Neoadjuvant anti-PD-1 induces pathological complete response (pCR) in 20% and any pathological response (pR) in 34% of patients with stage III melanoma.  

Combination pembrolizumab and lenvatinib (P+L) is active in patients with melanoma who have progressed on anti-PD-1 alone (LEAP-004). Adding lenvatinib to anti-PD-1 could enhance clinical benefit in the neoadjuvant setting, and provide melanoma tissue to gain translational insights into impact of lenvatinib on the tumour microenvironment.  

NeoPeLe (NCT04207086) is a phase II, open label, single arm study of 20 patients with resectable stage III melanoma treated with neoadjuvant P+L.  

**Objectives**  

**Primary:** To determine the RECIST and metabolic response at pembrolizumab plus lenvatinib  

**Secondary:** To determine the resectable stage III melanoma treated with neoadjuvant P+L.  

**Methods**  

**Stage IIIb-D**  

| Blood drug and funding support | Melanoma Institute Australia, The University of Sydney, 2. Faculty of Medicine and Health, The University of Sydney, 3. Royal Prince Alfred Hospital, 4. Chris O'Brien Lifehouse, 5. Concord Repatriation Hospital, 6. Charles Perkins Centre, The University of Sydney, 7. N劲t Health Pathology  

**Background**  

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- NeoPeLe (NCT04207086) is a phase II, open label, single arm study of 20 patients with resectable stage III melanoma treated with neoadjuvant P+L.  

**Methods**  

**Stage IIIb-D**  

- Histologically-confirmed  

- ECOG PS ≤1  

**Screening**  

- Blood for biomarkers at screening, Day 8, and weekly  

- CT/PET scans at screening, Wk 1  

- Surgical operability questionnaire screening and Wk 6  

- Pathologic response determined as per INMC criteria  

**Assessments**  

- CT/PET scans at Week 1, 6, and 22 in the first 6 weeks  

- Blood for biomarkers at screening, Day 8, and Wk 6  

**Treatment**  

- Neoadjuvant (pre-surgery): Pembrolizumab 200 mg IV on Day 1 and Day 22 plus lenvatinib 20 mg daily for 5 weeks  

- Adjunct (post-surgery): Pembrolizumab 200 mg IV 3 times weekly for 46 weeks  

**Results**  

- The majority of patients had a pathological response (75%) and most were a pCR (40%)  

- Pathological response did not correlate with the radiological RECIST response prior to surgery at Wk 6  

- Surgery was easier than expected in 13/20 (65%) and harder in 7/20 (35%); no correlation with path response  

**Figure 1. Pathological and Radiological RECIST Response at Week 6**  

<table>
<thead>
<tr>
<th>Pathological Response, n (%)</th>
<th>N=20</th>
<th>RECIST Response, n (%)</th>
<th>N=20</th>
<th>Objective Response Rate</th>
<th>N=20</th>
</tr>
</thead>
<tbody>
<tr>
<td>pCR</td>
<td>15 (75%)</td>
<td>pCR</td>
<td>15 (75%)</td>
<td>CR</td>
<td>4 (20%)</td>
</tr>
<tr>
<td>near-pCR</td>
<td>3 (15%)</td>
<td>PR</td>
<td>4 (20%)</td>
<td>PR</td>
<td>4 (20%)</td>
</tr>
<tr>
<td>pPR</td>
<td>8 (40%)</td>
<td>SD</td>
<td>11 (55%)</td>
<td>SD</td>
<td>11 (55%)</td>
</tr>
<tr>
<td>pNR</td>
<td>8 (40%)</td>
<td>PD</td>
<td>2 (10%)</td>
<td>PD</td>
<td>2 (10%)</td>
</tr>
</tbody>
</table>

**Figure 2. Event-free survival in total population (n=20)**  

- Three patients (4/20, 20%) had relapsed during follow-up;  

- Two patients had died at data cut off due to melanoma  

**Conclusions**  

- Neoadjuvant pembrolizumab + lenvatinib induced a high pathological response rate of 75% and a high major pathological response (pCR+near-pCR) rate of 55%  

- These results are higher than response rates reported for PD-1 monotherapy and similar to those reported for PD-1 + CTLA-4 combination therapy.  

- Lenvatinib appears to enhance the activity of PD-1 monotherapy  

- There was a low rate of recurrence in pathological responders (1/15)  

- Given this early promising data, recruitment to NeoPeLe was increased to a total of 40 patients and is ongoing.  

- Translational studies are underway.