Welcome
2013 CHICAGO MULTIDISCIPLINARY SYMPOSIUM in THORACIC ONCOLOGY
2012 Chicago Multidisciplinary Symposium in Thoracic Oncology
September 6-8, 2012

Friday, September 7, News Briefing
7:15 a.m. Central time

Moderated by Heather Wakelee, MD
Stanford University
Stanford, Calif.
• This symposium is co-sponsored by ASCO, ASTRO, IASLC and The University of Chicago.
• More than 700 attendees are expected.
• 348 abstracts will be presented.
• Please hold all questions until the end. Online participants may submit questions to the host via the online chat tool.
Results of a Global Phase II Study with Crizotinib in Advanced ALK-positive Non-small Cell Lung Cancer (NSCLC)

G. J. Riely¹, T. L. Evans², R. Salgia³, S. I. Ou⁴, S. N. Gettinger⁵, G. A. Otterson⁶, S. Lanzalone⁷, A. Polli⁷, A. T. Shaw⁸

¹Memorial Sloan-Kettering Cancer Center, New York, NY; ²University of Pennsylvania, Philadelphia, PA; ³University of Chicago, Chicago, IL; ⁴University of California at Irvine, Irvine, CA; ⁵Yale University School of Medicine, New Haven, CT; ⁶The Ohio State University, Columbus, OH; ⁷Pfizer Italy Srl, Milan, Italy; ⁸Massachusetts General Hospital Cancer Center, Boston, MA
Lung Adenocarcinomas

35% Unknown

- KRAS mutation
- EGFR mutation
- BRAF mutation
- ALK rearrangement
- MEK mutation
- PIK3CA mutation
- HER2 mutation
- ROS1 fusion
- RET translocation
- MET amplification
Background

• Anaplastic lymphoma kinase (ALK) gene rearrangements have been identified in approximately 3–5% of non-small cell lung cancers, most frequently occurring in adenocarcinomas\textsuperscript{1–3}

• Crizotinib (PF-02341066) is an oral ALK inhibitor

• In a phase 1 study of crizotinib, patients with ALK-positive lung cancer treated with 250 mg twice daily had a response rate of 61% and median PFS of 10 months.\textsuperscript{4}

• Here we present updated data from the subsequent phase 2 study of crizotinib in patients with previously treated, advanced ALK-positive NSCLC (NCT00932451)

Phase 2 Study of Crizotinib in ALK+ NSCLC

Key eligibility criteria:
• ALK+ NSCLC by central laboratory
• ECOG PS: 0–3
• ≥1 prior line of chemotherapy
• Stable/controlled brain metastases allowed

Treatment
- Crizotinib 250 mg po BID
  continuous daily dosing

Primary endpoints:
• ORR
• safety/tolerability

Study Design
• Phase II, single-arm, multicenter study; ~1100 patients (enrollment ongoing)
Phase 2 Study of Crizotinib in ALK+ NSCLC

Best Response of Indicator Lesions

<table>
<thead>
<tr>
<th>Response</th>
<th>Patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete Response</td>
<td>4</td>
<td>2%</td>
</tr>
<tr>
<td>Partial Response</td>
<td>151</td>
<td>58%</td>
</tr>
<tr>
<td>Stable Disease</td>
<td>69</td>
<td>27%</td>
</tr>
<tr>
<td>Progressive Disease</td>
<td>19</td>
<td>7%</td>
</tr>
</tbody>
</table>

Response-evaluable patients n=259

Decrease or increase from baseline (%)

- PD: Complete Response
- SD: Partial Response
- PR: Stable Disease
- CR: Progressive Disease

Graph showing the distribution of responses with bars indicating the decrease or increase from baseline.
Progression-free Survival

Median PFS 8 months (95% CI: 7–10)
28% of patients in follow-up for progression

Phase 2 Study of Crizotinib in ALK+ NSCLC
Phase 2 Study of Crizotinib in ALK+ NSCLC

Response of Brain Metastases to Crizotinib

- There were 18 patients with asymptomatic, non-irradiated brain metastases in the mature response-evaluable population who were evaluable for both brain and systemic disease

<table>
<thead>
<tr>
<th>Brain Response</th>
<th>N=18</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete Response</td>
<td>2 (11%)</td>
</tr>
<tr>
<td>Partial Response</td>
<td>2 (11%)</td>
</tr>
<tr>
<td>Stable Disease</td>
<td>12 (67%)</td>
</tr>
<tr>
<td>Progressive Disease</td>
<td>2 (11%)</td>
</tr>
</tbody>
</table>
Conclusions

- Crizotinib treatment led to a response rate of 60% and median PFS of 8 months.
- Crizotinib continued to show a good safety profile in patients with previously treated ALK-positive advanced NSCLC.
- Clinically meaningful improvement was observed in global QOL and in lung cancer symptoms such as fatigue, cough, dyspnea, chest pain.
- These data are consistent with the efficacy and safety findings previously reported and further support the use of crizotinib in patients with ALK-positive lung cancer.
RTOG 0214:
A Phase III Comparison of Prophylactic Cranial Irradiation versus Observation in Patients with Locally Advanced Non-Small Cell Lung Cancer: 5 Year Update

Elizabeth Gore, MD
Medical College of Wisconsin
Milwaukee, Wisc.

Elizabeth Gore, Rebecca Paulus, Stuart Wong, Alexander Sun, Gregory Videtic, Swati Dutta, Mohan Suntharalingam, Yuhchyau Chen, Laurie Gaspar, Hak Choy
Background

• 40-50% of patients develop brain metastases after treatment for lung cancer
• Studies in the 1980s showed that PCI decreases brain failures but did not improve survival
• Advances in radiation, addition of surgery improved local control
• Chemotherapy decreases failures outside the chest but does not enter the brain tissue
• The brain is undertreated with standard therapy
Study Question

• Do patients treated with PCI live longer?
• Is low dose brain radiation safe?
No progression after curative therapy for Stage IIIA/B NSCLC

Stage
1. IIIA
2. IIIB

Histology
1. SCCa
2. Non-SCCa

Treatment
1. Surgery
2. No Surgery

PCI 30Gy at 2Gy/Fx

Observation
Results

• Only 358 patients were enrolled
• Not enough patients to answer the primary question
• Survival not different
• Brain metastases were lower with PCI
• Patients with out PCI were twice as likely to fail in the brain only
CNS Metastasis

CNS Mets Failure (%) vs Months since Randomization

Patients at Risk
- PCI: 163
- Observation: 177

PCI
- Observation

Fail
- PCI: 19
- Observation: 39

Total
- PCI: 163
- Observation: 177

HR = 2.05 (1.19, 3.55)
p = 0.009

PCI 5 yr BM
- PCI: 17.3%
- Control: 26.8%
A Randomized, Open-Label, Phase III, Superiority Study of Pemetrexed (Pem) + Carboplatin (Cb) + Bevacizumab (Bev) Followed by Maintenance Pem + Bev versus Paclitaxel (Pac)+Cb+Bev Followed by Maintenance Bev in Patients with Stage IIIB or IV Non-Squamous Non-Small Cell Lung Cancer (NS-NSCLC)

Jyoti D. Patel¹, Mark A. Socinski², Edward B. Garon³, Craig H. Reynolds⁴, David R. Spigel⁵, Robert C. Hermann⁶, Jingyi Liu⁷, Susan C. Guba⁷, Philip Bonomi⁸, Ramaswamy Govindan⁹

¹Feinberg School of Medicine, Northwestern University, Chicago/IL; ²UPMC Cancer Pavilion, University of Pittsburgh, Pittsburgh/PA; ³University of California Los Angeles/Translational Oncology Research International, Los Angeles/CA; ⁴Ocala Oncology, Ocala/FL and US Oncology Research, Inc., Houston/TX; ⁵SCRI/Tennessee Oncology, PLLC, Nashville, TN; ⁶Northwest Georgia Oncology Centers, Marietta, GA; ⁷Eli Lilly and Company, Indianapolis/IN; ⁸Rush University Medical Center, Chicago/IL; ⁹Washington University School of Medicine, St. Louis/MO
Background

- Platinum-based chemotherapy combinations are recommended for first-line treatment of advanced NSCLC\(^1\)

- For patients with non-squamous NSCLC in the US, two regimens are widely used based upon survival improvements
  - Paclitaxel, carboplatin and bevacizumab\(^2\)
  - Pemetrexed and platinum\(^3\)

- Continuation maintenance therapy with pemetrexed after cisplatin and pemetrexed initial therapy has lead to improvements in survival\(^4,5\)

- In a single-arm phase II study, pemetrexed+carboplatin+bevacizumab followed by maintenance pemetrexed+bevacizumab demonstrated encouraging overall survival of 14.1 months and progression free survival of 7.8 mo\(^6\)

**Inclusion:**
- No prior systemic therapy for lung cancer
- PS 0/1
- Stage IIIB-IV NS-NSCLC
- Stable tx’t brain mets

**Exclusion:**
- Peripheral neuropathy Gr 1
- Uncontrolled pleural effusions

**PointBreak: Study Design**

- Randomized, open-label, phase III superiority study conducted in US
- Pemetrexed 500 mg/m²; Carboplatin AUC 6; Bevacizumab 15 mg/kg
- Paclitaxel 200 mg/m²; Carboplatin AUC 6; Bevacizumab 15 mg/kg

**Induction Phase**
q21d, 4 cycles

- Pemetrexed (folic acid & vitamin B₁₂) + Carboplatin + Bevacizumab

**Maintenance Phase**
q21d until PD

- Paclitaxel + Carboplatin + Bevacizumab
- Bevacizumab

**Randomized, 1:1**

**Stratified for:**
- PS (0 vs 1); sex (M vs F); disease stage (IIIB vs IV); measurable vs nonmeasurable disease
Censoring rate for Pem+Cb+Bev was 27.8%; for Pac+Cb+Bev was 27.2%
# PointBreak: CTCAEs (Version 3) Possibly Related to a Study Drug (Safety Population)

<table>
<thead>
<tr>
<th></th>
<th>Pem+Cb+ Bev (n=442) %</th>
<th>Pac+Cb+ Bev (n=443) %</th>
<th>Pem+Cb+ Bev (n=442) %</th>
<th>Pac+Cb+ Bev (n=443) %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Grade 1/2</td>
<td>Grade 1/2</td>
<td>Grade 3/4 (5)</td>
<td>Grade 3/4 (5)</td>
</tr>
<tr>
<td>Anemia†</td>
<td>31.0</td>
<td>24.4</td>
<td>14.5</td>
<td>2.7</td>
</tr>
<tr>
<td>Thrombocytopenia†</td>
<td>17.9</td>
<td>17.2</td>
<td>23.3</td>
<td>5.6</td>
</tr>
<tr>
<td>Neutropenia†</td>
<td>14.7</td>
<td>8.4</td>
<td>25.8</td>
<td>40.6</td>
</tr>
<tr>
<td>Febrile neutropenia †</td>
<td>0.2</td>
<td>0.2</td>
<td>1.4</td>
<td>4.1</td>
</tr>
<tr>
<td>Fatigue†</td>
<td>42.1</td>
<td>39.5</td>
<td>10.9</td>
<td>5.0</td>
</tr>
<tr>
<td>Hemorrhage GI/pulmonary</td>
<td>3.6</td>
<td>3.8</td>
<td>1.8 (0.5)</td>
<td>0.5 (0.7)</td>
</tr>
<tr>
<td>Thromboembolic event</td>
<td>0.5</td>
<td>0.2</td>
<td>3.2</td>
<td>2.0</td>
</tr>
<tr>
<td>Neuropathy/sensory†</td>
<td>11.8</td>
<td>35.7</td>
<td>0.0</td>
<td>4.1</td>
</tr>
<tr>
<td>Alopecia*</td>
<td>6.6</td>
<td>36.8</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Other Grade 5 Events (Pem Arm/Pac Arm %)</td>
<td>Includes: CNS ischemia (0.2/0.7); Cardiac events (0.2/0.7); ARDS (0.5/0); Infection (0.2/0); Other Hemorrhage (0.2/0.2)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
PointBreak: Conclusions

- The primary endpoint of superior OS was not met in this trial: 12.6 mo (Pem+Cb+Bev followed by Pem+Bev) vs 13.4 mo (Pac+Cb+Bev followed by Bev) (HR 1.00, \( P=0.949 \)). There was no improvement in survival.
- Pem+Cb+Bev followed by Pem+Bev had superior median PFS compared with Pac+Cb+Bev followed by Bev: 6.0 vs 5.6 mo (HR 0.83, \( P=0.012 \))
- The toxicity profiles differed and both regimens demonstrated tolerability
  - Pem+Cb+Bev followed by Pem+Bev had significantly more drug related anemia, thrombocytopenia, and fatigue compared with Pac+Cb+Bev
  - Pac+Cb+Bev followed by Bev had significantly more study drug related neutropenia, febrile neutropenia, sensory neuropathy, and complete alopecia

Sandler et al. *NEJM*, 2006
Q and A
To arrange an interview with any of the authors or for additional information, please contact Michelle Kirkwood or Nicole Napoli in the Press Room at 312-595-3188 or via email at michellek@astro.org or nicolen@astro.org.