment: temozolomide and bevacizumab
  - Challenge for new agents: ability to cross the blood brain barrier
- Bevacizumab resistance is critical for evaluation, new treatments are needed
- Immunotherapy is focus of future studies

Self-Assessment Questions

?

Self-Assessment Questions

Which of the following is the most common presenting symptom of a Glioblastoma?

a. Seizures
b. Headaches
c. Aphasia
d. Cognitive changes
e. Visual field defects

Self-Assessment Questions

Which of the following is the first-line treatment for newly diagnosed Glioblastoma?

a. Bevacizumab
b. Irinotecan
c. Temozolomide
d. Lomustine
e. Carboplatin

Self-Assessment Questions

Bevacizumab now has FDA approval for the treatment of newly diagnosed Glioblastoma?

a. True
b. False

Self-Assessment Questions

Vaccine therapy, such as Rindopepimut, uses the EGFR-vIII target as a novel treatment of Glioblastoma?

a. True
b. False