ESMO 2012
Highlight on Lung Cancer

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The Chinese University of Hong Kong
New Options
New Biomarkers
New Targets
New Options
New Biomarkers
New Targets
PROFILE 1007: Crizotinib vs Chemotherapy (2\textsuperscript{nd}/3\textsuperscript{rd} line therapy)

Key entry criteria
- ALK+ by central FISH testing
- Stage IIIB/IV NSCLC
- 1 prior chemotherapy (platinum-based)
- ECOG PS 0–2
- Measurable disease
- Treated brain metastases allowed

Randomize

N=318

Endpoints
- Primary
  - PFS (RECIST 1.1, independent radiology review)
- Secondary
  - ORR, DCR, DR
  - OS
  - Safety
  - Patient reported outcomes (EORTC QLQ-C30, LC13)

CROSSOVER TO CRIZOTINIB ON PROFILE 1005

- Crizotinib 250 mg BID PO, 21-day cycle (n=159)
- Pemetrexed 500 mg/m\textsuperscript{2} or Docetaxel 75 mg/m\textsuperscript{2} IV, day 1, 21-day cycle (n=159)

*aStratification factors: ECOG PS (0/1 vs 2), brain metastases (present/absent), and prior EGFR TKI (yes/no)
ORR\textsuperscript{a} by Independent Radiologic Review

ORR ratio: 3.4 (95\% CI: 2.5 to 4.7); \(P<0.001\)

Crizotinib (n=173)
PEM/DOC (n=174)

\begin{itemize}
\item Crizotinib (n=172)
\item PEM (n=99)
\item DOC (n=72)
\end{itemize}
Primary Endpoint: PFS by Independent Radiologic Review (ITT Population)

![Graph showing survival rates and event counts for Crizotinib and PEM/DOC treatments.]

More than an option! It is a new standard!

<table>
<thead>
<tr>
<th></th>
<th>Crizotinib (n=173)</th>
<th>PEM/DOC (n=174)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events, n (%)</td>
<td>100 (58)</td>
<td>127 (73)</td>
</tr>
<tr>
<td>Median, mo</td>
<td>7.7</td>
<td>3.0</td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>0.49 (0.37 to 0.64)</td>
<td></td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

No. at risk
- Crizotinib: 173, 93, 38, 11, 2, 2, 0
- PEM/DOC: 174, 49, 15, 4, 1, 0

PEM/DOC, pemetrexed/docetaxel
Intercalated combination
NVALT-10: Design

**Patients**
- Locally advanced or metastatic NSCLC (IIIB-IV)
- Failed first line platinum therapy
- WHO PS 0-2

**Combination therapy**

**Squamous**
- Erlotinib 150mg p.o. day 2-16
- + Docetaxel 75 mg/m² day 1 q3 weeks

**Non-Squamous**
- Erlotinib 150mg p.o. day 2-16
- + Pemetrexed 500 mg/m² day 1 q3 weeks

**Mono therapy**

**Squamous and Non Squamous**
- Erlotinib 150mg p.o. daily

Primary endpoint: PFS

Chemotherapy planned 4 cycles
Erlotinib until disease progression

Aerts et al ESMO 2012
PFS and OS

Adjusted for stratification factors: $p = 0.09$, HR = 0.78 (0.59 - 1.04)

Adjusted for stratification factors: $p = 0.02$, HR = 0.67 (0.50 - 0.93)
**FASTACT-2 (MO22201; CTONG0902) study design**

<table>
<thead>
<tr>
<th>Screening</th>
<th>Study treatment</th>
<th>Maintenance phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previously untreated stage IIIB/IV NSCLC, PS 0/1 (n=451)</td>
<td>Gemcitabine 1,250mg/m² (d1, 8) + carboplatin AUC=5 or cisplatin 75mg/m² (d1) + erlotinib 150mg/day (d15–28); q4wks x 6 cycles GC-erlotinib (n=226)</td>
<td>Erlotinib 150mg/day → PD</td>
</tr>
<tr>
<td></td>
<td>1:1; stratified by stage, histology, smoking status and chemo regimen</td>
<td>Erlotinib 150mg/day</td>
</tr>
<tr>
<td></td>
<td>Gemcitabine 1,250mg/m² (d1, 8) + carboplatin AUC=5 or cisplatin 75mg/m² (d1) + placebo (d15–28); q4wks x 6 cycles GC-placebo (n=225)</td>
<td>Placebo → PD</td>
</tr>
</tbody>
</table>

**Primary endpoint:** PFS with IRC confirmation

**Secondary endpoints:** subgroup analyses, OS in all patients and subgroups, ORR, duration of response, TTP, NPR at 16 weeks, safety, QoL

NSCLC = non-small cell lung cancer; PS = performance status; PD = disease progression; AUC = area under the curve; q4wks = every 4 weeks; IRC = independent review committee; OS = overall survival; ORR = objective response rate; TTP = time to progression; NPR = non-progression rate; QoL = quality of life
OS in ITT population (22 Jun 2012)

HR = 0.79 (95% CI 0.64–0.99)  
\( p = 0.0420 \)

Erlotinib (n=226)  
Placebo (n=225)

E 226 219 202 191 176 165 154 138 129 114 98 85 68 52 39 23 9 6 1 0
P 225 218 206 185 168 156 138 120 103 92 78 68 53 37 24 13 6 4 0 0

Time (months)
PFS and OS in **EGFR Mut+** subgroup (22 Jun 2012)

**PFS**

- Erlotinib (n=49) vs Placebo (n=48)
  - HR=0.48 (0.27–0.84)  
  - p=0.0092

**OS**

- Erlotinib (n=49) vs Placebo (n=48)
  - HR=0.25 (0.16–0.39)  
  - p<0.0001
PFS and OS in \textit{EGFR WT} subgroup (22 Jun 2012)

**PFS**

- Erlotinib (n=69)
- Placebo (n=67)
- HR=0.97 (0.69–1.36)
- p=0.8467

**OS**

- Erlotinib (n=69)
- Placebo (n=67)
- HR=0.77 (0.53–1.11)
- p=0.1612
Intercalated combination of chemotherapy and EGFR TKI benefit mostly patients with EGFR mutation but remains as an option for patients with UNKNOWN mutation status.
CATS TRIAL (Cisplatin And TS-1 TRIAL)
Treatment Schema

- Advanced NSCLC
- PS 0 or 1
- 20-74 years
- No prior chemotherapy

Control arm (DP) n=305
- Docetaxel: 60mg/m² d1
- Cisplatin: 80mg/m² d1
- repeated every 3-4 weeks

Experimental arm (SP) n=303
- S-1: 40-60mg*/body b.i.d d1-21
- Cisplatin: 60mg/m² d8
- repeated every 4-5 weeks

*According to body surface area
- BSA < 1.25 m²  80 mg/day
- 1.25=<BSA <1.5  100 mg/day
- BSA >=1.5  120 mg/day

Randomized
- Stratified by
  Gender (Male/Female)
  Stage (IIIB/IV/postoperative)
  histology (Adeno/Non-adeno)

- Follow-up : Jan/2009 - Jun/2011
- Enrolled : N=608

Sakai et al ESMO 2012 Abst 1234PD
Overall survival

<table>
<thead>
<tr>
<th></th>
<th>SP (n=301)</th>
<th>DP (n=295)</th>
<th>SP (n=251)</th>
<th>DP (n=247)</th>
<th>SP (n=50)</th>
<th>DP (n=48)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
<td>301</td>
<td>295</td>
<td>251</td>
<td>247</td>
<td>50</td>
<td>48</td>
</tr>
<tr>
<td><strong>Events</strong></td>
<td>244</td>
<td>236</td>
<td>247</td>
<td>236</td>
<td>48</td>
<td>48</td>
</tr>
<tr>
<td><strong>HR (96.4% CI)</strong></td>
<td>1.013 (0.837-1.227)</td>
<td>1.239 (0.819-1.874)</td>
<td>1.013 (0.837-1.227)</td>
<td>1.239 (0.819-1.874)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Median OS</strong></td>
<td>17.1 months (13.7-20.3)</td>
<td>16.1 months (14.0-18.5)</td>
<td>17.1 months (13.7-20.3)</td>
<td>16.1 months (14.0-18.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>95% CI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

**Overall survival probability (%)**

- **Docetaxel + CDDP**
- **S-1 + CDDP**

**Time From Random Assignment (months)**

**Median Overall Survival by Histology**

- **Non-squamous**
  - SP (n=251): Median OS (M) (95% CI) = 17.4 (14.6-20.7) HR (95% CI) = 0.973 (0.797-1.187)
  - DP (n=247): Median OS (M) (95% CI) = 19.1 (14.6-21.4) HR (95% CI) = 1.239 (0.819-1.874)

- **Squamous**
  - SP (n=50): Median OS (M) (95% CI) = 12.3 (8.1-15.8) HR (95% CI) = 1.239 (0.819-1.874)
  - DP (n=48): Median OS (M) (95% CI) = 11.7 (8.9-17.7) HR (95% CI) = 1.239 (0.819-1.874)
Patients responded to EORTC QLQ-C30 3 times:
1. before each treatment
2. 1 week after the first dose of cisplatin
3. at the end of the second course.

A higher score of LC-13 represents a worse condition in lung cancer-associated symptoms, treatment-related side effects and pain.

S1 + Cisplatin should be considered one of the first line options.
New Standard
New Biomarkers
New Targets
Molecular findings in 95 patients from the EURTAC trial (All pts with EGFR mutations)

<table>
<thead>
<tr>
<th></th>
<th>Total (N=95) N (%)</th>
<th>Erlotinib (N=50) N (%)</th>
<th>Chemotherapy (N=45) N (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EML4-ALK</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Detected</td>
<td>15 (15.79)</td>
<td>11 (22.00)</td>
<td>4 (8.89)</td>
<td>0.0968</td>
</tr>
<tr>
<td>Not detected</td>
<td>79 (83.16)</td>
<td>39 (78.00)</td>
<td>40 (88.89)</td>
<td></td>
</tr>
<tr>
<td>No data</td>
<td>1 (1.05)</td>
<td>0 (0.00)</td>
<td>1 (2.22)</td>
<td></td>
</tr>
<tr>
<td><strong>T790M mutation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not detected</td>
<td>59 (62.11)</td>
<td>32 (64.00)</td>
<td>27 (60.00)</td>
<td>0.6882</td>
</tr>
<tr>
<td>Detected</td>
<td>36 (37.89)</td>
<td>18 (36.00)</td>
<td>18 (40.00)</td>
<td></td>
</tr>
<tr>
<td><strong>TP53 mutation status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mutated</td>
<td>23 (24.21)</td>
<td>10 (20.00)</td>
<td>13 (28.89)</td>
<td>0.5953</td>
</tr>
<tr>
<td>Wild-type</td>
<td>58 (61.05)</td>
<td>33 (66.00)</td>
<td>26 (57.78)</td>
<td></td>
</tr>
<tr>
<td>No data</td>
<td>13 (13.68)</td>
<td>7 (14.00)</td>
<td>6 (13.33)</td>
<td></td>
</tr>
<tr>
<td><strong>BIM expression</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low/intermediate</td>
<td>53 (55.79)</td>
<td>26 (52.00)</td>
<td>27 (60.00)</td>
<td>0.5418</td>
</tr>
<tr>
<td>High</td>
<td>30 (31.58)</td>
<td>16 (32.00)</td>
<td>14 (31.11)</td>
<td></td>
</tr>
<tr>
<td>No data</td>
<td>12 (12.63)</td>
<td>8 (16.00)</td>
<td>4 (8.89)</td>
<td></td>
</tr>
</tbody>
</table>

Rosell et al ESMO 2012
Multivariate analyses

- Multivariate analyses included sex, smoking status, PS, treatment group, brain mets, bone mets, type of EGFR mutation, T790M, BIM, TP53 and EML4-ALK

- **Markers of longer PFS**
  - erlotinib (HR, 0.36; P=0.0005)
  - high BIM expression (HR, 0.55; P=0.033)

- **Markers of longer OS**
  - high BIM expression (HR, 0.47; P=0.025)
**EGFR del 19 / L858R w/ or w/out**

- **T790M**
- **BIM mRNA**
- **TP53**
- **EML4/ALK**

**Compensatory survival pathways that can inhibit BIM**

- **ROR1 (Pan-HER i)**
- **ZNF217 (β-TGF i)**
- **GATA2/STAT5/BCL2**
- **NOTCH3 (Gsi), HES1, Numb**
- **ADAM17 (MEK i)**
- **Tankyrases 1&2 (TNKS)**

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**Seshagiri et al. Nature 2012**

- **erlotinib**

**HR = 2.46 (p=0.04)**

**Baumgart et al. Cancer Res 2010**

**Seshagiri et al. Nature 2012**

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**Vienna ESMO Congress 2012**

[wesmo2012.org]
LACE-Bio Pooled Analysis of the Prognostic and Predictive Value of $TP53$ mutations in Completely Resected Non Small Cell Lung Cancer (NSCLC)


- Mutations in the Tumour Suppressor Gene $TP53$ (encoding p53) occur in about 50% of Stage II-III NSCLC.

- This study has assessed the prognostic and predictive value of $TP53$ mutations for survival after cis-platin-based adjuvant therapy in a pooled analysis of 4 randomized trials (IALT, ANITA, CALGB, JBR10; n=1209 patients)

- Hazard ratio (HR; 95% CI) were estimated with a Cox model stratified on trial and adjusted for gender, age and clinico-pathological variables (histology, T and N status). A test was considered significant if p-value was inferior to 0.01.
LACE-Bio Pooled Analysis of the Prognostic and Predictive Value of *TP53* mutations in Completely Resected Non Small Cell Lung Cancer (NSCLC)

<table>
<thead>
<tr>
<th><em>TP53</em> mutation</th>
<th>Chemotherapy group (Nb deaths / Nb patients)</th>
<th>Control group (Nb deaths / Nb patients)</th>
<th>HR for event CT vs. no CT [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wild-Type n=772</td>
<td>153/377</td>
<td>190/395</td>
<td>0.77 [0.62;0.96] p=0.02</td>
</tr>
<tr>
<td>Mutant n=432</td>
<td>127/233</td>
<td>100/199</td>
<td>1.05 [0.81;1.37] p=0.71</td>
</tr>
<tr>
<td>HR for event Mutant vs. WT [95% CI]</td>
<td>1.39 [1.09;1.77] p=0.008</td>
<td>1.02 [0.79;1.30] p=0.90</td>
<td>Test for interaction p53*treatment p=0.07</td>
</tr>
</tbody>
</table>
The European Thoracic Oncology Platform Lungscape project: A way to bridge NSCLC molecular characteristics and clinical data

New Standard
New Biomarkers
New Targets
Selumetinib for KRAS mutation

<table>
<thead>
<tr>
<th></th>
<th>Selumetinib + docetaxel</th>
<th>Placebo + docetaxel</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Best objective response (RECIST 1.0), number (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CR</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>PR</td>
<td>16 (37.2)*</td>
<td>0</td>
</tr>
<tr>
<td>SD ≥6 weeks</td>
<td>19 (44.2)</td>
<td>20 (50.0)</td>
</tr>
<tr>
<td>PD</td>
<td>8 (18.6)</td>
<td>18 (45.0)</td>
</tr>
<tr>
<td>Not evaluable</td>
<td>0</td>
<td>2 (5.0)</td>
</tr>
<tr>
<td>Median DoR, days</td>
<td>182</td>
<td>-</td>
</tr>
</tbody>
</table>

1-sided p value
*11 confirmed, 5 unconfirmed
§One patient was classed as non-evaluable due to non-evaluable non-target lesions and would have had a partial response according to RECIST 1.1 criteria

Janne et al ESMO 2012
Progression Free Survival

• There was a statistically and clinically significant improvement in PFS
  – 71/83 events (85.5%): selumetinib + docetaxel 35/43, placebo + docetaxel 36/40

<table>
<thead>
<tr>
<th></th>
<th>Median PFS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selumetinib + docetaxel, N=43</td>
<td>5.3 mo</td>
</tr>
<tr>
<td>Placebo + docetaxel, N=40</td>
<td>2.1 mo</td>
</tr>
<tr>
<td>HR 0.58; 80% CI 0.42, 0.79; 1-sided p=0.0138*</td>
<td></td>
</tr>
</tbody>
</table>

Symbols represent censored observations
**Target expression:**
NeuGc GM3 is a tumor specific antigen, expressed in melanoma, breast cancer, lung cancer and several neuroectodermal pediatric tumors.

**Mechanism of Action:** Racotumomab induces a specific Ab3 (IgM and IgG) and cellular response against NeuGcGM3.
Phase II/III, multicentric, randomized, double blind and placebo-controlled.

Two stages in the trial:
Stage 1 - 15 immunizations during a period of one year.
Stage 2 - Follow up for all patients. Blind was opened and monthly re-immunizations continued only for patients receiving racotumomab. Vaccination continued beyond progression (no second line therapy) until worsening PS or unacceptable toxicity.

Vaccination Schedule:

<table>
<thead>
<tr>
<th>Induction Period</th>
<th>Maintenance Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 doses every 14 days</td>
<td>10 doses every 28 days (1 year of treatment)</td>
</tr>
</tbody>
</table>

176 patients with:
NSCLC Stages IIIB/IV
After completion of standard first line chemotherapy (CT) and
Response: PR, CR, SD.
Overall Survival (OS) Analyses

### OS (ITT)

<table>
<thead>
<tr>
<th>Arm</th>
<th>Mean</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>Racotumomab</td>
<td>15.7</td>
<td>8.3</td>
</tr>
<tr>
<td>Events: 73</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>10.6</td>
<td>6.3</td>
</tr>
<tr>
<td>Events: 77</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### OS (PPP)

<table>
<thead>
<tr>
<th>Arm</th>
<th>Mean</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>Racotumomab</td>
<td>18.9</td>
<td>10.9</td>
</tr>
<tr>
<td>Events: 54</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>11.4</td>
<td>6.9</td>
</tr>
<tr>
<td>Events: 58</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

OS Rate

<table>
<thead>
<tr>
<th>OS Rate</th>
<th>6 m</th>
<th>12 m</th>
<th>18 m</th>
<th>24 m</th>
</tr>
</thead>
<tbody>
<tr>
<td>Racotumomab</td>
<td>68</td>
<td>38</td>
<td>23</td>
<td>17</td>
</tr>
<tr>
<td>Placebo</td>
<td>55</td>
<td>24</td>
<td>11</td>
<td>7</td>
</tr>
</tbody>
</table>

PPP: Includes only patients who received ≥ 5 doses of Racotumomab (77% of patient population)

Log rank test, p= 0.02
Stimuvax: Randomized Phase II Overall Survival

Survival distribution function

Survival time (months)

n=88

n=83

Stimuvax

Censored Stimuvax

Control

Censored control

<table>
<thead>
<tr>
<th></th>
<th>BSC</th>
<th>Stimuvax + BSC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median follow-up, months</td>
<td>56</td>
<td>51</td>
</tr>
<tr>
<td>Median survival, months [95% CI]</td>
<td>13.0 [11.2–16.2]</td>
<td>17.2 [12.9–24.2]</td>
</tr>
<tr>
<td>Hazard ratio [95% CI]; p-value</td>
<td>0.75 [0.53–1.04]; p=0.09</td>
<td></td>
</tr>
<tr>
<td>1-year survival rate, %</td>
<td>55</td>
<td>63</td>
</tr>
<tr>
<td>2-year survival rate, %</td>
<td>27</td>
<td>41</td>
</tr>
<tr>
<td>3-year survival rate, %</td>
<td>17</td>
<td>31</td>
</tr>
</tbody>
</table>

Targeting c-MET with Mab against Hepatocyto growth factor

Key entry criteria:
- Stage IIIb/IV NSCLC
- Treatment-naïve
- Adenocarcinoma histology
- Asian, non-smoker or light former smoker

Treatment
- Gefitinib: 250 mg daily
- Ficlatuzumab: 20 mg/kg every 2 wks in 28-day cycles

Study endpoints
- Primary: ORR
- Secondary: PFS, OS

Stratification:
- ECOG PS
- Smoking history
- Gender

Crossover permitted: ficlatuzumab plus gefitinib (progressive disease after initial response, partial response or stable disease >3 months)

Early discontinuations, non-responders, or pts who do not want to participate in crossover

<table>
<thead>
<tr>
<th>Event/Censored</th>
<th>Median PFS (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FG</td>
<td>70/24</td>
</tr>
<tr>
<td>G</td>
<td>79/15</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Event/Censored</th>
<th>Median OS (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FG</td>
<td>30/64</td>
</tr>
<tr>
<td>G</td>
<td>35/59</td>
</tr>
</tbody>
</table>

FG=ficlatuzumab plus gefitinib; G=gefitinib; ITT=intent-to-treat; NA=not applicable; OS=overall survival; PFS=progression-free survival.
Biomarker selected subgroup

**c-Met low**

**PFS**
- HR (95% CI) = 0.63 (0.33, 1.21)
- P = 0.1574

<table>
<thead>
<tr>
<th>Group</th>
<th>Event/Censored</th>
<th>Median PFS (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FG</td>
<td>17/5</td>
<td>7.3 (2.7, 11.1)</td>
</tr>
<tr>
<td>G</td>
<td>21/2</td>
<td>2.8 (1.9, 4.7)</td>
</tr>
</tbody>
</table>

**OS**
- HR (95% CI) = 0.79 (0.33, 1.92)
- P = 0.6082

<table>
<thead>
<tr>
<th>Group</th>
<th>Event/Censored</th>
<th>Median OS (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FG</td>
<td>9/13</td>
<td>17.8 (13.3, NA)</td>
</tr>
<tr>
<td>G</td>
<td>11/12</td>
<td>16 (10.1, NA)</td>
</tr>
</tbody>
</table>

**ORR, % (95% CI)**
- FG: 41 (21, 64)
- G: 22 (8, 44)

Mok et al ESMO 2012 Abst 1198
### What is news EGFR TKI

<table>
<thead>
<tr>
<th>Abst #</th>
<th>Study design</th>
<th>Result</th>
<th>Remark</th>
</tr>
</thead>
<tbody>
<tr>
<td>1226</td>
<td>Dacomitinib in EGFR mutants</td>
<td>PFS 18.2 months</td>
<td>Highest PFS so far (sample size 46)</td>
</tr>
<tr>
<td>Kris</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1227</td>
<td>Afatinib/Cetuximab in TKI resistance</td>
<td>RR 40%</td>
<td></td>
</tr>
<tr>
<td>Janjigian</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>T790M +ive 38%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>T790M –ive 47%</td>
<td></td>
</tr>
<tr>
<td>1252</td>
<td>Afatinib in uncommon mutations</td>
<td>L858R + T790M (1PR, 11.0 mo; 3SD, 9.6+ mo, 8.5 mo and 6.7 mo); Others: lower response rate</td>
<td>It works but not as good as sensitive mutations</td>
</tr>
<tr>
<td>Yang</td>
<td></td>
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</tr>
<tr>
<td>1225</td>
<td>Second line erlotinib + pemetrexed vs erlotinib vs pemetrexed</td>
<td>E + P vs E vs P Med PFS 7.4 vs 3.8 vs 4.4 months</td>
<td>Not sure if incidence of mutations are the same in all 3 arms</td>
</tr>
<tr>
<td>Lee</td>
<td></td>
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</tbody>
</table>
## New disappointment

<table>
<thead>
<tr>
<th>Abst #</th>
<th>Study design</th>
<th>Agent</th>
<th>Remark</th>
</tr>
</thead>
<tbody>
<tr>
<td>916</td>
<td>MISSION: Sorafenib vs placebo</td>
<td>Sorafenib</td>
<td>We need biomarker for anti-angiogenesis</td>
</tr>
<tr>
<td>2347</td>
<td>FORTIS-M: Talactoferrin vs BSC</td>
<td>Talactoferrin</td>
<td>Targeted immunotherapy is the future</td>
</tr>
</tbody>
</table>