Biological and clinical prognostic factors in patients with advanced non-small-cell cancer (NSCLC) treated by erlotinib: preliminary results of the ERMETIC cohort

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Abstract # 8079

Sequencing (n=297)

<table>
<thead>
<tr>
<th>Type of specimens</th>
<th>Sequencing (n=297)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biopsy-cytology</td>
<td>205 (71)</td>
</tr>
<tr>
<td>Cytology</td>
<td>63 (22)</td>
</tr>
<tr>
<td>Wiltype</td>
<td>222 (78)</td>
</tr>
<tr>
<td>- non amplifiable</td>
<td>80 (27)</td>
</tr>
<tr>
<td>- mutated</td>
<td>142 (48)</td>
</tr>
<tr>
<td>- wild type</td>
<td>246 (83)</td>
</tr>
<tr>
<td>- non amplifiable</td>
<td>19 (6)</td>
</tr>
<tr>
<td>- mutated</td>
<td>38 (13)</td>
</tr>
</tbody>
</table>

Overall survival was defined as the delay between the start of treatment and the date of death whatever the cause or date of last follow up for the patient alive. The cut-off data for analysis was April 1st 2009. The median follow-up (inverted Kaplan-Meier method) was 15.6 months.

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Cohort Size</th>
<th>HR [95% CI]</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EGFR IHC</td>
<td>10%</td>
<td>1.00 [1.00-1.00]</td>
<td>0.88</td>
</tr>
<tr>
<td>K-Ras</td>
<td>1%</td>
<td>1.00 [1.00-1.00]</td>
<td>0.88</td>
</tr>
<tr>
<td>Stage</td>
<td>IIIB-IV</td>
<td>1.00 [1.00-1.00]</td>
<td>0.88</td>
</tr>
</tbody>
</table>

The Kaplan-Meier method was used to draw survival curves. Cox model was used for prognostic analyses. Clinical factors were studied in univariate and multivariate analysis. Factors with p-value inferior to 0.20 were kept in the model. Each Biological factor was studied in univariate analysis and then added to the clinical model.

The present work shows preliminary results of objective 2 ERMETIC project, including:

- Description analysis of ERMETIC prospective cohort
- Overall survival analysis based on clinical characteristics
- Descriptive analysis of 2 biomarkers (EGFR IHC and sequencing of EGFR exons 18-21 and K-Ras exon 2)
- Overall survival analysis based on clinical and biological factors restricted to a subpopulation of patients having results of at least 3 biomarkers available

**BACKGROUND**

**EGFR-TKis, and especially Erlotinib, are authorized in Europe for the treatment of metastatic NSCLC after failure of at least one line of chemotherapy.**

Although, it has been suggested that biomarkers (EGFR over-expression, EGFR gene polysomy/amplification and EGFR and K-Ras mutations) are predictors of EGFR-TKis efficacy, they are not used in clinical practice.

In order to help implementation of these biomarkers in France, the French National Cancer Institute and French Ministry for Health have granted a 2-year multicentric prospective project entitled: **ERMETIC**

**ERMETIC** project had 3 consecutive objectives, with specific design:

- Objective 1: to validate several techniques for the detection of molecular alterations in the EGFR pathway applicable on paraffin-embedded specimens obtained from NSCLC.
- Objective 2: to select and hierarchized clinical, pathological and biological predictors of EGFR-TKis response and clinical benefit based on a large prospective clinical cohort of stage IIIb-IV NSCLC.
- Objective 3: to determine the best strategy to prescribe EGFR-TKis i.e. based or not on EGFR-TKis biomarkers response, in term of cost-effectiveness

**AIM**

The present work shows preliminary results of objective 2 ERMETIC project, including:

- Description analysis of ERMETIC prospective cohort
- Overall survival analysis based on clinical characteristics
- Descriptive analysis of 2 biomarkers (EGFR IHC and sequencing of EGFR exons 18-21 and K-Ras exon 2)
- Overall survival analysis based on clinical and biological factors restricted to a subpopulation of patients having results of at least 3 biomarkers available

**RESULTS**

**STATISTICAL METHODS**

The Kaplan-Meier method was used to draw survival curves. Cox model was used for prognostic analyses. Clinical factors were studied in univariate and multivariate analysis. Factors with p-value inferior to 0.20 were kept in the model. Each Biological factor was studied in univariate analysis and then added to the clinical model.

**CONCLUSION**

**ERMETIC** project confirms in a large non-selected European population:

- The efficacy of erlotinib on previously treated advanced NSCLC
- The independent prognostic value of smoking habits and PS on overall survival of patients treated by erlotinib

**ERMETIC** project shows in clinical practice:

- The possibility to perform EGFR and K-Ras sequencing in paraffin-embedded biopsies
- The independent prognostic value of EGFR and K-Ras mutations on survival of patients receiving erlotinib

**EGFR-TKI treatment**

**Prognostic value of Clinical factors**

**Prognostic value of Biological factors**

**Patients characteristics**

**Overall survival and Free-Of-Progression survival**

EGFR mutation - 25 (8.5%) : 5% exon 18-21, K-Ras mutation - 24 (8.1%) : EGFR and K-Ras mutations, mutually exclusive

Prognostic value of clinical and biological factors in patients with 5 biomarkers available.