Introduction

Immunotherapy is currently the first-line treatment for patients with metastatic non-small cell lung cancer (NSCLC). However, only a small proportion of patients can achieve a long-term response from ICIs. Rechallenge with immune checkpoint inhibitors (ICI) after disease progression provides interesting clinical outcomes for selected patients. Prior identification of patients who could benefit from this strategy remains an open question. Inflammation has been demonstrated to have a major role in the development and progression of cancer. Indeed, this causes an increase in the proportion of circulating neutrophils, monocytes and platelets at the detriment of lymphocytes, the main leukocyte subtype involved in an effective anti-tumour immune response. It has previously been shown that inflammation scores can identify patients who respond to rechallenge. However, they have never been investigated as predictive biomarkers of response with rechallenge. Here, we analyzed the independent predictive value of several inflammation scores in a cohort of patients that received a rechallenge with ICIs or chemotherapy only during their history of disease.

Objective of the Study

Identification of inflammation scores predicting a longer Progression Free Survival (PFS) and Overall Survival (OS) with ICI rechallenge independently from clinical factors that have already been shown as associated with a good response to this strategy according to the literature.

Material and Methods

This is a national, multicenter, retrospective cohort including 187 advanced NSCLC patients that receive at least one line of immunotherapy and for which biological data were available. Patients were then divided into:

- “Rechallenge” cohort (Re) (N = 81): patients that received a ICI rechallenge during their history of disease and that are followed in 23 French oncologic centers.
- “No Rechallenge” cohort (NR) (N = 106): patients that received at least one line of chemotherapy after the first ICI. Patients that received another ICI during their history of disease were excluded. Patients included in this cohort were followed at the CHU Grenoble-Alpes.

Biological data were collected at C1D1 (> 15 days) of rechallenge or chemotherapy regimen post-ICI. Inflammation scores cut-off were estimated by ROC curves. Cox proportional hazard models were used in the study.

Evaluation of prognostic and predictive value of inflammation scores:

We evaluated the inflammation score as biomarkers of interest by constituting ROC curves (AUC > 0.7 and p < 0.05). Then, we identified prognostic cut-offs able to stratify patients in responders and non-responders (time to treatment failure > or ≤ 3 months) to the “Rechallenge” cohort. The selected threshold of each inflammation score is represented on the table 2.

A longer PFS and OS were found in patients scored as “low” in consistent manner across the 4 inflammation scores. These results were confirmed by a multivariate analysis adjusted on confounding factors including including smoking status, first ICI duration, best response obtained, reason for stopping, intercurrent treatments between the first ICI and the rechallenge and the ECOG status at the time of the rechallenge (table 2).

While NLR and dNLR confirmed their prognostic value in the “No Rechallenge” group, MLR and PLR scores were not able to discriminate responder from non-responder patients treated with chemotherapy (Fig 2). MLR and PLR inflammation scores are therefore predictive of response to rechallenge by immunotherapy.

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Table 2 : Selected threshold and survival and multivariate analysis for each inflammation score

![Table 2](image)

Table: 3- Evaluation of prognostic and predictive value of inflammation scores

<table>
<thead>
<tr>
<th>Score</th>
<th>Selected Threshold</th>
<th>OS (months)</th>
<th>p-value</th>
<th>PFS (Months)</th>
<th>p-value</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>MLR</td>
<td>4.2</td>
<td>12</td>
<td>0.0016</td>
<td>4</td>
<td>0.0059</td>
<td>0.19 [0.07 - 0.49]</td>
</tr>
<tr>
<td>dNLR</td>
<td>2.1</td>
<td>25</td>
<td>0.0034</td>
<td>2</td>
<td>0.0003</td>
<td>0.17 [0.06 - 0.46]</td>
</tr>
<tr>
<td>NLR</td>
<td>0.61</td>
<td>26</td>
<td>0.0011</td>
<td>5</td>
<td>0.0015</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PLR</td>
<td>188.3</td>
<td>Non reached</td>
<td>0.002</td>
<td>7</td>
<td>0.0014</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Contribution of inflammation scores for each cohort

![Figure 1](image)  
**Figure 1:** Survival curve representing OS and PFS of the two cohorts since introduction of the 2nd ICI.

- **Figure 2:** Survival curve representing OS since rechallenge (A and B) or introduction of chemotherapy (C and D) depending on MLR and PLR value.

- **Rechallenge by ICI is an interesting strategy for selected patients and provides long term clinical responses.**

- **According to our results NLR and dNLR had a prognostic rather than predictive value in NSCLC treated with rechallenge. In contrast, PLR and MLR demonstrated a predictive value of response to rechallenge.**

References:


Conflict of interest : ICI is the spouse of an Atraxone employee, she received personal fees from Roche, Merck, Pierre Fabre and Chiesi and Bristol Myers Squibb, and she received research grants from Bristol Myers Squibb and AstraZeneca.