Systemic Therapy for Small Cell Lung Cancer
Paul A. Bunn, Jr, MD, Dudley Professor, Univ. of Colorado Cancer Center, Aurora, CO, USA

Consultant: Amgen, Allos, AstraZeneca, Abraxis, Bayer, Biodesix, Boehringer-Ingelheim, Bristol-Myers Squibb, Daiichi-Sankyo, Eli Lilly, GlaxoSmithKline, Merck, Novartis, OSI/Genentech/Roche, Poniard, Sanofi Aventis
Epidemiology
- ~26,000 cases in US annually
- Worldwide
  - 10-20% of lung ca in males
  - 10-30% in women
- Causes 35,000-40,000 of 160,000 lung cancer deaths annually

Etiology
- TOBACCO 90%
- Other respiratory carcinogens, underlying lung disease, familial clusters

SEER = Surveillance, Epidemiology, and End Results.
SCLC Biology

• Tumor suppressor loss/silencing
  – 3p loss in 90% of tumors
    • FHIT, VHL, RAR, RassF1
  – Other genes: p53, RB in 80-90%
  – Aberrant methylation: RASSF1

• Expression of activating genes
  – MYC, BCL-2

• Cellular pathways
  – GRP, IGF, c-KIT, TGF-b, PKC, PI3K
Survival by IASLC proposed TNM stage

Years After Enrollment

Deaths / N

Median in Months

<table>
<thead>
<tr>
<th>Stage</th>
<th>Deaths / N</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>17 / 25</td>
<td>31</td>
</tr>
<tr>
<td>IB</td>
<td>14 / 19</td>
<td>35</td>
</tr>
<tr>
<td>IIA</td>
<td>8 / 15</td>
<td>68</td>
</tr>
<tr>
<td>IIB</td>
<td>84 / 101</td>
<td>17</td>
</tr>
<tr>
<td>IIIA</td>
<td>332 / 384</td>
<td>13</td>
</tr>
<tr>
<td>IIIB</td>
<td>424 / 481</td>
<td>12</td>
</tr>
<tr>
<td>IV</td>
<td>1400 / 1439</td>
<td>8</td>
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</table>
## Phase III Trials in Extensive SCLC: Prior to 2000

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Ref</th>
<th>MST (mo)</th>
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</thead>
<tbody>
<tr>
<td>CAV vs CAV/PE</td>
<td>Evans</td>
<td>*8.0 vs 9.6</td>
</tr>
<tr>
<td>CAV vs PE vs CAV/PE</td>
<td>Fukuoka</td>
<td>9.9vs9.9vs11.8</td>
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<tr>
<td>CAV vs PE vs CAV/PE</td>
<td>Roth</td>
<td>8.3vs8.6vs8.1</td>
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<tr>
<td>VIP vs VP</td>
<td>Loehrer</td>
<td>*9.1 vs 7.3</td>
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</tbody>
</table>

*p<0.05
<table>
<thead>
<tr>
<th>Any New Treatment Options?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chemotherapy</strong></td>
</tr>
<tr>
<td>• Topo I Inhibitors</td>
</tr>
<tr>
<td>– Irinotecan</td>
</tr>
<tr>
<td>– Topotecan</td>
</tr>
<tr>
<td>• Dose intensification</td>
</tr>
<tr>
<td>• Pemetrexed</td>
</tr>
<tr>
<td>• Radiation</td>
</tr>
<tr>
<td>• Maintenance</td>
</tr>
<tr>
<td>• Picoplatin</td>
</tr>
<tr>
<td>• Amrubicin</td>
</tr>
<tr>
<td><strong>Targeted Agents</strong></td>
</tr>
<tr>
<td>• Antiangiogenics</td>
</tr>
<tr>
<td>• HDAC inhibitors</td>
</tr>
<tr>
<td>• BCL2 inhibitors</td>
</tr>
</tbody>
</table>
Irinotecan vs Etoposide & Cisplatin: ED SCLC

Noda et al. 2002

Lara et al. 2009

Overall Survival (% of patients)

months

Overall Survival (%)

Time Since Enrollment (months)

Events/n  Median (95% CI)
CDDP/CPT-11 288/324 9.9 (9.2 to 11.1)
CDDP/VP16 285/327 9.1 (8.4 to 9.9)

IP (n = 221)
EP (n = 110)

P = .74

IP: median 9.3 months (0.1-32.6)
1 year 35%, 2 years 8.0%
EP: median 10.2 months (0.3-44.6)
1 year 35.2%, 2 years 7.9%
### Meta analysis EP vs IP

Jiang et al. J. Thor. Oncol. 5,867,2010

![Graph](image)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Camptothecin Events</th>
<th>Camptothecin Total at Risk</th>
<th>Etoposide Events</th>
<th>Etoposide Total at Risk</th>
<th>O-E Variance</th>
<th>Weight</th>
<th>Hazard Ratio</th>
<th>Hazard Ratio</th>
<th>Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
<td>Total</td>
<td></td>
<td></td>
<td>Expl(O-E) / V</td>
<td>Expl(O-E) / V</td>
<td></td>
</tr>
<tr>
<td>1.1.1 Topotecan versus Etoposide</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Enoiri 2006</td>
<td>309</td>
<td>389</td>
<td>299</td>
<td>395</td>
<td>7.3</td>
<td>149.6</td>
<td>23.7%</td>
<td>1.05</td>
<td>[0.89, 1.23]</td>
</tr>
<tr>
<td>Hoogen 2003</td>
<td>290</td>
<td>346</td>
<td>299</td>
<td>334</td>
<td>-10.03</td>
<td>140.22</td>
<td>22.3%</td>
<td>0.93</td>
<td>[0.79, 1.10]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>599</td>
<td>589</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.99</td>
<td>[0.88, 1.11]</td>
</tr>
<tr>
<td></td>
<td>Total events</td>
<td>599</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.99</td>
<td>[0.88, 1.11]</td>
</tr>
<tr>
<td></td>
<td>Heterogeneity: Chi²&lt;sup&gt;2&lt;/sup&gt; = 1.05, df = 1 (P = 0.31); I² = 5%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td>0.99</td>
<td>[0.88, 1.11]</td>
</tr>
<tr>
<td></td>
<td>Test for overall effect: Z = 0.16 (P = 0.87)</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td>0.99</td>
<td>[0.88, 1.11]</td>
</tr>
<tr>
<td>1.1.2 Irinotecan versus Etoposide</td>
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<td></td>
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<td></td>
<td>0.99</td>
<td>[0.88, 1.11]</td>
</tr>
<tr>
<td>Hanna 2006</td>
<td>209</td>
<td>221</td>
<td>100</td>
<td>110</td>
<td>-6.82</td>
<td>67.73</td>
<td>10.7%</td>
<td>0.90</td>
<td>[0.71, 1.15]</td>
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<tr>
<td>Hermes 2008</td>
<td>101</td>
<td>105</td>
<td>101</td>
<td>104</td>
<td>-16.38</td>
<td>47.68</td>
<td>7.6%</td>
<td>0.71</td>
<td>[0.53, 0.94]</td>
</tr>
<tr>
<td>Lara 2009</td>
<td>288</td>
<td>324</td>
<td>285</td>
<td>327</td>
<td>-10.93</td>
<td>147.23</td>
<td>23.4%</td>
<td>0.93</td>
<td>[0.79, 1.09]</td>
</tr>
<tr>
<td>Noda 2002</td>
<td>58</td>
<td>77</td>
<td>65</td>
<td>72</td>
<td>-18.15</td>
<td>35.53</td>
<td>5.6%</td>
<td>0.60</td>
<td>[0.43, 0.83]</td>
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<tr>
<td>Schrevel 2009</td>
<td>89</td>
<td>106</td>
<td>101</td>
<td>110</td>
<td>-8.23</td>
<td>42.13</td>
<td>6.7%</td>
<td>0.82</td>
<td>[0.61, 1.11]</td>
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<tr>
<td>Subtotal (95% CI)</td>
<td>745</td>
<td>652</td>
<td></td>
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<td></td>
<td>0.82</td>
<td>[0.61, 1.11]</td>
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<tr>
<td></td>
<td>Total events</td>
<td>1344</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.82</td>
<td>[0.61, 1.11]</td>
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<tr>
<td></td>
<td>Heterogeneity: Chi²&lt;sup&gt;2&lt;/sup&gt; = 7.25, df = 4 (P = 0.12); I² = 45%</td>
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<td>[0.61, 1.11]</td>
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<tr>
<td></td>
<td>Test for overall effect: Z = 3.28 (P = 0.001)</td>
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<td>0.82</td>
<td>[0.61, 1.11]</td>
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<tr>
<td></td>
<td>Subtotal (95% CI)</td>
<td>1568</td>
<td></td>
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<td></td>
<td>0.82</td>
<td>[0.61, 1.11]</td>
</tr>
<tr>
<td></td>
<td>Total events</td>
<td>1568</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.82</td>
<td>[0.61, 1.11]</td>
</tr>
<tr>
<td></td>
<td>Heterogeneity: Chi²&lt;sup&gt;2&lt;/sup&gt; = 12.73, df = 6 (P = 0.05); I² = 53%</td>
<td></td>
<td></td>
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<td>0.82</td>
<td>[0.61, 1.11]</td>
</tr>
<tr>
<td></td>
<td>Test for overall effect: Z = 2.52 (P = 0.011)</td>
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<td></td>
<td></td>
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<td></td>
<td></td>
<td>0.82</td>
<td>[0.61, 1.11]</td>
</tr>
<tr>
<td></td>
<td>Subtotal (95% CI)</td>
<td>1568</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.82</td>
<td>[0.61, 1.11]</td>
</tr>
<tr>
<td></td>
<td>Total events</td>
<td>1568</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.82</td>
<td>[0.61, 1.11]</td>
</tr>
<tr>
<td></td>
<td>Heterogeneity: Chi²&lt;sup&gt;2&lt;/sup&gt; = 4.44, df = 1 (P = 0.04); I² = 77.9%</td>
<td></td>
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<td></td>
<td>0.82</td>
<td>[0.61, 1.11]</td>
</tr>
<tr>
<td></td>
<td>Test for subgroup differences: Chi²&lt;sup&gt;2&lt;/sup&gt; = 4.44, df = 1 (P = 0.04); I² = 77.9%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.82</td>
<td>[0.61, 1.11]</td>
</tr>
</tbody>
</table>

Topotecan PO vs. BSC for Relapsed SCLC

**Overall Survival**

- **RR 7%, SD 44%**

<table>
<thead>
<tr>
<th>Arm</th>
<th>Med Surv.</th>
<th>6-mo Surv</th>
</tr>
</thead>
<tbody>
<tr>
<td>BSC</td>
<td>13.9 wk</td>
<td>26%</td>
</tr>
<tr>
<td>Topo</td>
<td>25.9 wk</td>
<td>49%</td>
</tr>
</tbody>
</table>

O’ Brien et al, JCO 2006
Any New Treatment Options?

Chemotherapy
- Topo I Inhibitors
  - Irinotecan
  - Topotecan
- Dose intensification
- Pemetrexed
- Radiation
- Maintenance

Targeted Agents
- Picoplatin
- Amrubicin
- Antiangiogenics
- HDAC inhibitors
- BCL2 inhibitors
Intensified Chemotherapy

Jiang et al. Lung Cancer 65,214,2009
## Randomized Trial of TEP vs EP in Extensive SCLC

<table>
<thead>
<tr>
<th>Rx</th>
<th>No. Pts.</th>
<th>OR</th>
<th>CR</th>
<th>MS</th>
<th>1YS</th>
<th>%GR</th>
<th>Febrile</th>
</tr>
</thead>
<tbody>
<tr>
<td>EP</td>
<td>74</td>
<td>48%</td>
<td>4%</td>
<td>11.5</td>
<td>46%</td>
<td>39%</td>
<td>13%</td>
</tr>
<tr>
<td>TEP+G</td>
<td>62</td>
<td>50%</td>
<td>3%</td>
<td>10.5</td>
<td>46%</td>
<td>44%</td>
<td>24%</td>
</tr>
</tbody>
</table>

*Proc. ASCO. 2000;19:484a.*
Phase III Pemetrexed/CB vs Etop/CB

**Eligibility**
- ES-SCLC
- PS 0-2
- No prior chemo

**Stratification factors**
- Center
- PS
- LDH
- Gender
- Age
- No. metastatic sites
- History of brain metastases

**Pemetrexed/CB**
- Pem 500 mg/m², d 1
- Cb AUC 5, d 1
- every 21 days x 6 cycles
- Prophylactic folic acid, B₁₂, dexamethasone

**Etop/CB**
- E 100 mg/m², d 1, 2, 3
- Cb AUC 5, d 1
- every 21 days x 6 cycles

**Results**
- Median (95% CI)
  - Pem-Cb: 3.68 (3.38, 4.2)
  - E-Cb: 5.32 (5.03, 5.85)
- Log rank p<.0001
- PFS HR = 1.79 (90% CI: 1.49, 2.15)

*Socinski, ASCO 2008*
PCI in ED SCLC: Time to Symptomatic brain mets & Survival

**Time to Sx. Br. Mets**

- 1 year: 14.6% vs. 40.4%
- HR: 0.27 (0.16-0.44)
- $p<0.001$

**Overall Survival**

- 1 year: 27.1% vs. 13.3%
- HR: 0.68 (0.52-0.88)  $p=0.003$

![Graphs showing time to symptomatic brain mets and overall survival](image-url)
More extensive RT for ED SCLC?
Ongoing trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>Selection</th>
<th>Standard arm</th>
<th>Experimental arm</th>
<th>Primary endpoint</th>
<th>Expected enrollment</th>
</tr>
</thead>
<tbody>
<tr>
<td>CREST</td>
<td>CR or PR after 4–6 cycles</td>
<td>No thoracic RT</td>
<td>30 Gy/10 fx, 2 wk, once daily to thorax</td>
<td>Overall survival</td>
<td>460</td>
</tr>
<tr>
<td>RTOG 0937</td>
<td>CR or PR after 4–6 cycles platinum-based chemotherapy</td>
<td>No RT to thorax or disease sites</td>
<td>45 Gy/15 fx, 3 wk, once daily to thorax and maximum of 3 residual distant metastasis sites (or 40 Gy/10 fx)</td>
<td>Overall survival</td>
<td>154</td>
</tr>
</tbody>
</table>
Maintenance Therapy for SCLC: Hanna Trial

Hanna, Ann Oncol 13: 95, 2002

**SCLC-ED**

* N = 233

Cis/Etop/Ifos x4 cycles

**CR/PR/SD**

**RAND**

* N = 144

Etoposide 50 mg PO 21 of 28 days x 3

**Observation**

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Maintenance</th>
<th>Observation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progression-Free Surv (mo)</td>
<td>8.2</td>
<td>6.5</td>
</tr>
<tr>
<td>Median Survival (mo)</td>
<td>12.2</td>
<td>11.2</td>
</tr>
<tr>
<td>1-year Survival (%)</td>
<td>51.4</td>
<td>40.3</td>
</tr>
<tr>
<td>3-year Survival (%)</td>
<td>8.8</td>
<td>1.8</td>
</tr>
</tbody>
</table>

- An appropriate place for minimally toxic targeted therapies?
Results of Maintenance Chemo in SCLC
Topotecan vs Placebo: ECOG

- Progression-free survival significantly better with maintenance topotecan (3.7 vs. 2.3 mo)

- Overall survival was no different (9.3 vs. 8.9 mo)

- Grade 4 neutropenia 60%, thrombocytopenia 13%

- Grade 4/5 infection 1.8%
Any New Treatment Options?

Chemotherapy
- Topo I Inhibitors
  - Irinotecan
  - Topotecan
- Dose intensification
- Pemetrexed
- Radiation
- Maintenance

Targeted Agents
- Picoplatin
- Amrubicin
- Antiangiogenics
- HDAC inhibitors
- BCL2 inhibitors
Picoplatin in SCLC: SPEAR Phase III Trial

- Phase 3 SPEAR (Study of Picoplatin Efficacy After Relapse) Trial
- Enrollment completed in March 2009
- 401 patients enrolled at over 100 sites

Secondary line SCLC patients*

Randomized 2:1

Picoplatin* + BSC n=266

BSC alone n=133

Primary endpoint:
Overall Survival
Secondary endpoints:
Progression-Free Survival, Objective Response Rate, Disease Control Rate, Safety

*Prior platinum therapy; failed or progressed by ≤6 months. PS 0–2; life expectancy >8 weeks. Picoplatin 150 mg/m² IV q3w

*Until disease progression or unacceptable toxicity

Negative Trial: Primary endpoint not met but crossover complicated analysis
EORTC 08062 – Phase 2 1st Line SCLC

- Small Cell Lung Cancer (SCLC)
- Extensive Disease
- No prior chemotherapy
- ECOG performance status 0-2
- Measurable disease
Ph. II Amrubicin vs Topotecan in relapsed SCLC

<table>
<thead>
<tr>
<th></th>
<th>Amrub n=50</th>
<th>Topo n=26</th>
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</thead>
<tbody>
<tr>
<td><strong>ORR</strong></td>
<td>44%</td>
<td>15%</td>
</tr>
<tr>
<td><strong>CR</strong></td>
<td>12</td>
<td>3.8</td>
</tr>
<tr>
<td><strong>PR</strong></td>
<td>32</td>
<td>11.5</td>
</tr>
<tr>
<td><strong>SD</strong></td>
<td>22</td>
<td>34.6</td>
</tr>
<tr>
<td><strong>PD</strong></td>
<td>26</td>
<td>34.6</td>
</tr>
</tbody>
</table>

Phase III Trial Failed to Meet Primary Endpoint: 2011 WCLC
Any New Treatment Options?

## Chemotherapy
- **Topo I Inhibitors**
  - Irinotecan
  - Topotecan
- **Dose intensification**
- **Pemetrexed**
- **Radiation**
- **Maintenance**

## Targeted Agents
- **Antiangiogenics**
- **HDAC inhibitors**
- **BCL2 inhibitors**

- **Picoplatin**
- **Amrubicin**
Phase II Cediranib (AZD2171) Recurrent SCLC - CA Consortium

- PI: Suresh Ramalingam MD
- Cediranib daily

- Results
  - Cediranib 45 mg: 7/12 pts did not complete 4 wks tx due to toxicity.
  - Cediranib 30 mg: 13 pts
  - Most common DLT fatigue (grade 2-3 in 6/25)
  - PR/SD: 1/8 (36%)
  - Median PFS 8 wks

Recurrence s/p one prior platin-based regimen

ECOG  PS 0-2
Measurable disease
No brain mets
Phase I Cediranib + EP

Incurable lung ca for whom EP is appropriate

PS 0-2

Treated Brain mets

Cediranib Dose levels
1. 30 mg
-1. 20 mg
-2. 15 mg

EP/cediranib x 6 followed by cediranib maint.

• PI: John Heymach MD
• Sponsor: Astra Zeneca
• Primary endpoint: safety
  – “3+3+3” design
  – 12 patients at MTD
• Secondary endpoints:
  – PFS/OS, PK, toxicity
• Exploratory
  – Plasma CAF profiling
  – CECs, RTK + monocytes
  – Pharmacogenetics
• Status: activated 2/08 (SWOG sites)
Phase II Sorafenib Recurrent SCLC- SWOG S0435

Recurrence s/p prior platin-regimen
Zubrod PS 0-1
Asymptomatic brain mets
Cohorts: Sensitive and Resistant (> or < 90 day prog. free after chemotx)

- PI: Barbara Gitlitz MD
- Sorafenib 400 mg po bid
- Primary endpoint  response rate
  - Two stage design 20/40 each cohort
- Secondary endpoints:
  - PFS/OS, toxicity
- Exploratory
  - B RAF mutation
  - VEGFR-2, VEGF, KIT expression
  - Plasma VEGF

<table>
<thead>
<tr>
<th></th>
<th>Sensitive N= 40</th>
<th>Refractory</th>
<th>N=39</th>
</tr>
</thead>
<tbody>
<tr>
<td>PR/SD (%)</td>
<td>2/12 (35)</td>
<td>1/13 (36)</td>
<td></td>
</tr>
<tr>
<td>Med PFS/OS mo</td>
<td>2/7</td>
<td>2/5</td>
<td></td>
</tr>
<tr>
<td>Derm toxicity gr3</td>
<td>25%</td>
<td>Flu-like gr 3/4</td>
<td>14%</td>
</tr>
</tbody>
</table>
Phase I Sorafenib + Topotecan

- PI: Joseph Leach MD
- Sponsor: Onyx-Bayer
- Sorafenib daily
- Primary endpoint: safety with dose esc. of sorafenib
- Secondary endpoints:
  - PFS/OS, toxicity
- Status: Accruing at 400 mg bid PRs in 2/8 pts

Recurrence s/p one prior platin-based regimen

ECOG  PS 0-2

Evaluable disease

Treated stable brain mets

Topotecan 4 mg/m² iv wkly
ZD6474 vs Placebo in 2nd Line SCLC

**PFS**

1-sided $P = .51$

HR = 1.01 (80% CI, 0.75 to 1.36)

- Blue line: Vandetanib
- Yellow line: Placebo

**OS**

1-sided $P = .90$

HR = 1.43 (80% CI, 1.00 to 2.05)

- Blue line: Vandetanib
- Yellow line: Placebo

Angiogenesis inhibitors in SCLC

25,3945,2007
Bevacizumab in ES SCLC: E3501

**REGISTRATION**

P - 60 mg/m² day 1
E - 120 mg/m² days 1 to 3
*Bevacizumab 15 mg/kg
day 1 q3 weeks x 4

*Bevacizumab 15 mg/kg
day 1 q3 week

*Anti-VEGF 15 mg/kg every 3 weeks until progressive disease.
Correlatives - pre- and post-treatment serum VEGF levels
Phase I-II Sunitinib + EP  CALGB

ED SCLC

PS 0-1 (I)
PS 0-2 (II)

No brain mets

Phase I EP/sunit.

Phase II monotx (35 days)

Followed by
EP/sunitinib and sunitinib maintenance

• PI: Neal Ready MD
• Primary endpoint
  – Phase I: safety- MTD sunitinib
  – Phase II: Response to sunitinib
    10 month survival rate
• Secondary endpoints:
  – PFS/OS, toxicity
• Accrual 6 pts in phase I –
  – sunitinib 37.5 mg
  – delays due to neutropenia
  – revision to include G-CSF
  – No other unexpected toxicity

• Status: active
Antiangiogenics

• No relevant clinical activity in RPII and III trials
  – In combination with standard EP
  – As single agent or in maintenance (ZD 6474, thalodimide)

• Excessive toxicity when used in combination with RT
Other Novel Therapies

- **HDAC inhibitors**: Insufficient activity to proceed to phase III studies

- **PARP Inhibitors**: Proposed ECOG Ep/cis +/- ABT 888 (Veliparib)

- **Bcl2 inhibitors**: Antisense Bcl-2 possibly detrimental; Phase I ABT 263

*ASCO 2009 – Based on Farmer H et al., Nature 2005;434:917-21; Bryant HE et al., Nature 2005;434:913-7*
Iniparib itself is not a PARP Inhibitor – an active metabolite is proposed.
The Past and Future

- **Planned**
  - Hedgehog inhibitors
  - Neuropeptide inhibitors

- **Not active**
  - Matrix metalloproteases
  - Imatinib (c-Kit + SCLC)
  - mTor inhibitor
  - Dasatinib
Save the date!

October 27 - 31, 2013
Breceptin Mechanism of action:
Biased or partial agonist leading to apoptosis

G protein coupled receptor

- PLC
- Src
- Ras/Raf
- MEKK

Ca^2+
P KC
MAPK
JNK
Meanwhile...

- Clinicaltrials.gov search:
  - All SCLC studies 694 hits
  - All SCLC studies open 237 hits
  - All SCLC studies open +intervention 191 hits
    - 68 RT
    - Same + phase II 97 hits
    - Same + phase III 17 hits
      - 8 RT
      - 9 chemotherapy
      - 0 targeted agents