Highlights of 2015
Thoracic Cancers

Caicun Zhou

Shanghai Pulmonary Hospital, Tongji University, Shanghai, China
• Chemotherapy
• Targeted therapy
• Immunotherapy
• Other
Lung Adjuvant Cisplatin Evaluation: A Pooled Analysis by the LACE Collaborative Group

Study objective: To evaluate the addition of bevacizumab to adjuvant chemotherapy in early stage resected NSCLC.

Key patient inclusion criteria:
- Resected
- Stage IB (≥4cm)–IIIA
- 6–12 weeks post-op
- No prior chemotherapy
- ECOG PS 0–1 (n=1,501)

Stratification:
- Cisplatin doublet, stage, histology, gender

Chemotherapy regimens q3w:
- Cisplatin 75 mg/m² D1 combined with any of the following:
  - vinorelbine 30 mg/m² D1, 8
  - docetaxel 75 mg/m² D1
  - gemcitabine 1200 mg/m² D1, 8
  - pemetrexed 500 mg/m² D1

Primary endpoint: OS
Secondary endpoints: DFS, safety

Randomized Phase III Trial of Adjuvant Chemotherapy with or without Bevacizumab in Resected NSCLC: Results of E1505

Wakelee HA, et al. J Thorac Oncol 2015; 10 (9, suppl 2); abstr PLEN04.03
Overall Survival

OS hazard ratio (B:A): 0.99
95% CI: (0.81-1.21)
p=0.93

Goal: Inc. mOS
From 66-83.5 mo

Disease Free Survival

DFS hazard ratio (B:A): 0.98
95% CI: (0.84-1.14)
p=0.75
**Customized BRCA1 Adjuvant Treatment in Stage II-II NSCLC (SCAT)**

**Resected NSCLC R0 pN1 / pN2**

**CONTROL**
- T1 BRCA1
- T2 BRCA1
- T3 BRCA1

**EXPERIMENTAL**
- Docetaxel/Cis
- Gem/Cis
- Docetaxel/Cis
- Docetaxel

**Statification factors:**
- Stage: N1 vs. N2
- Age ≤65 vs >65 y
- Histology: Non-SCC vs. SCC
- Type of resection: Lobectomy vs Pneumonectomy

Planned number of patients : 432 (amended)
CT should be started before 8 weeks after surgery
PORT in N2 patients

**EudraCT: 2007-000067-15**
**NCTgov:00478699**

Presented By Mark Socinski at 2015 ASCO Annual Meeting

SLIDES ARE THE PROPERTY OF THE AUTHOR. PERMISSION REQUIRED FOR REUSE.
Results/1 (cut-off March 15th 2015): Overall survival

HR = 0.86 (0.59-1.27)

DFS

HR = 1.00 (0.71-1.43)

Presented By Mark Socinski at 2015 ASCO Annual Meeting
<table>
<thead>
<tr>
<th>Trial</th>
<th>Stage</th>
<th>Therapy</th>
<th>Marker</th>
</tr>
</thead>
<tbody>
<tr>
<td>SWOG 0720</td>
<td>I</td>
<td>± Chemotherapy (cis/gem)</td>
<td>ERCC1/RRM1</td>
</tr>
<tr>
<td>ITACA</td>
<td>II-III</td>
<td>Cisplatin/Pemetrexed</td>
<td>ERCC1/TS</td>
</tr>
<tr>
<td>SCAT</td>
<td>II-III A</td>
<td>Platinum/Docetaxel</td>
<td>BRCA1</td>
</tr>
<tr>
<td>MAGRIT</td>
<td>IB-III A</td>
<td>MAGE A3 Vaccine</td>
<td>MAGE-A3</td>
</tr>
<tr>
<td>TASTE</td>
<td>II-III A</td>
<td>Erlotinib vs CDDP Pem</td>
<td>ERCC1/EGFR mut</td>
</tr>
<tr>
<td>RADIANT</td>
<td>IB-III A</td>
<td>Erlotinib vs Placebo</td>
<td>EGFR FISH or IHC+</td>
</tr>
<tr>
<td>SELECT</td>
<td>I and I NO</td>
<td>Erlotinib</td>
<td>EGFR mutation</td>
</tr>
<tr>
<td>GACT</td>
<td>II-III A N+</td>
<td>Gefitinib vs CDDP Vinorelbine</td>
<td>EGFR mutation</td>
</tr>
</tbody>
</table>
Nedaplatin plus docetaxel versus cisplatin plus docetaxel for advanced or relapsed squamous cell carcinoma of the lung (WJOG 5208L): a randomized, open label, phase 3 trial

• Study objective:
  – To determine the efficacy and safety of the combination of nedaplatin + docetaxel vs. cisplatin + docetaxel in patients with advanced or relapsed squamous cell carcinoma of the lung

Key patient inclusion criteria
• 20–74 years of age
• Stage IIIb/IV squamous cell carcinoma of the lung or recurrence
• Chemotherapy-naïve
• ECOG PS 0–1 (N=350)

Up to 6 cycles of:
Nedaplatin 100 mg/m² IV Q3W + Docetaxel 60 mg/m² IV Q3W (n=175)

Up to 6 cycles of:
Cisplatin 80 mg/m² IV Q3W + Docetaxel 60 mg/m² IV Q3W (n=175)

Stratification
• Stage (IIIb, IV, or recurrent, gender, institution)

Primary endpoint
• OS

Secondary endpoints
• PFS, RR, and AEs

### Efficacy Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Nedaplatin + Docetaxel (n=177)</th>
<th>Cisplatin + Docetaxel (n=172)</th>
<th>HR (90% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>OS, months</strong></td>
<td>13.6</td>
<td>11.4</td>
<td>0.81 (0.67, 0.98)</td>
<td>0.037</td>
</tr>
<tr>
<td><strong>PFS, months</strong></td>
<td>4.9</td>
<td>4.5</td>
<td>0.83 (0.69, 1.00)</td>
<td>0.050</td>
</tr>
<tr>
<td><strong>ORR</strong></td>
<td>55.8%</td>
<td>53.0%</td>
<td>NA</td>
<td>0.663</td>
</tr>
<tr>
<td><strong>Nausea</strong></td>
<td>4.0%</td>
<td>13.4%</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td><strong>Fatigue</strong></td>
<td>3.4%</td>
<td>10.9%</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td><strong>Thrombocytopenia</strong></td>
<td>9.0%</td>
<td>0%</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td><strong>Neutropenia</strong></td>
<td>82.5%</td>
<td>70.3%</td>
<td>NA</td>
<td></td>
</tr>
</tbody>
</table>

*aGr 3 or more AEs*

A Randomized, Phase III Study Comparing Carboplatin/Paclitaxel or Carboplatin/Paclitaxel/Bevacizumab with or without Concurrent Cetuximab in Patients with Advanced NSCLC: SWOG S0819

• Study objective
  – To evaluate the effect of adding cetuximab to carboplatin/paclitaxel or carboplatin/paclitaxel/bevacizumab in patients with advanced NSCLC

Key patient inclusion criteria
• Stage IV NSCLC treatment-naïve patients (n=1,333)

Primary endpoint
♦ OS (entire study), PFS (EGFR FISH)

Secondary endpoints
♦ OS and PFS by bevacizumab appropriate, safety

Stratification
• Appropriate use of bevacizumab, smoking status, stage M1a vs. M1b

Paclitaxel + carboplatin + bevacizumab* (n=657)
Bevacizumab*

Paclitaxel + carboplatin + bevacizumab* + cetuximab (n=656)
Bevacizumab* + cetuximab

Herbst R, et al. J Thorac Oncol 2015; 10 (9, suppl 2) abstr PLEN04.01
Key Results

S0819 RESULTS: ENTIRE STUDY POPULATION

Overall Survival

<table>
<thead>
<tr>
<th>Treatment</th>
<th>N</th>
<th>Events</th>
<th>Median in Months</th>
<th>95% Conf. Int.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cetuximab Arm</td>
<td>656</td>
<td>536</td>
<td>10.9</td>
<td>(9.8 - 12.0)</td>
</tr>
<tr>
<td>Control Arm</td>
<td>857</td>
<td>558</td>
<td>9.4</td>
<td>(8.7 - 10.3)</td>
</tr>
</tbody>
</table>

P = 0.34
HR = 0.94 (0.84 - 1.06)

Progression Free Survival

<table>
<thead>
<tr>
<th>Treatment</th>
<th>N</th>
<th>Events</th>
<th>Median in Months</th>
<th>95% Conf. Int.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cetuximab Arm</td>
<td>656</td>
<td>629</td>
<td>4.8</td>
<td>(4.2 - 5.2)</td>
</tr>
<tr>
<td>Control Arm</td>
<td>857</td>
<td>632</td>
<td>4.5</td>
<td>(4.2 - 4.9)</td>
</tr>
</tbody>
</table>

P = 0.68
HR = 0.98 (0.87 - 1.09)

Herbst R, et al. J Thorac Oncol 2015; 10 (9, suppl 2) abstr PLEN04.01
● Chemotherapy
● Targeted therapy
● Immunotherapy
● Other
# First line EGFR TKI vs chemotherapy in EGFR mut+ NSCLC

<table>
<thead>
<tr>
<th>Trial</th>
<th>ORR</th>
<th>PFS</th>
<th>ORR</th>
<th>PFS</th>
<th>ORR</th>
<th>PFS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TKI</td>
<td>Chemo</td>
<td>TKI</td>
<td>Chemo</td>
<td>TKI</td>
<td>Chemo</td>
</tr>
<tr>
<td>IPASS Mut+</td>
<td>71.2</td>
<td>47.3</td>
<td>9.5</td>
<td>6.3</td>
<td>21.6</td>
<td>21.9</td>
</tr>
<tr>
<td>First-Signal</td>
<td>84.6</td>
<td>37.5</td>
<td>8.4</td>
<td>6.7</td>
<td>30.6</td>
<td>26.5</td>
</tr>
<tr>
<td>WJTOG</td>
<td>62.1</td>
<td>32.2</td>
<td>9.2</td>
<td>6.3</td>
<td>30.9</td>
<td>NR</td>
</tr>
<tr>
<td>NEJ002</td>
<td>73.7</td>
<td>30.7</td>
<td>10.8</td>
<td>5.4</td>
<td>27.7</td>
<td>26.6</td>
</tr>
<tr>
<td>OPTIMAL</td>
<td>83</td>
<td>36</td>
<td>13.7</td>
<td>4.6</td>
<td>22.6</td>
<td>28.8</td>
</tr>
<tr>
<td>EURTAC</td>
<td>58</td>
<td>15</td>
<td>9.7</td>
<td>5.2</td>
<td>19.3</td>
<td>19.5</td>
</tr>
<tr>
<td>LUX-Lung3</td>
<td>58.1</td>
<td>22.6</td>
<td>11.1</td>
<td>6.9</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>LUX-Lung6</td>
<td>66.9</td>
<td>23</td>
<td>11</td>
<td>5.6</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>
**Study design**

- Stage IIIB/IV adenocarcinoma of the lung
- **EGFR mutation** (Del19 and/or L858R) in the tumor tissue*
- No prior treatment for advanced/metastatic disease
- ECOG PS 0/1
- Treatment beyond progression allowed if deemed beneficial by investigator
- RECIST assessment performed at Weeks 4, 8 and every 8 weeks thereafter until Week 64, and every 12 weeks thereafter

**Primary endpoints:**
- PFS (independent)
- TTF
- OS

**Secondary endpoints:**
- ORR
- Time to response
- Duration of response
- Duration of disease control
- Tumor shrinkage
- HRQoL
- Safety

---

*Central or local test
†Dose modification to 50, 30, 20 mg permitted in line with prescribing information
PFS by independent review

<table>
<thead>
<tr>
<th></th>
<th>Afatinib (n=160)</th>
<th>Gefitinib (n=159)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median PFS (months)</td>
<td>11.0</td>
<td>10.9</td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>0.73 (0.57–0.95)</td>
<td></td>
</tr>
<tr>
<td>p value</td>
<td></td>
<td>0.0165</td>
</tr>
</tbody>
</table>
## Survival Summary of 3rd generation EGFR-TKIs

<table>
<thead>
<tr>
<th>Study</th>
<th>Drugs</th>
<th>Population</th>
<th>N</th>
<th>ORR</th>
<th>DCR</th>
<th>PFS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase I study</td>
<td>AZD9291</td>
<td>Pre-treated T790M +</td>
<td>127</td>
<td>61%</td>
<td>95%</td>
<td>9.6</td>
</tr>
<tr>
<td>AURA study Phase II extension cohort</td>
<td>AZD9291</td>
<td>Pre-treated T790M +</td>
<td>201</td>
<td>61%</td>
<td>91%</td>
<td>NR</td>
</tr>
<tr>
<td>AURA2 Phase II Study</td>
<td>AZD9291</td>
<td>Pre-treated T790M +</td>
<td>210</td>
<td>71%</td>
<td>92%</td>
<td>8.6</td>
</tr>
<tr>
<td>Phase I study</td>
<td>CO1686</td>
<td>Pre-treated T790M +</td>
<td>46</td>
<td>59%</td>
<td>93%</td>
<td>13.1</td>
</tr>
<tr>
<td>Phase I/II study</td>
<td>HM61713</td>
<td>Pre-treated T790M +</td>
<td>34</td>
<td>58.8% (dose&gt;650 mg)</td>
<td>97.1% (dose&gt;650 mg)</td>
<td>NR</td>
</tr>
</tbody>
</table>
AZD9291, a mutant-selective EGFR inhibitor, as first-line treatment for EGFR-mutation (+) NSCLC: Results from a phase 1 expansion cohort

Ramalingam SS, et al. ASCO 2015  abstr 8000
How to improve efficacy of EGFR TKI

• Plus chemotherapy
  FASTACT II EGFR mutant
    PFS: 16.8 months in Chemo+erlotinib
    6.9 months in Chemo+placebo
  NEJ 005: Concurrent vs Sequential combination
    PFS: 18.3 months in concurrent
    15.3 months in sequential
• Plus bevacizumab
  PFS: 16.0 months in Beva + erlotinib
  9.7 months in erlotinib
Randomized Trial of Gefitinib with and without Pemetrexed as First-Line Therapy in East-Asian Patients with Advanced NS NSCLC with EGFR Mutations

- **Study objective**
  - To evaluate whether the addition of pemetrexed to gefitinib prolongs PFS in treatment-naïve East-Asian patients with advanced non-squamous NSCLC with activating **EGFR** mutations

**Key patient inclusion criteria**
- Confirmed advanced (stage IV) or recurrent NS NSCLC
- Activating **EGFR** mutations
- No prior systemic CT, immunotherapy or biologic therapy
- ECOG PS ≤1
- ≥18 years (n=191)

**Primary endpoint**
- PFS

**Secondary endpoints**
- OS, ORR, DOR, QoL, safety

**Primary treatment arms**
- Oral gefitinib 250 mg/day + pemetrexed 500 mg/m² IV D1 q3w (n=126)
- Oral gefitinib 250 mg/day (n=65)

## Key Results

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Gefitinib + pemetrexed</th>
<th>Gefitinib</th>
<th>HR (95%CI); p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median PFS, months</td>
<td>15.8</td>
<td>10.9</td>
<td>0.68 (0.48, 0.96); p=0.029*</td>
</tr>
<tr>
<td>PFS: Exon 19 deletion</td>
<td>17.1</td>
<td>11.1</td>
<td>0.67 (0.43, 1.05); p=0.078*</td>
</tr>
<tr>
<td>PFS: Exon 21 point mutation</td>
<td>12.6</td>
<td>10.9</td>
<td>0.58 (0.33, 1.01); p=0.054*</td>
</tr>
<tr>
<td>Median DOR, months</td>
<td>15.4</td>
<td>11.3</td>
<td>0.74 (0.50, 1.08); p=0.122</td>
</tr>
<tr>
<td>ORR, %</td>
<td>80.2</td>
<td>73.8</td>
<td>p=0.358</td>
</tr>
<tr>
<td>≥1 TEAE, %</td>
<td>93.7</td>
<td>92.3</td>
<td></td>
</tr>
<tr>
<td>≥1 Grade 3/4 TEAE, %</td>
<td>40.5</td>
<td>18.5</td>
<td></td>
</tr>
<tr>
<td>≥1 SAE, %</td>
<td>8.7</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>Discontinued treatment due to AE, %</td>
<td>15.1</td>
<td>7.7</td>
<td></td>
</tr>
<tr>
<td>Gefitinib treatment interruption due to AE, %</td>
<td>33.3</td>
<td>15.4</td>
<td></td>
</tr>
</tbody>
</table>

- First-line gefitinib + pemetrexed prolonged PFS vs. gefitinib for East-Asian patients with EGFR mutation-positive NS NSCLC
- First-line gefitinib + pemetrexed was associated with an acceptable safety profile

*2-sided p-value

BELIEF trial: Phase II trial of erlotinib (E) and bevacizumab (B) in patients with advanced NSCLC with activating EGFR mutations with and without T790M mutation.

- **Study objective**
  - To estimate PFS in patients with nonsquamous NSCLC with or without EGFR T790M mutation, treated with first-line bevacizumab and erlotinib

**Key patient inclusion criteria**
- Metastatic or locally-advanced nonsquamous NSCLC
- Centrally confirmed EGFR mutations (exon 19 deletion or L858R)
- Unsuitable for surgery or radiotherapy

(n=1,135 screened)

**Primary endpoint**
- PFS

**Secondary endpoints**
- Safety, correlation of PFS with mutations

Stahel RA, et al. Ann Oncol 2015; 26 (suppl 6); abstr 3BA
Key results

- Erlotinib + bevacizumab had a toxicity profile consistent with previous experience
- With the exception of a single patient, tumor shrinkage was seen in all cases
- CR was observed in 8.1% of T790+ patients and 5.6% of T790- patients
- PR was seen in 62.2% and 73.6%, respectively

<table>
<thead>
<tr>
<th>Events/N</th>
<th>Median PFS, months (95%CI)</th>
<th>12-month PFS, % (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>57/109</td>
<td>13.8 (10.3, 21.3)</td>
</tr>
<tr>
<td>T790M+</td>
<td>15/37</td>
<td>16.0 (13.1, NE)</td>
</tr>
<tr>
<td>T790M-</td>
<td>42/72</td>
<td>10.5 (9.2, 16.2)</td>
</tr>
</tbody>
</table>

Stahel RA, et al. Ann Oncol 2015; 26 (suppl 6); abstr 3BA
Alectinib in Crizotinib-Refractory ALK-Rearranged NSCLC: A Phase II Global Study.

Ou SI, et al. JCO 2015

- **All population ORR:** 50%
- **All population PFS:** 8.9 months
- **CNS ORR:** 57%
- **CNS DOR:** 10.3 months
• Chemotherapy
• Targeted therapy
• Immunotherapy
• Other
Nivolumab

CheckMate 057 study design

Key patient inclusion criteria
• Stage IIIb/IV non-squamous NSCLC
• Known PD-L1 expression
• ECOG PS 0–1
• Failed 1 prior platinum doublet
(n=582)

Primary endpoint
• OS

Nivolumab 3 mg/kg IV Q2W (n=292)
PD or toxicity

Docetaxel 75 mg/m² IV Q3W (n=290)
PD or toxicity

CheckMate 017 study design

Key patient inclusion criteria
• Squamous NSCLC
• Stage IIIb/IV
• ECOG PS 0–1
• 1 prior platinum doublet
• Pre-treatment tumor samples available
(n=272)

Primary endpoint
• OS

Nivolumab 3 mg/kg IV Q2W (n=135)
PD or toxicity

Docetaxel 75 mg/m² IV Q3W (n=137)
PD or toxicity


CheckMate 057 non-SQ

<table>
<thead>
<tr>
<th></th>
<th>Nivolumab (n=292)</th>
<th>Docetaxel (n=290)</th>
</tr>
</thead>
<tbody>
<tr>
<td>mPFS, months</td>
<td>2.3</td>
<td>4.2</td>
</tr>
<tr>
<td>HR 0.92 (95% CI 0.77, 1.11); p=0.3932</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1-year PFS rate=13%

CheckMate 017 SQ

<table>
<thead>
<tr>
<th></th>
<th>Nivolumab (n=135)</th>
<th>Docetaxel (n=137)</th>
</tr>
</thead>
<tbody>
<tr>
<td>mPFS, months</td>
<td>3.6 (2.1, 4.9)</td>
<td>2.8 (2.1, 3.5)</td>
</tr>
<tr>
<td>HR 0.62 (95% CI 0.47, 0.81); p=0.0004</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1-year PFS rate=21%


## CheckMate 057 Key Results

<table>
<thead>
<tr>
<th>PD-L1 Expression Level</th>
<th>Nivolumab n</th>
<th>Docetaxel n</th>
<th>Unstratified HR (95% CI)</th>
<th>Interaction p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>OS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥1%</td>
<td>123</td>
<td>123</td>
<td>0.59 (0.43, 0.82)</td>
<td>0.0646</td>
</tr>
<tr>
<td>&lt;1%</td>
<td>108</td>
<td>101</td>
<td>0.90 (0.66, 1.24)</td>
<td></td>
</tr>
<tr>
<td>≥5%</td>
<td>95</td>
<td>86</td>
<td>0.43 (0.30, 0.63)</td>
<td></td>
</tr>
<tr>
<td>&lt;5%</td>
<td>136</td>
<td>138</td>
<td>1.01 (0.77, 1.34)</td>
<td>0.0004</td>
</tr>
<tr>
<td>≥10%</td>
<td>86</td>
<td>79</td>
<td>0.40 (0.26, 0.59)</td>
<td></td>
</tr>
<tr>
<td>&lt;10%</td>
<td>145</td>
<td>145</td>
<td>1.00 (0.76, 1.31)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Not quantifiable at baseline</td>
<td>61</td>
<td>66</td>
<td>0.91 (0.61, 1.35)</td>
<td></td>
</tr>
<tr>
<td><strong>PFS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥1%</td>
<td>123</td>
<td>123</td>
<td>0.70 (0.53, 0.94)</td>
<td>0.0227</td>
</tr>
<tr>
<td>&lt;1%</td>
<td>108</td>
<td>101</td>
<td>1.19 (0.88, 1.61)</td>
<td></td>
</tr>
<tr>
<td>≥5%</td>
<td>95</td>
<td>86</td>
<td>0.54 (0.39, 0.76)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>&lt;5%</td>
<td>136</td>
<td>138</td>
<td>1.31 (1.01, 1.71)</td>
<td></td>
</tr>
<tr>
<td>≥10%</td>
<td>86</td>
<td>79</td>
<td>0.52 (0.37, 0.75)</td>
<td></td>
</tr>
<tr>
<td>&lt;10%</td>
<td>145</td>
<td>145</td>
<td>1.24 (0.96, 1.61)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Not quantifiable at baseline</td>
<td>61</td>
<td>66</td>
<td>1.06 (0.73, 1.56)</td>
<td></td>
</tr>
</tbody>
</table>
## CheckMate 017 Key Results

<table>
<thead>
<tr>
<th>PD-L1 Expression</th>
<th>Patients n</th>
<th>Unstratified HR (95%CI)</th>
<th>Interaction p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Nivolumab</td>
<td>Docetaxel</td>
<td></td>
</tr>
<tr>
<td><strong>OS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥1%</td>
<td>63</td>
<td>56</td>
<td>0.69 (0.45, 1.05)</td>
</tr>
<tr>
<td>&lt;1%</td>
<td>54</td>
<td>52</td>
<td>0.58 (0.37, 0.92)</td>
</tr>
<tr>
<td>≥5%</td>
<td>42</td>
<td>39</td>
<td>0.53 (0.31, 0.89)</td>
</tr>
<tr>
<td>&lt;5%</td>
<td>75</td>
<td>69</td>
<td>0.70 (0.47, 1.02)</td>
</tr>
<tr>
<td>&lt;10%</td>
<td>81</td>
<td>75</td>
<td>0.70 (0.49, 0.99)</td>
</tr>
<tr>
<td>Not quantifiable</td>
<td>18</td>
<td>29</td>
<td>0.39 (0.19, 0.82)</td>
</tr>
<tr>
<td>≥10%</td>
<td>36</td>
<td>33</td>
<td>0.58 (0.33, 1.02)</td>
</tr>
<tr>
<td>&lt;10%</td>
<td>81</td>
<td>75</td>
<td>0.70 (0.49, 0.99)</td>
</tr>
</tbody>
</table>

**Survival benefit with nivolumab was independent of PD-L1 expression**
Patients
Advanced NSCLC
Confirmed PD after ≥1 line of chemotherapy
No active brain metastasis
ECOG PS 0-1
PD-L1 TPS ≥1%
No serious autoimmune disease
No ILD or pneumonitis requiring systemic steroids

Stratification factors:
ECOG PS (0 vs 1)
Region (East Asia vs non-East Asia)
PD-L1 status (TPS≥50% vs 1-49%)

Endpoints in the TPS≥50% stratum and TPS ≥1% population
Primary: PFS and OS
Secondary: ORR, duration of response, safety
Atezolizumab monotherapy vs docetaxel in 2L/3L NSCLC: Primary analyses for efficacy, safety and predictive biomarkers from a randomized phase II study (POPLAR)

- **Study objective**
  - To examine the efficacy and safety of atezolizumab in patients with advanced NSCLC

- **Key patient inclusion criteria**
  - Metastatic or locally advanced NSCLC
  - Second- or third-line
  - Disease progression on a prior platinum therapy (n=287)

- **Primary endpoint**
  - OS in ITT and PD-L1 expression subgroups

- **Secondary endpoints**
  - PFS, ORR and DOR in ITT and PD-L1 expression subgroups, safety

Vansteenkiste J, et al. Ann Oncol 2015; 26 (suppl 6); abstr 14LBA
Key Results

- Patients with higher PD-L1 expression had better outcomes with atezolizumab than with docetaxel.
- Atezolizumab was well tolerated with fewer treatment-related Grade 3/4 AEs (12% atezolizumab; 39% docetaxel) despite a longer treatment duration (3.7 vs. 2.1 months).

Atezolizumab was associated with significant improvements in OS in the ITT population (12.6 months versus 9.7 months, HR 0.73 [95%CI 0.53, 0.99], p=0.040)

• Chemotherapy
• Targeted therapy
• Immunotherapy
• Other
Bevacizumab 15mg/kg plus cisplatin-pemetrexed (CP) triplet versus CP doublet in Malignant Pleural Mesothelioma (MPM): Results of the IFCT-GFPC-0701 MAPS randomized phase 3 trial

- Study objective
  - To determine whether the addition of bevacizumab to cisplatin-pemetrexed improves survival in patients with MPM

Key patient inclusion criteria
- Histologically proven MPM
- No prior chemo
- No cardiovascular comorbidities
- ECOG PS 0–2
- (n=448)

Primary endpoint
- OS

Secondary endpoints
- PFS, QoL, biomarkers, pharmacoeconomic outcomes

Stratification
- Histology (epitheloid vs. sarcomatoid/mixed), center, ECOG PS (0–1 vs. 2), smoking status

(ARM A) Six 21-day cycles of:
  Pemetrexed 500 mg/m² D1 + cisplatin 75 mg/m² D1
Surveillance

(ARM B) Six 21-day cycles of:
  Pemetrexed 500 mg/m² D1 + Cisplatin 75 mg/m² D1 + Bevacizumab 15 mg/kg D1
Maintenance Bevacizumab 15 mg/kg D1 Q21D until PD or toxicity

Key results

<table>
<thead>
<tr>
<th></th>
<th>BEV+CIS-PEM</th>
<th>CIS-PEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median OS, months</td>
<td>18.82</td>
<td>16.07</td>
</tr>
<tr>
<td>HR (95%CI); p-value</td>
<td>0.76 (0.61, 0.94); p=0.015</td>
<td></td>
</tr>
<tr>
<td>Median PFS, months</td>
<td>9.59</td>
<td>7.48</td>
</tr>
<tr>
<td>HR (95%CI); p-value</td>
<td>0.61 (0.50, 0.75); p&lt;0.0001</td>
<td></td>
</tr>
</tbody>
</table>

Adding bevacizumab to pemetrexed + cisplatin significantly increased PFS (2 months) and OS (2.75 months) and with manageable increase of toxicity

Scherpereel A, et al. J Thorac Oncol 2015; 10 (9, suppl 2; abstr ORAL11.01)
Conclusions

- Nedaplatin + docetaxel improves PFS and OS in advanced or relapsed SQCC.
- Afatinib is slightly superior to gefitinib in 1\textsuperscript{st}-line treatment for EGFR mutant lung cancer.
- 3\textsuperscript{rd} generation EGFR TKIs have demonstrated a encouraging clinical benefit in T790M (+) NSCLC.
- EGFR-TKI; plus pemetrexed or bevacizumab showed promising efficacy in EGFR (+) patients.
- PD1 and PD-L1 inhibitor improve OS for NSCLC compared with docetaxel.
- The triplet pemetrexed, cisplatin, and bevacizumab is a new 1\textsuperscript{st} line treatment paradigm for pleural mesothelioma.
Thank you!
Afatinib versus erlotinib as second-line treatment of patients with advanced squamous cell carcinoma of the lung (LUX-Lung 8): an open-label randomized controlled phase 3 trial.

- Study objective:
  - To compare the efficacy and safety of afatinib, an irreversible ErbB family blocker, and erlotinib, a reversible EGFR TKI, in patients with squamous cell lung carcinoma

Key patient inclusion criteria
- Stage IIIB/IV SCC
- PD after ≥4 cycles of a first-line platinum-doublet
- ECOG PS 0−1
- Adequate organ function (N=795)

Stratification
- Ethnicity (East Asian vs. non-East Asian)

Primary endpoint
- PFS

Secondary endpoints
- OS, ORR, DCR, tumor shrinkage, patient reported outcomes, safety

Afatinib 40 mg QD\textsuperscript{a} (n=398) → PD

Erlotinib 150 mg QD\textsuperscript{b} (n=397) → PD

\textsuperscript{a}dose escalation/reduction permitted; \textsuperscript{b}dose reduction permitted

### PFS and OS

<table>
<thead>
<tr>
<th></th>
<th>Afatinib n=398</th>
<th>Erlotinib n=397</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median PFS, months</strong></td>
<td>2.6 (2.0, 2.9)</td>
<td>1.9 (1.9, 2.1)</td>
</tr>
<tr>
<td>(95% CI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HR (95% CI)</strong></td>
<td>0.81 (0.69, 0.96)</td>
<td></td>
</tr>
<tr>
<td><strong>p-value</strong></td>
<td>0.0103</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Afatinib n=398</th>
<th>Erlotinib n=397</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median OS, months</strong></td>
<td>7.9 (7.2, 8.7)</td>
<td>6.8 (5.9, 7.8)</td>
</tr>
<tr>
<td>(95% CI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HR (95% CI)</strong></td>
<td>0.81 (0.69, 0.95)</td>
<td></td>
</tr>
<tr>
<td><strong>p-value</strong></td>
<td>0.0077</td>
<td></td>
</tr>
</tbody>
</table>