Phase II of gefitinib (IRESSA) administered as first-line treatment in patients with non-resectable pneumonic-type adenocarcinoma (P-ADC)

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**IFCT-0401 TRIAL**

**Abstract**

**Background (1)**
- Pneumonic-type adenocarcinoma (P-ADC)
- Primary lung ADC:
  - Pathological pneumonic presentation (multifocal or diffuse)
  - Usually referred to histologically as ADC with BAC feature (ADC-WBF) (2004 WHO Classification)
- Age > 18 years old
- Performance status ≤ 2 (WHO)
- Adequate blood biological parameters

**Eligibility criteria**
- Pathologically/cytologically proven ADC-P
- Non-resectable disease
- 3-month expected survival
- No prior radiotherapy or chemotherapy
- Age > 18 years old
- Performance status ≤ 2 (WHO)

**Background (2)**
- Effectiveness of chemotherapy questionable in ADC-WBF
- Resistant, less or more sensitive to chemotherapy than other lung cancers?
- Rationale for treatment of ADC-WBF by TI-EGR:
  - EGFR overexpression by tumor cells more frequent = importance of EGFR pathway (AKT phosphorylation)
  - BAC feature is predictive of response to TI-EGR (p53 and p21)
  - High frequency of EGFR mutation leading to major response to TI-EGR

**Biological markers**
- Centralized pathologic review
- Immunochemistry and SISH expression
  - EGFR, HER2, p53, p21, p-AKT
- Mutation analysis
  - EGFR exon 18-21 sequencing
  - 12 codon ras (ASO-PCR)
- Collection of serum:
  - Inclusion & one more month treatment
  - EGFR ligands and shedding EGFR extracellular domain

**Characteristics of the 50 first patients**
- Males: 22 (44%)
- Females: 28 (56%)
- Median age: 64.9 (range 27-80)
- Performance Status (PS):
  - PS 0: 22
  - PS 1: 10
  - PS 2: 7
  - PS > 2:
- WHO criteria
- Smoking habits
  - 18 non-smokers (NS) (including 17 females)

**IFCT-0401 Schedule**

**RESULTS**

**Effectiveness (1)**

*All patients were evaluable for response*

<table>
<thead>
<tr>
<th>Partial response</th>
<th>6 (12%)</th>
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<tbody>
<tr>
<td>Disease control</td>
<td>15 (30%)</td>
</tr>
<tr>
<td>Static disease</td>
<td>9 (18%)</td>
</tr>
<tr>
<td>Progressive</td>
<td>38 (70%)</td>
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</tbody>
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**Results**

- Clinical presentation at inclusion
  - 46 thoracic diseases:
    - 40 bi-lobar diseases: 6 with extra-thoracic metastasis
    - 6 un-lobar diseases after pneumonectomy
  - 2 unilateral diseases with extra-thoracic metastasis
  - 2 unilateral diseases non-resectable for inadequate pulmonary function tests

**Feasibility - Toxicity**

- Dermatological toxicity
  - Grade 0-2:
  - Grade 3:
  - Grade 4:

**Patients outcome**

17/20 patients eligible for post-trial treatment received chemotherapy

**Results**

- No patients were lost for follow-up
- Duration of disease control for the first 50 patients:
  - Longer: +13.5 months
  - Range: [5.1 +13.5] months
- Median time to progression: not evaluable
- Overall survival: median not achieved

**Discussion**

**Conclusions**

- Final study with 83 patients (ASCO 2006)
- Next trial profiled:
  - Randomized phase II on first-line BAC treatment strategy
  - Optimization of taxan-based chemotherapy and TKI EGFR...