Efficacy of current immunotherapies in patients (pt) with metastatic non-small cell lung cancer (NSCLC) harboring KRAS mutations

BACKGROUND

Approximately 20% of lung adenocarcinomas harbor KRAS mutations (mut), an oncogene that has the ability to alter the tumor immune microenvironment. The most common mutation found in ~40% of cases is KRAS G12C, which has been related with tobacco exposure. Despite the immune-related nature of KRAS driven tumors, they are genomically heterogenous and the efficacy of immunotherapy (IT) according to KRAS mut type has not been well elucidated.

The objective of this study is to describe a cohort of pt with KRAS-mutant NSCLC treated with IT and evaluate the clinical outcomes.

METHODS

A retrospective cohort of KRAS-mutated NSCLC pt treated at the Catalan Institute of Oncology in Badalona between June/2013 and June/2020 were included. KRAS status was determined by cobas® KRAS mut test, a real-time PCR test designed for the identification of mut in codons 12, 13 and 61; and NGS panels (Oncomine Solid) in the most recent cases (2020).

PD-L1 in tumor cells was determined by immunohistochemistry assay (VENTANA PD-L1 SP263) and was categorized as: negative <1%, low 1-49% and high 50-100%.

Chi-square test for categorical variables and Kaplan Meier test for categorical variables were performed.

RESULTS

Of the 103 pt included: 73% were male, median age at diagnosis: 62. 97% were current/former smokers, and 69% had stage IV at diagnosis. KRAS mutation type: 46% harbored KRAS G12C and 54% KRAS non-G12C. All pt were treated with IT for advanced disease: 97% with antiPD(L)1 based regimens.

1. Patient characteristics

<table>
<thead>
<tr>
<th>Gender</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking status</td>
<td>Current or former</td>
<td>Never</td>
</tr>
<tr>
<td>Performance status</td>
<td>PS 0-1</td>
<td>PS 2-3</td>
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<tr>
<td>Schedule of treatment</td>
<td>1st line IT</td>
<td>2nd line IT</td>
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</tbody>
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2. Patient characteristics by KRAS mut mutation

Of the 103 pt included: 10% harbored KRAS G12C and 90% non-G12C. mPFS G12C = 10.1m and mPFS nonG12C = 16.7m. mOS G12C = 36.2m and mOS nonG12C = 26.3m.

3. Response to IT by KRAS mut

4. Progression free survival according to KRAS mut type

5. Overall survival according to KRAS mut type

6. Progression free survival according to line of treatment with IT

CONCLUSIONS

• Although KRAS G12C mut tumors exhibited higher PDL1 expression, no differences were observed in mPFS compared to KRAS nonG12C in our cohort, probably due to the IT-based treatment heterogeneity. Concerning OS, no differences were observed between both groups.

• Starting 1st line IT based regimens improved mPFS, regardless of KRAS mut type.

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