Bevacizumab in combination with temozolomide and regional radiation therapy for up-front treatment of patients with newly-diagnosed glioblastoma

Design and analysis of single-arm Phase II clinical trial for maximal information.

Albert Lai, M.D., Ph.D.
Associate Professor-in-Residence
UCLA Neuro-oncology Program
Department of Neurology

Controversies dealing with the clinical trials
Feb. 1st, 2013
Early randomized trial data is now available. How did we do?
Background Objectives

• Review current standard of care for glioblastoma (GBM)
  – Upfront versus recurrent
• Discuss MGMT methylation as a predictive biomarker
• Discuss emergence of recurrent treatment with bevacizumab
• Discuss timing of bevacizumab treatment either upfront versus at recurrence
Glioblastoma (GBM)

- Most common primary malignant brain tumor
  - Approx. 13,000 new cases per year in the United States
- ~15-20 month median overall survival with treatment
- Highly vascularized tumor with high levels of basal vascular endothelial growth factor (VEGF) production
- Reasons for poor outcome
  - Tumor cell migration/invasion
  - Relatively chemo and radiation insensitive
  - Molecular heterogeneity
- Personalized therapies will be required
Phase III Study Established Radiation + Temozolomide as Standard of Care for Newly-Diagnosed GBM

Concomitant TMZ/RT*  Adjuvant TMZ

0  6  10  14  18  22  26  30  Weeks

Surgery

Temozolomide 75 mg/m^2 po qd for 6 weeks (Bactrim given), then 150-200 mg/m^2 po qd day 1-5 q 28 days for 6 cycles

Regional fractionated RT daily — 30 x 200 cGy
Total dose 60 Gy

Standard of Care Outcome for Newly-Diagnosed Glioblastoma (GBM)

- TMZ + radiation (RT) is better than RT alone
- Modest improvement from 12.1 to 14.6 months median overall survival
- Improvement in 12-month progression-free survival from 9.1% to 26.9% (PFS 5.0 to 6.9 months)
- TMZ/RT can be the backbone for other upfront trials

Tumor MGMT Promoter Methylation Associated with Increased Benefit From TMZ

- MGMT promoter methylation associated with improved outcome for those treated with RT/TMZ (dark blue vs orange)
  - Median survival of 12.7 months vs 21.7
- Those without MGMT promoter methylation derive minimal benefit from TMZ (dark blue vs red)
  - 11.8 vs 12.7
- MGMT methylation is also prognostic (RT only) (red vs light blue)
  - 11.8 vs 15.3

Promoter Methylation Results in Gene Silencing of MGMT

**Unmethylated CpG Island of a Tumor Suppressor Gene**

Activators, Histone Acetyltransferases (HATs) and the Basal Transcriptional Machinery Protect the Island

\[ \text{Normal Cell} \]

CpG

RNA Transcription

**Hypermethylated CpG Island**

Transcriptional Repressors, Histone Deacetylases (HDACs), Histone Methyltransferases (HMTs), DNA Methyltransferases (DNMTs) and Methyl-CpG Binding Proteins (MBDs) “Invade” the Island

\[ \text{Cancer Cell} \]

Transcription is Abolished

**Fig. B3.** Diagram of CpG island methylation of gene expression. Cancer cells commonly have hypermethylation of promoter CpG islands. This results in interference of transcriptional machinery leading to silencing of gene expression. Taken from (Esteller 2005).

**MGMT IHC**

High protein expression

Low protein expression
MGMT Promoter Methylation Can Be Determined by PCR-based Tests Performed on Paraffinized Tissue

Methylation specific PCR

Bisulfite methylation sequencing

Un-methylated MGMT promoter

Methylated MGMT promoter
Bevacizumab (BV)

- Humanized anti-VEGF antibody administered intravenously
- Anti-angiogenic and anti-edema effects
- FDA approved as single agent for recurrent glioblastoma in May 2009
Vascular Endothelial Growth Factor

- Homodimer, MW 45,000
- Central pathway in tumor biology
- Endothelial cell mitogen, survival factor, and permeability factor
- Promotes blood vessel formation and edema

Anti-VEGF therapy with Avastin (bevacizumab) has promising activity against GBM

- GBM is a highly vascularized tumor that produces high levels of VEGF.
- VEGF promotes blood vessel formation and edema.
- Avastin is an antibody delivered intravenously that neutralizes VEGF.

Features of Recurrent GBM Response to Avastin and Chemotherapy (CPT-11)

Before

6 wks after

Decreased contrast enhancement

Decreased edema
Phase II Randomized Study BRAIN (AVF3708g) for Recurrent GBM - Both arms received BV

167 patients with glioblastoma in first or second relapse
Prior radiotherapy and temozolomide
Stratification by
- Karnofsky score
- First, second relapse

Bevacizumab (n=85)
Bevacizumab + irinotecan (n=82)

First progressive disease (PD)

Optional post-PD phase
Bevacizumab + irinotecan (n=44)

• Primary endpoints:
  - Objective response rate, and
  - 6-month PFS (PFS6) by independent radiologic review

• Clinical, neurocognitive, and tumor assessments by MRI were performed every 6 weeks
## BRAIN Efficacy Outcomes

<table>
<thead>
<tr>
<th>IRF-Determined Outcome</th>
<th>BEV (n=85)</th>
<th>BEV+CPT-11 (n=82)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em><em>Objective response rate</em>, n (%)</em>*</td>
<td>24 (28.2)</td>
<td>31 (37.8)</td>
</tr>
<tr>
<td>Complete response</td>
<td>1 (1.2)</td>
<td>2 (2.4)</td>
</tr>
<tr>
<td>Partial response</td>
<td>23 (27.1)</td>
<td>29 (35.4)</td>
</tr>
<tr>
<td><strong>6-Month PFS (%) (compare with ~20% as control)</strong></td>
<td>42.6</td>
<td>50.3</td>
</tr>
<tr>
<td><strong>Median overall survival, months (95% CI)</strong></td>
<td>9.3</td>
<td>8.9</td>
</tr>
<tr>
<td></td>
<td>(8.2 to 11.8)</td>
<td>(7.9 to 11.9)</td>
</tr>
</tbody>
</table>

*Based on modified Macdonald criteria.
**Based on July 2008 cutoff.

IRF=Independent radiology facility, BEV=bevacizumab, CPT-11=irinotecan; PFS=progression-free survival, CI=confidence interval.
Corticosteroid Dose Decreases Over Time for All Patients With Baseline Use

Baseline corticosteroid dose was the average dose within 4 days prior to first treatment. All corticosteroids were converted to decadron equivalent dose. BEV=bevacizumab; CPT-11=irinotecan.
Nonstandardized Controlled Oral Word Association test scores (not presented) were stable for most patients.
BEV=bevacizumab; CPT-11=irinotecan; DR=Delayed Recall; HVLT-R=Hopkins Verbal Learning Test-Revised; IRF=independent review facility; RECOG=Recognition; TMTA=Trail Making Test Part A; TMTB=Trail Making Test Part B; TR=Total Recall.
BV appears to improve survival and QOL.

No non-BV arm.
FDA Approval for single-agent BV in May 2009 based on the BRAIN study

• Does this trial tell us whether BV is actually helpful?

• How does BV really work?
  – Anti-angiogenic
  – Direct anti-tumor
  – Potentiation of concomitant chemotherapy
  – Anti-edema, corticosteroid reduction

• Would it be better to use BV upfront instead of waiting till recurrence?
Phase II Study of Bevacizumab Plus Temozolomide During and After Radiation Therapy for Patients With Newly Diagnosed Glioblastoma Multiforme


See accompanying editorial on page 124
Upfront trial of BV, RT and TMZ

• Can we provide useful preliminary data to guide large randomized trials (now ongoing)
• What is the optimal time to initiate BV?
• Could early use of BV preferentially improve outcomes for MGMT unmethylated patients?
• Are there other subgroups that may preferentially benefit?
Study Rationale and Design

- To investigate whether bevacizumab is safe and effective for up-front treatment of GBM
  - 70 Patient Open-label Multicenter Non-randomized phase II trial
    - UCLA, Kaiser Permanente Northern and Southern California
    - Genentech-sponsored trial
  - Bevacizumab is combined with standard backbone of RT/TMZ
  - Bevacizumab given concurrently with radiation
    - exploit possible synergy (e.g. neutralize VEGF induced by RT)
  - Frozen tissue collection required for correlative molecular analysis
Study Objectives

- Primary endpoint
  - Overall survival (from diagnosis)
- Secondary endpoints
  - Progression-free survival (from diagnosis)
    - Response retrospectively determined by imaging (T1 contrast and T2 changes) using modified Levin criteria\(^1\) or clinical deterioration
  - Feasibility, toxicity and safety
  - Correlative tissue analysis
    - MGMT promoter methylation
    - Gene expression, copy number, and methylation profiling

\(^1\)Levin et al. 1977
Inclusion and Exclusion Criteria

- GBM or GS
- Frozen tissue collection at diagnosis
- Age ≥ 18 yo
- KPS ≥ 60
- Adequate bone marrow, liver, and renal function
- Treatment to commence within 3-6 weeks from surgery

- No previous RT or chemo
- No Gliadel wafer
- No prior history of active malignancy in previous 3 years
- History cerebral or myocardial infarction in previous 6 months
- Major surgery (excluding craniotomy) within 28 days of treatment
- BP >150/100
- Urine protein:creatinine ratio > 1.0
- Anti-coagulation acceptable
BV + RT/TMZ Study Schema

Treatment arm

A

Bevacizumab
Temozolomide
Radiation

0 6 wks

Recurrence
This was not a randomized prospective study

- Report single-arm results
- Compare with published historical benchmark-2005 trial (14 mo)
  - Overall survival has increased (18-20 mo)
- Derive control group from same patient population (UCLA/KPLA)
Comparison with a derived UCLA/KPLA historical control
# Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Current study (n=70)</th>
<th>UCLA/KPLA control (n=110)</th>
<th>EORTC-NCIC (n=287)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Enrollment by site</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>UCLA</td>
<td>38 54%</td>
<td>61 55%</td>
<td>-</td>
</tr>
<tr>
<td>Kaiser</td>
<td>32 46%</td>
<td>49 45%</td>
<td>-</td>
</tr>
<tr>
<td><strong>Age, years</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>57.4</td>
<td>59.4</td>
<td>56</td>
</tr>
<tr>
<td>Range</td>
<td>31.3 - 75.8</td>
<td>20.5 - 90</td>
<td>19 - 70</td>
</tr>
<tr>
<td>&lt;50</td>
<td>15 21%</td>
<td>30 27%</td>
<td>95 33%</td>
</tr>
<tr>
<td>≥50</td>
<td>55 79%</td>
<td>80 73%</td>
<td>192 67%</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>39 56%</td>
<td>70 64%</td>
<td>185 64%</td>
</tr>
<tr>
<td>Female</td>
<td>31 44%</td>
<td>40 36%</td>
<td>102 36%</td>
</tr>
<tr>
<td><strong>Karnofsky Performance Status (KPS)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>100</td>
<td>8 11%</td>
<td>13 12%</td>
<td>-</td>
</tr>
<tr>
<td>90</td>
<td>27 39%</td>
<td>62 56%</td>
<td>-</td>
</tr>
<tr>
<td>80</td>
<td>27 39%</td>
<td>23 21%</td>
<td>-</td>
</tr>
<tr>
<td>70</td>
<td>5 7%</td>
<td>8 7%</td>
<td>-</td>
</tr>
<tr>
<td>60</td>
<td>3 4%</td>
<td>4 4%</td>
<td>-</td>
</tr>
<tr>
<td><strong>Extent of surgery</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biopsy</td>
<td>2 3%</td>
<td>23 21%</td>
<td>48 17%</td>
</tr>
<tr>
<td>Sub Total resection</td>
<td>40 57%</td>
<td>40 36%</td>
<td>126 44%</td>
</tr>
<tr>
<td>Gross Total resection</td>
<td>28 40%</td>
<td>47 43%</td>
<td>113 39%</td>
</tr>
<tr>
<td><strong>Recursive Partitioning Analysis (RPA)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Class III</td>
<td>9 13%</td>
<td>27 25%</td>
<td>42 15%</td>
</tr>
<tr>
<td>Class IV</td>
<td>32 46%</td>
<td>45 41%</td>
<td>152 53%</td>
</tr>
<tr>
<td>Class V</td>
<td>29 41%</td>
<td>37 34%</td>
<td>93 32%</td>
</tr>
<tr>
<td>Class VI</td>
<td>0 0%</td>
<td>1 1%</td>
<td>0 0%</td>
</tr>
<tr>
<td><strong>Follow up (month)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>24.2</td>
<td>41.8</td>
<td>61</td>
</tr>
<tr>
<td>Range</td>
<td>12-40</td>
<td>29-58</td>
<td>-</td>
</tr>
<tr>
<td><strong>Deaths</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>48</td>
<td>69%</td>
<td>89 81%</td>
<td></td>
</tr>
<tr>
<td><strong>Recurrent treatment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Progressed</td>
<td>56 80%</td>
<td>96 87%</td>
<td>272 95%</td>
</tr>
<tr>
<td>Progressed with chemotherapy</td>
<td>39 56%</td>
<td>64 58%</td>
<td>148 52%</td>
</tr>
<tr>
<td>Progressed with BV</td>
<td>29 41%</td>
<td>57 52%</td>
<td>-</td>
</tr>
<tr>
<td><strong>MGMT promoter methylation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methylated</td>
<td>29 41%</td>
<td>28 39%</td>
<td>46 43%</td>
</tr>
<tr>
<td>Unmethylated</td>
<td>41 59%</td>
<td>43 61%</td>
<td>60 57%</td>
</tr>
<tr>
<td><strong>IDH1 Mutational status</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wild type</td>
<td>65 93%</td>
<td>68 96%</td>
<td>-</td>
</tr>
<tr>
<td>R132H</td>
<td>5 7%</td>
<td>3 4%</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>BV/TMZ/RT (n=70)</td>
<td>UCLA / Kaiser control (n=110)</td>
<td>EORTC-NCIC (Stupp, 2005) (n=287)</td>
</tr>
<tr>
<td>---------------------------</td>
<td>------------------</td>
<td>-------------------------------</td>
<td>----------------------------------</td>
</tr>
<tr>
<td><strong>Radiotherapy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median from diagnosis to RT (weeks)</td>
<td>4.14 (3 - 6.9)</td>
<td>4.29 (0.9 – 10.6)</td>
<td>5 (1.7 - 10.7)</td>
</tr>
<tr>
<td>Median total dose of RT delivered (range)</td>
<td>6000 Gy (4200-6000)</td>
<td>-</td>
<td>60 Gy (12–62)</td>
</tr>
<tr>
<td>RT Completed (&gt;90% (%))</td>
<td>91%</td>
<td>-</td>
<td>95%</td>
</tr>
<tr>
<td>RT Interruption/Delay (%)</td>
<td>10%</td>
<td>-</td>
<td>32%</td>
</tr>
<tr>
<td><strong>Temozolomide</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Received &gt;90% of planned concomitant TMZ</td>
<td>89%</td>
<td>-</td>
<td>92%</td>
</tr>
<tr>
<td>Interruption/discontinuation during RT</td>
<td>17%</td>
<td>-</td>
<td>13%</td>
</tr>
<tr>
<td>Achieved full dose during maintenance (of 64)</td>
<td>45%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Interruption during maintenance (of 64)</td>
<td>41%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Bevaczumab</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Received &gt;90% of planned concomitant Bevaczumab</td>
<td>84%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Interruption/discontinuation during RT</td>
<td>16%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Interruption during maintenance (of 64)</td>
<td>42%</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

1Stupp et al., 2005
Hematological toxicity of study group.

| Hematoxicity         | BV+TMZ/RT   | UCLA/Kaiser RT/TMZ | EORTC-NCIC RT/TMZ Control
|----------------------|-------------|---------------------|-----------------------------
|                      | *During RT* | *Post RT* | *During RT* | *Post RT* |                  |
| Anemia               | 2%          | 2%        | 2%          | 0%        | 1%               |
| Leukopenia           | 5%          | 10%       | 7%          | 0%        | 7%               |
| Lymphopenia          | 46%         | 60%       | 41%         | 42%       | Not reported     |
| Neutropenia          | 6%          | 21%       | 6%          | 9%        | 7%               |
| Thrombocytopenia     | 6%          | 19%       | 10%         | 7%        | 12%              |

1Stupp et al., 2005
<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Number of Patients</th>
<th>Grade 3+4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Patients</td>
<td>Grade 3</td>
</tr>
<tr>
<td>CNS cerebrovascular ischemia</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>CNS hemorrhage</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Dizziness/lightheadedness/syncope</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Elevated ALT</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Elevated AST</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Elevated creatinine</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Epistaxis</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Fatigue</td>
<td>14</td>
<td>0</td>
</tr>
<tr>
<td>GI Bleed</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>GI perforation</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Hyponatremia</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Ocular</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Other infection</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Seizure</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Venous thrombosis/pulmonary embolism</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Wound infection</td>
<td>4</td>
<td>0</td>
</tr>
</tbody>
</table>
BV improves PFS compared to control group whereas OS is not improved.

**Table 2. Cox Proportional Hazard Analysis of Treatment Group**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Progression-Free Survival</th>
<th>Overall Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hazard Ratio</td>
<td>P</td>
</tr>
<tr>
<td>Sex, female</td>
<td>0.59</td>
<td>.0091</td>
</tr>
<tr>
<td>MGMT, methylated</td>
<td>0.47</td>
<td>.0002</td>
</tr>
<tr>
<td>RPA class, III/IV</td>
<td>0.68</td>
<td>.0550</td>
</tr>
</tbody>
</table>

Abbreviations: MGMT, O6-methylguanine DNA methyltransferase; RPA, recursive partitioning analysis.
MGMT Promoter Methylation is Associated with Improved PFS and OS
Pre-specified subset analysis
Prespecified Subgroup analysis for OS shows that MGMT Unmethylated Group may actually do worse with BV.
Pre-specified Subgroup Analysis of Combined RPA V/VI (poor prognosis) Classes Show Early Benefit in OS Between Control and Treatment Arms
Pre-specified Subgroup analysis of Age<,>50 for OS shows worse outcome for <50 patients
PHASE III Ongoing studies

- **RTOG 0825 (720 pt)**
  - PHASE III DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL OF CONVENTIONAL CONCURRENT CHEMORADIATION AND ADJUVANT TEMOZOLOMIDE PLUS BEVACIZUMAB VERSUS CONVENTIONAL CONCURRENT CHEMORADIATION AND ADJUVANT TEMOZOLOMIDE IN PATIENTS WITH NEWLY DIAGNOSED GLIOBLASTOMA

- **ROCHE AVAGLIO (920 pt)**
  - Phase III A randomized, double-blind, placebo-controlled trial to evaluate the efficacy on survival and the tolerability of bevacizumab, radiotherapy (RT) and temozolomide (TMZ) followed by bevacizumab and TMZ, vs placebo, RT and TMZ followed by placebo and TMZ in patients with newly diagnosed glioblastoma.
Interim results of Roche Avaglio

• A 4.4 month improvement in median PFS was observed when people with newly diagnosed glioblastoma received Avastin in combination with radiation and chemotherapy compared to those who received radiation and chemotherapy plus placebo (10.6 months vs. 6.2 months, respectively). Interim results for OS did not reach statistical significance (HR=0.89; p=0.2135). Final data on OS are expected in 2013.
Conclusions

• Our study is not a randomized study.
• Promising activity for PFS in relation historical control
• For OS, BV at progression in control arm may nullify overall survival benefit of BV upfront
• Subgroup analysis shows that MGMT U group is not rescued, that age <50 may do worse, RPA III/VI may do better.
• Study arm appears tolerable
  – Toxicity signal consistent with prior BV studies
  – May be more neutropenia, thrombocytopenia
  – May be less RT interruption
• Single-arm MGMT methylation survival advantage persists with BV
• Phase III study needed to validate these findings
  – ROCHE AVAGLIO, and RTOG 0825
• Correlative studies are required to identify patients that will derive the most (or least) benefit from the addition of BV upfront
Final thoughts

• Well-designed (and analyzed) single arm Phase II study can provide very useful information and early look to guide design of randomized trials (safety and efficacy).

• Subset analysis can guide clinicians as to which groups will derive the most benefit.

• Multivariate analyses must include clinical and molecular variables.

• QOL assessments may be instrumental
Acknowledgements

- Patients, families and Caregivers
- Data-Gabriele Tsung, Emese Filka
- Data analysis/Statistics-Anh Tran
- Database-Michael Quinn, Siliconmed
- Kaiser Northern and Southern California
- UCLA Neuro-oncology Team
- JCCC GCRC
- Genentech
References

UCLA Brain Tumor Program

• UCLA Neuro-Oncology Clinical Team
  – Timothy Cloughesy
  – Albert Lai
  – Leia Ngiemphu
  – Nanette Fong
  – Stacey Green
  – Dan Gamboa
  – Melissa Depillo
  – Dillon Marks
  – Claudia Garcia
• Fellow-Xiao Tang Kong
• Siliconmed
  – Michael Quinn

• UCLA Brain Cancer P.I.
  – Stan Nelson
  – Linda Liau
  – Steve Horvath
  – William Partridge
  – Andrew Charles
  – Hong Wu
  – William Yong
  – Harley Kornblum
  – Robert Prins

• Henry E. Singleton Brain Tumor Program