Introduction

• Immune checkpoint inhibitors (ICIs) are the first-line therapy for NSCLC patients without actionable mutations
• Less than 50% of patients benefit
• Early identification of no durable benefit (NDB) enables treatment discontinuation
• This reduces immune-related toxicity and treatment costs

Study aims

1. Externally validate a blood-based model (CM 2022) to predict which patients will not benefit from ICIs
2. Assess added value next to radiological response assessment (RECIST)

Methods

• Prediction of NDB (progressive disease, stable disease or † < 6 months) in 242 metastatic NSCLC patients
• Blood-based model (CM 2022): random forest model based on CYFRA, CEA, NSE at day 0 and week 6 of ICI treatment
• CM 2022 was added to radiological evaluation by RECIST at 6-8 weeks

Results

<table>
<thead>
<tr>
<th></th>
<th>Sens (95% CI)</th>
<th>Spec (95% CI)</th>
<th>PPV (95% CI)</th>
<th>NPV (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CM 2022</td>
<td>38 (35 – 41)</td>
<td>96 (95 – 97)</td>
<td>88 (86 – 90)</td>
<td>66 (63 – 69)</td>
</tr>
<tr>
<td>RECIST</td>
<td>33 (30 – 36)</td>
<td>96 (95 – 97)</td>
<td>87 (84 – 89)</td>
<td>64 (61 – 67)</td>
</tr>
<tr>
<td>Combined model*</td>
<td>21 (18 – 23)</td>
<td>100 (100 – 100)</td>
<td>100 (100 – 100)</td>
<td>61 (58 – 65)</td>
</tr>
</tbody>
</table>

*Combined model = prediction of NDB by CM 2022 and progressive disease by RECIST 6-8 weeks after ICI initiation

Conclusion

• CM 2022 predicts NDB with a specificity of 96% and PPV of 88%
• Addition of RECIST score improves specificity and PPV to 100%
• Serological (CM 2022) and radiological response assessment (RECIST) are complementary when predicting NDB
• Combined model achieves hazards ratios of 22 (95% CI 12 – 42) for PFS and 4 (95% CI 3 – 7) for OS

Clinical implications

• After 6-8 weeks of ICIs, treatment can safely be stopped in patients with NDB prediction by CM 2022 and PD by RECIST
• After 6-8 weeks of ICIs our advice is:
  - PR/SD & CM 2022 + Continue ICIs
  - PR/SD & CM 2022 - CT-scan in 6 weeks
  - PD & CM 2022 - Stop ICIs
  - PD & CM 2022 +