A phase II study assessing the benefit of cisplatin re-introduction (stop and go strategy) in patients with advanced non-squamous non-small cell lung cancer (NSCLC): The IFCT-1102 BUCIL study (a Better Use of Cisplatin in Lung Cancer).

French Cooperative Thoracic Intergroup (IFCT): Aix Marseille University, Assistance Publique Hôpitaux de Marseille, Marseille, France; Institut de Cancérologie de l'Ouest, Saint Herblain, France; Centre Francois Baclesse, Caen, France; Centre Hospitalier De Chassy - Service de Pneumologie, Chassy, France; Hôpital Tarn, AP-HP et Service de Médecine Pierre et Marie Curie, Paris, Paris, France; Emile Muller Hospital, Mulhouse, France; Institut Sainte Catherine, Angers, France; Hospital Lyon Sud, Pierre-Béclère, France; Le Mans Regional Hospital, Le Mans, France; University Hospital of Strasbourg, France; Strasbourg, France; IFCT, Paris, France; Intergroup Francophone de Cancérologie Thoracique, Paris, France; CRU, Caen, France; Institut de Cancérologie de l'Ouest - site Reims Guedochien, Saint Herblain, France

**ABSTRACT**

**BACKGROUND**

Pemetrexed plus cisplatin combination is now recognized as standard of care in the first line management of patients with advanced non-squamous non-small cell lung cancer (NSCLC) (Kuang et al, 2009). However, adding bevacizumab to first line pemetrexed plus cisplatin has not been studied in NSCLC patients receiving standard chemotherapy. In this context, the current study was designed to evaluate the benefit of the reintroduction of cisplatin in patients already treated with pemetrexed plus cisplatin in the first line setting. The main endpoint was overall survival (OS) in patients with advanced NSCLC and squamous histology.

**STUDY DESIGN**

**OBJECTIVES**

**KEY INCLUSION CRITERIA**

- Histologically or cytologically documented stage IV non-squamous NSCLC, or EGF receptor (EGFR) mutation positive NSCLC at progression
- Measurable disease (at least one lesion) according to RECIST V1.1 outside a previous radiation field
- Age ≥ 18 years
- ECOG Performance Status: 0 or 1
- Adequate renal function: serum creatinine ≤ 1.5x ULN
- Adequate bone marrow function
- Written informed consent

**STUDY POPULATION**

- 113 patients
- 86% squamous NSCLC
- 57.5% required cisplatin dose reduction
- 37 patients (32.5%) received 3 cycles of chemotherapy
- 109 patients were assessable for response
- Median age 60.6 y (36.0-87.5)
- 50% of patients were assessable for progression
- Median follow-up (months): 9.6 (1.1-39.4)
- Median OS: 23.4 mo. (11.8-40.7)
- Median PFS: 7.7 mo. (5.1-11.3)

**OUTCOME**

- **Overall Response Rate**
  - 15.4% (6/40)
- **Progression Free Survival (PFS)**
  - Median: 7.7 mo. (5.1-11.3)
- **Overall Survival (OS)**
  - Median: 23.4 mo. (11.8-40.7)
  - 10% progression at 12 mo.

**FLOW CHART**

**PRIMARY OBJECTIVE**

- Proportion of patients receiving 3 cycles of chemotherapy without dose reduction of cisplatin/carboplatin during the 2nd sequence of treatment

**OVERVIEW OF TOXICITIES (sequence 2)**

<table>
<thead>
<tr>
<th>Grade 3-4 Toxicity</th>
<th>N (N=65)</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neutropenia</strong></td>
<td>31 (47.7)</td>
<td></td>
</tr>
<tr>
<td>Transient or permanent moderate toxicity</td>
<td>1 (1.5)</td>
<td></td>
</tr>
<tr>
<td><strong>Alopecia</strong></td>
<td>2 (3.1)</td>
<td></td>
</tr>
<tr>
<td><strong>Nausea</strong></td>
<td>18 (27.7)</td>
<td></td>
</tr>
<tr>
<td><strong>Thrombocytopenia</strong></td>
<td>21 (32)</td>
<td></td>
</tr>
</tbody>
</table>

**CONCLUSIONS**

Although the stringent endpoint was not met, this study highlighted that a "stop and go" strategy using a platinum-based chemotherapy with bevacizumab continuation beyond progression, compares favourably with standard schedule, deserving to be further studied in non-squamous advanced NSCLC.