Multimodal predictive model of response to neoadjuvant chemotherapy and biochemistry for surgically resectable stage IIIA non-small cell lung cancer (NSCLC)

1 Highlights

- Results from the NADIM trial support the addition of neoadjuvant nivolumab to platinum-based chemotherapy in patients with resectable stage IIIA NSCLC (Provencio et al., Lancet Oncol, 2020).
- Pathological complete response (pCR) could potentially be used as an important surrogate endpoint for survival.

We present here a re-analysis of the NADIM cohort aiming to develop a machine learning algorithm to predict the pCR status based on multimodal baseline data.

Our findings suggest that multimodal baseline data can help predict the pathological complete response (pCR), in patients with resectable stage IIIA NSCLC receiving neoadjuvant chemomunotherapy.

2 Background

- The NADIM trial (NCT0381689), led by the Spanish Lung Cancer Group, assessed the antitumor activity and safety of neoadjuvant chemomunotherapy for resectable stage IIIA NSCLC.
- Patients received neoadjuvant nivolumab and paclitaxel-carboplatin for three cycles before surgical resection, followed by one year of adjuvant nivolumab.

![Figure 1. High-level overview of the NADIM trial design.](image)

- At 24 months, progression-free survival (PFS) was 77%, suggesting that neoadjuvant chemomunotherapy represents a promising option in this setting.
- Pathological complete response (pCR) could potentially be used as an important surrogate endpoint for survival.

We present here a re-analysis of the NADIM cohort aiming to develop a machine-learning algorithm to predict the pCR status based on multimodal baseline data.

3 Materials & Methods

- **Patients.** 46 patients were enrolled in the NADIM trial, and 28 had a complete set of data available for this retrospective study.
- **Data.** We combined baseline clinical data (e.g., age, smoking status), biological data (e.g., tumor histology), genomics data (e.g., tumor mutations), radiology reports, and radiomics analysis of the baseline chest CT scan in a multimodal analysis powered by machine learning algorithms (Table 1).

<table>
<thead>
<tr>
<th>Clinical data</th>
<th>Imaging data</th>
<th>Genomics data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, gender,</td>
<td>Over 200 radiomics features (e.g., AUC)</td>
<td>Tumor histology, TMB</td>
</tr>
<tr>
<td>Smoking status, EOCG score,</td>
<td></td>
<td>40-gene panel</td>
</tr>
<tr>
<td>pCR, PFS,</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Complete blood count</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Creatinine, LDH,</td>
<td></td>
</tr>
</tbody>
</table>

4 Results

**Patient characteristics (Table 2)**
- Among the 28 analyzed patients, there were 22 males and 6 females, aged between 41 and 77 years old (mean: 64 years).
- 18 patients (64%) achieved pCR while 10 patients (36%) did not.
- 18 patients (64%) achieved pCR while 10 patients (36%) did not.
- Among the 28 analyzed patients, there were 22 males and 6 females, aged between 41 and 77 years old (mean: 64 years).
- 18 patients (64%) achieved pCR while 10 patients (36%) did not.

**Overall model performance**
- An XGBoost algorithm with a linear base learner correctly predicted 20 pCR status out of 28 from multimodal baseline data (Table 3).
- The model reached an AUC of 0.65, a precision of 75%, a sensitivity of 83%, and a specificity of 50%. Accuracy was 71%, and the F1 score was 0.79.

**Predicted**

<table>
<thead>
<tr>
<th>pCR</th>
<th>Non-pCR</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>3</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>

**Predictive features**
- Features with the highest weight in the algorithm were a mix of radiological, radiomics, biological, genomics, and clinical features, highlighting the importance of a truly multimodal analysis.
- Withdrawing a specific data modality (e.g., radiomics or biological features) led to a decrease of -13% in the AUC.
- Individual features with the most predictive power included blood-based markers such as platelet levels and several radiomics features, notably intensity-based and texture-based indicators (Figure 2).

5 Conclusions and perspectives

This study is, to our knowledge, the first to offer a multimodal analysis of the response to neoadjuvant treatment for surgically resectable stage IIIA NSCLC and is a proof of concept that a machine learning algorithm can be used to predict the pCR in this context.

Results suggest that multimodal baseline data can help predict pCR, with specific importance of radiomics texture indicators measured at baseline or over time (delta-radiomics) and blood-based indicators such as platelets and HLR.

The key limitation of this study lies in the small sample size that restricted a proper assessment of the predictive value of less frequent events, such as gene mutations. Moreover, it does not guarantee the high stability of the overall model performance at this stage.

These preliminary results are being validated in the ongoing NADIM II trial, which will significantly expand the sample size (NCT03838159).


Pending: This work has been supported by a grant from Region Nouvelle Aquitaine (France). The information provided in this poster presents products or concepts in development. They are not products available for sale and not intended for use in diagnostic procedures or treatment decisions.