What’s New in Neuro-Oncology: Updates from Recent ASCO Meetings

Sponsored by the University of Chicago Brain Tumor Center & the Heinrich Kluver Memorial Lectureship Endowment
Welcome and Introduction

Infiltrating gliomas remain the most common and, therefore, vexing, clinical problem in neuro-oncology. Significant advances in patient outcomes have been slow, despite substantial investments of creative thinking, time, energy, and financial resources. Our goals are: 1) to review recent clinical trial results and 2) to discuss their impact on future directions and challenges in providing optimal care.
PROBLEMS UNIQUE TO NEURO-ONCOLOGY

- Small changes in tumor size and location can have significant impact on functional status.
- Brain anatomy and physiology limit therapeutic options.
  - Surgery
  - Radiotherapy
  - Chemotherapy
PROGRAM

• Bevacizumab in Glioblastoma
  • M. Kelly Nicholas, MD, PhD

• Anaplastic Gliomas
  • Rimas Lukas, MD

• Combining Chemotherapy and Radiotherapy in Low Grade Gliomas
  • Steve Chmura, MD, PhD

DISCUSSION
Bevacizumab in Glioblastoma: Results of Randomized Clinical Trials and Future Directions

M. Kelly Nicholas, MD, PhD
Associate Professor
University of Chicago
Clinical Developments in Glioblastoma


SURGERY
STEROIDS
RADIOThERAPY
NITROSOUREAS
GLIADEL®
TEMOZOLOMIDE
BEVACIZUMAB
NOVOCURE®

THE UNIVERSITY OF CHICAGO MEDICINE & BIOLOGICAL SCIENCES
Bev in Newly Diagnosed GBM

• 2013 ASCO Presentations
  – RTOG-0825
    • Prospective PCRCT: “SOC” +/- Bev
  – AvAglio (first at SNO, 11/12)
    • Prospective PCRCT: SOC +/- Bev
  – Glarius
    • SOC vs. Bev/CPT-11
      – Unmethylated MGMT promoter
  – BINGO
    • SOC with Bev (open-ended dosing)
Bevacizumab in newly diagnosed GBM: The phase III data

**AVAglia** | **RTOG-0825**
---|---
$n = 921$ | $n = 637$

**Similarities:**
- Both prospective, randomized, and placebo-controlled
- Both allowed for cross-over from placebo to Bev at progression
- Primary endpoints were OS and PFS
- Shared secondary endpoints:
  - symptom burden
  - QOL and neuro-cognitive function
  - adverse events
Bevacizumab in newly diagnosed GBM:
The phase III data

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<th>AVAglio</th>
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**Differences:**

- AvaGlio used TMZ adjuvantly for 6 cycles but continued Bev/P to progression
- RTOG-0825 used TMZ and Bev/P adjuvantly for 12 cycles
  (note: Placebo-to-Bev crossover could extend treatment)
- Differences in Image interpretation, including statistics
- RTOG:
  - 9 gene signature (required adequate tissue for eval)
  - Advanced imaging component
**OS**

Bev = 15.7  
P = 16.1

**PFS**

Bev = 10.7  
P = 7.3

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**AVAglio**

Bev = 16.8  
P = 16.7

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**AVAglio**

Bev = 10.6  
P = 6.2
Bev in the World of Regulatory Agencies

- **Food and Drug Administration**
  - Accelerated approval for recurrent GBM stands for now

- **European Medicines Agency**
  - Not currently approved for any indication

- **Japanese Ministry of Health and Welfare**
  - approved for all malignant gliomas regardless of stage
Progression Free Survival

- Generally defined as the length of time from study entry/treatment onset to documented progression (usually radiographic +/- concurrent worsening of symptoms.
  - RECIST
  - MacDonald
  - RANO
Progression Free Survival

pre-Bev to post-Bev

DWI/ADC changes
Progression and QOL

Post-Bev progression
QOL in AVAglio and RTOG-0825

• AVAglio
  • HrQOL better with Bev
  • Steroids less with Bev
  • KPS better longer with Bev

• RTOG-0825
  • HrQOL worse with Bev
  • Neuro-cognitive function worse with Bev
  • Symptom burden worse with Bev
Predictive Markers: RTOG-0825

The 9-gene platform was not predictive of response in 0825.

Those with both favorable MGMT and 9-gene status had worse outcomes.

Focus now on a 42-gene profile.

A multigene predictor of outcome in glioblastoma.
Colman H et al.
GLIOBLASTOMA

Targeting Angiogenesis:
Where do we stand?
Targeting Angiogenesis in Glioblastoma: where do we stand?

• Bevacizumab is one of several angiogenesis inhibitors under investigation in GBM.
• Based upon evidence to date, there is no survival advantage to using Bev in newly diagnosed GBM.
• A more detailed explanation of recent clinical trial findings is warranted.
• Further clinical trials are essential.