Background: Patients with epidermal growth factor receptor (EGFR) mutant advanced non-small cell lung cancer receiving first-line EGFR-tyrosine kinase inhibitor (TKI) inevitably developed disease progression after 9-13 months.

Methods: Before 1st January 2017, patients were investigated for resistance mechanisms upon failure of first-line EGFR-TKI by means of tissue re-biopsy or liquid biopsy to detect secondary T790M mutation in plasma cell free tumor-DNA (cfDNA) if tissue re-biopsy could not be performed. After that, liquid biopsy followed by tumor re-biopsy if cfDNA was negative for T790M mutation or if the patients had rapidly enlarging tumors.

Results: Of 45 patients who were tested, 31 (68.9%) underwent tissue re-biopsy and 14 (31.1%) underwent liquid biopsy as the first investigation to determine the presence of T790M mutation. For the latter group, 4 (8.9%) subsequently also had tumor re-biopsy. T790M mutation was detected in 30 (66.7%) of the 45 patients. C-Met amplification was tested in 7 T790M mutation-negative patients for possible recruitment into a clinical trial with 4 showing C-Met amplification. Small cell lung cancer transformation and ALK rearrangement were detected in 2 (5.7%) and in 1 (2.9%) of the re-biopsy tissue specimens, respectively. The resistance mechanisms in 8 patients (17.8%) was unknown. In short, two-third (66.7%) of our patients had T790M mutation upon first-line EGFR-TKI failure; while another one-third (33.3%) failed first-line EGFR-TKI due to other resistance mechanisms.

Conclusions: T790M mutation is the commonest acquired resistance mechanism causing first-line EGFR-TKI treatment failure. There was no difference in the clinical and treatment characteristics between patients with and without acquired T790M mutation as causes of resistance to first-line EGFR-TKI treatment.

Legal entity responsible for the study: Chai Chee Shee, Liam Chong Kin

### Table: 430P Demographic, clinical and treatment characteristics of 45 patients with first-line EGFR-TKI treatment failure

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total number of patients (n = 45)</th>
<th>Patients with T790M mutation (n = 30)</th>
<th>Resistance mechanism other than T790M (n = 15)</th>
<th>P value of univariate analysis*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, No. (%) Male Female</td>
<td>18 (40.0) 27 (60.0)</td>
<td>13 (43.3) 17 (56.7)</td>
<td>5 (33.3) 10 (66.7)</td>
<td>0.780</td>
</tr>
<tr>
<td>Smoking history, No. (%) Never smoker or current smoker</td>
<td>39 (80.0) 9 (20.0)</td>
<td>22 (73.3) 8 (26.7)</td>
<td>14 (93.3) 1 (6.7)</td>
<td>0.963</td>
</tr>
<tr>
<td>EGFR mutation subtype, No. (%)</td>
<td>26 (57.8) 16 (35.6)</td>
<td>17 (56.7) 12 (40.0)</td>
<td>9 (60.0) 4 (26.7)</td>
<td>0.999</td>
</tr>
<tr>
<td>Treatment received, No. (%)</td>
<td>34 (75.5) 11 (24.5)</td>
<td>22 (73.3) 8 (26.7)</td>
<td>12 (80.0) 5 (20.0)</td>
<td>0.484</td>
</tr>
<tr>
<td>Best tumour response, No. (%)</td>
<td>38 (84.4) 6 (13.3)</td>
<td>27 (90.0) 2 (6.7)</td>
<td>11 (73.3) 4 (26.7)</td>
<td>-</td>
</tr>
<tr>
<td>Progression-free-survival on first-line EGFR-TKI, months</td>
<td>13.0</td>
<td>13.0</td>
<td>11.7</td>
<td>0.538</td>
</tr>
</tbody>
</table>