AFATINIB* LUX-LUNG 3 & 6 CLINICAL TRIALS:

The largest and most robust clinical registration trial programme in EGFR mutation-positive NSCLC to date

**PRIMARY ENDPOINT**

MEDIAN PROGRESSION-FREE SURVIVAL BY INDEPENDENT REVIEW

SHOWN HERE IN PATIENTS WITH COMMON MUTATIONS

- **Chemotherapy**
- **Afatinib**

LUX-Lung 3: Afatinib* vs. pemetrexed/cisplatin

Primary and secondary endpoints of the trial were in patients with EGFR mutation positive NSCLC

- **Presented at ASCO 2012**

<table>
<thead>
<tr>
<th>Months</th>
<th>Patients with most common EGFR mutations (del19 and L858R-pre-planned subgroup analysis, 89% of each study population)**</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.9</td>
<td>Afatinib*</td>
</tr>
<tr>
<td>13.6</td>
<td>Chemotherapy</td>
</tr>
</tbody>
</table>

**CONSISTENT ACROSS BOTH TRIALS, AFATINIB* DEMONSTRATED:**

- Better quality of life
- Tumour shrinkage
- Improvements in disease-related symptoms

**SECONDARY ENDPOINT**

MEDIAN OVERALL SURVIVAL

SHOWN HERE IN PATIENTS WITH COMMON MUTATIONS

- **Chemotherapies**
- **Afatinib**

LUX-Lung 3 & 6 combined subgroup post-hoc analysis: Afatinib* vs. chemotherapies

Consistent with LUX-Lung 3, results from LUX-Lung 6 substantiate the efficacy of afatinib* in delaying tumour growth in lung cancer patients with EGFR mutations, when compared with standard chemotherapy

- **Presented at ASCO 2014**

<table>
<thead>
<tr>
<th>Months</th>
<th>Patients with most common EGFR mutations (del19 and L858R)</th>
</tr>
</thead>
<tbody>
<tr>
<td>24.3</td>
<td>Afatinib*</td>
</tr>
<tr>
<td>27.3</td>
<td>Chemotherapy</td>
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</table>

<table>
<thead>
<tr>
<th>Months</th>
<th>Patients with del19 mutation</th>
</tr>
</thead>
<tbody>
<tr>
<td>20.7</td>
<td>Afatinib*</td>
</tr>
<tr>
<td>31.7</td>
<td>Chemotherapy</td>
</tr>
</tbody>
</table>

**ADVERSE EVENTS:**

- **Afatinib** treatment in LUX-Lung 3 and LUX-Lung 6 rarely led to discontinuation of therapy (6% and 8% respectively) and were as expected with EGFR inhibition.

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**LUX-Lung 3:** Afatinib* vs. pemetrexed/cisplatin

**LUX-Lung 6:** Afatinib* vs. gemcitabine/cisplatin

**MEDIAN OVERALL SURVIVAL**
(secondary endpoint)

**Patients with del19 mutation**

- In a subgroup analysis of LUX-Lung 3 and LUX-Lung 6, afatinib* prolonged survival of lung cancer patients with the most common type of EGFR mutation (deletion in exon 19 of the EGFR gene) compared with standard chemotherapy by a median of more than 12 months in both the trials.

- In a combined post-hoc analysis of the trials, this translated to a 41% reduction in the risk of death for patients with del19 mutation.

- In the overall patient population, there was no significant overall survival benefit of afatinib compared with chemotherapy (28.16 vs. 28.22 months for LUX-Lung 3 and 23.1 vs. 23.5 months for LUX-Lung 6).

- Overall survival analysis of LUX-Lung 3 & 6 presented at ASCO 2014.

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LUX-Lung 3 and LUX-Lung 6 showcase the growing evidence of the superiority of afatinib over standard of care chemotherapies (pem/cis) and (gem/cis).

345 LUX-LUNG 3 PATIENTS – RECRUITMENT COMPLETE
364 LUX-LUNG 6 PATIENTS – RECRUITMENT COMPLETE

Inclusion criteria
- Pathologically confirmed diagnosis of Stage IIIIB “wet” or Stage IV adenocarcinoma of the lung (AJCC Version 6 Staging)
- Epidermal Growth Factor Receptor mutation detected by central laboratory analysis of tumour biopsy material
- ECOG score of 0 or 1

LUX-Lung 3
- Argentina
- Australia
- Austria
- Belgium
- Brazil
- Canada
- Chile
- Croatia
- Czech Republic
- Denmark
- Estonia
- Finland
- France
- Germany
- Hungary
- Ireland
- Italy
- Japan
- Korea
- Malaysia
- Netherlands
- New Zealand
- Norway
- Peru
- Philippines
- Poland
- Portugal
- Romania
- Russia
- Singapore
- Slovakia
- Spain
- Sweden
- Switzerland
- Taiwan
- Thailand
- UK
- Ukraine
- USA

LUX-Lung 6
- China
- Rep. of Korea
- Thailand

LUX-Lung 3 & 6 Trial Design

Patients with adenocarcinoma of the lung with tumours harbouring EGFR mutations
(LUX-Lung 3: Global patient population, LUX-Lung 6: Asian patient population)

Randomisation

2:1

Afatinib*
(Irreversible ErbB Family Blocker)

LUX- Lung 3: PEMETREXED / CISPLATIN
(Chemotherapy)

LUX-Lung 6: GEMCITABINE / CISPLATIN
(Chemotherapy)

Primary endpoint: Progression-free survival (PFS)
Secondary endpoints: Quality of Life, Tumour Shrinkage, Disease Related Symptoms, Overall Survival, Safety
Grade ≥3 Adverse Events (AEs)

**LUX-Lung 3**
(Afatinib* vs pemetrexed/cisplatin)

- The most common drug-related adverse events observed in the afatinib* treatment arm were diarrhoea, rash and paronychia
- The most common drug-related adverse events observed in the chemotherapy arm were nausea, decreased appetite, and vomiting
- There was a low discontinuation rate associated with treatment-related adverse events in the trial (6% discontinuation rate for afatinib*; 12% for chemotherapy)
- 1% of patients in the afatinib* arm discontinued treatment due to diarrhoea

**LUX-Lung 6**
(Afatinib* vs gemcitabine/cisplatin)

- The most common adverse events observed in the afatinib* treatment arm were diarrhoea, rash/acne and stomatitis/mucositis (inflammation of mouth and throat)
- The most common drug-related adverse events observed in the chemotherapy arm were neutropenia (an abnormally low level of neutrophils, a type of white blood cell), vomiting and leukopenia (a decrease in the number of white blood cells)
- There was a low discontinuation rate associated with treatment-related adverse events in the trial (6% discontinuation rate for afatinib*; 40% for chemotherapy)
- 2% of patients in the afatinib* arm discontinued treatment due to rash/acne and none discontinued due to diarrhoea

ADVERSE EVENTS:¹ ²

Adverse events with afatinib* treatment in LUX-Lung 6 and LUX-Lung 3 rarely led to discontinuation of therapy and were as expected with EGFR inhibition.


Further results

**BETTER QUALITY OF LIFE**

Patients on afatinib* experienced significantly better quality of life (e.g. at work and during household activities) than those on chemotherapies, as measured by lung cancer standard questionnaires.

**TUMOUR SHRINKAGE**

Afatinib* achieved significant and sustained tumour shrinkage (objective response) versus chemotherapies as measured by independent review.

- **LUX-LUNG 3**
  - 23% PEM/CIS
  - 56% AFATINIB*

- **LUX-LUNG 6**
  - 23% GEM/CIS
  - 67% AFATINIB*

**IMPROVED SYMPTOMS**

More patients taking afatinib* experienced improvement of symptoms such as cough, dyspnea (shortness of breath) and pain (as measured by standard lung cancer questionnaires).

- **Cough**
- **Shortness of breath (dyspnea)**
- **Pain**


**CONSISTENT ACROSS BOTH TRIALS, AFATINIB* DEMONSTRATED**

- Better quality of life
- Tumour shrinkage
- Improvements in disease-related symptoms