Does Denosumab offer Survival Benefits? Our Experience with Denosumab in Metastatic Non-Small Cell Lung Cancer Patients Treated with Immune-Checkpoint Inhibitors.

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Background
• Immune checkpoint inhibitors (ICIs) have revolutionized the treatment of non-small-cell lung cancer (NSCLC).
• Denosumab is widely used to prevent skeletal-related events of bone metastases in solid tumors¹.
• In both preclinical and clinical studies, denosumab have shown some anti-tumor properties and synergistic effect with Immune checkpoint inhibitors².

Methods
• Retrospective data from a tertiary cancer center from 2015-2020.
• Stage IV non-small cell lung cancer patients who received denosumab within 30 days of Immune checkpoint inhibitors (pembrolizumab, nivolumab, atezolizumab, ipilimumab) were included.

Results
• We identified 69 patients with NSCLC who received immune checkpoint inhibitors (ICIs) and denosumab concurrently.
• All the patients had skeletal metastasis, and 37.7% had brain metastases.
• Median duration of denosumab and ICIs overlap therapy was 1.5 months.

Figure 1: A: Kaplan-Meier estimate of Overall survival (OS) subgroups by duration of denosumab and ICI overlap (11.5 months vs. 3.6 months, P=0.0005). B: Kaplan-Meier estimate of OS subgroups by line of therapy i.e., first line vs. second line (8.9 vs 3.9 months, P=0.03). C: Kaplan-Meier estimate of OS subgroups by brain metastases (7.7 vs. 3.6 months, P= 0.16). D: Kaplan-Meier estimate of OS subgroups by skeletal metastases (7.7 vs. 4.0 months, P= 0.2).

Table 3: Best Radiographic response

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<thead>
<tr>
<th>Radiographic response</th>
<th>ORR</th>
<th>DCR</th>
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<tbody>
<tr>
<td>CR = 3 (4.3%)</td>
<td>18.8%</td>
<td>40.6%</td>
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<tr>
<td>PR = 10 (14.5%)</td>
<td>66.7%</td>
<td>15.8%</td>
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<td>SD = 15 (21.6%)</td>
<td>60.0%</td>
<td>60.0%</td>
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<td>PD = 41 (62.3%)</td>
<td>58.5%</td>
<td>31.5%</td>
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Figure 2: A: Kaplan-Meier estimate of progression free survival (PFS) subgroups by duration of denosumab and ICI overlap (6.0 months vs. 1.9 months, P=0.006). B: Kaplan-Meier estimate of PFS subgroups by line of therapy i.e., first line vs. second line (4.3 vs 1.8 months, P=0.006). C: Kaplan-Meier estimate of PFS subgroups by brain metastases (3.9 vs. 2.1 months, P= 0.2) . D: Kaplan-Meier estimate of PFS subgroups by skeletal metastases (3.7 vs. 2 months, P= 0.1).

Conclusions
• The duration of ICIs and denosumab overlap had a significant impact on overall survival (OS) and progression free survival (PFS).
• Importantly, among the 13 patients who achieved complete response (CR) and partial response (PR), six-month survival rate was 100% and one-year survival rate was 69.2%.
• This study provides real world experience combining ICIs with denosumab in Stage IV NSCLC patients with significant brain and skeletal metastatic burden, as well as considerable proportion receiving ICI as second line of therapy.

References