An Open-Label, Multi-Drug, Biomarker-Directed, Phase II Platform Study in Patients with Non-Small Cell Lung Cancer, who Progressed on an anti-PD(L)-1 Therapy

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Institut Gustave Roussy, Villejuif and Paris-Sud University, Paris, France

On behalf of the HUDSON study group

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Disclaimer

Disclosures

Contracted/supported research grants

Abbvie, Amgen, AstraZeneca, BeiGene, Blueprint Medicines, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Cristal Therapeutics, Daiichi-Sankyo, Eli Lilly, GSK, Ignyta, IPSEN, Inivata, Janssen, Merck KGaA, MSD, Nektar, Onxeo, OSE immunotherapeutics, Pfizer, Pharma Mar, Roche-Genentech, Sanofi, Servier, Spectrum Pharmaceuticals, Takeda, Tiziana Pharma, Tolero Pharmaceuticals

The HUDSON clinical study is ongoing, data presented may not yet be mature and are subject to change.

The HUDSON clinical study is sponsored by AstraZeneca.
HUDSON study design

- Locally advanced or metastatic NSCLC
- Previous platinum-based chemotherapy
- Failed Anti-PD(L)1 treatment
- Biopsiable disease
- Targetable EGFR, ALK, ROS1, BRAF, MET or RET alterations were excluded

Group A: biomarker matched (n=85)

Group B: biomarker non-matched (n=177)

Central molecular screen† (n=617)

Primary resistance‡ (n=74)

Acquired resistance§ (n=103)

Primary endpoint:
- Overall response rate

Secondary endpoints:
- Progression-free survival
- Overall survival
- Disease control rate
- Safety and tolerability

†Immunohistochemistry was also performed. ‡PD on ICI within 24 weeks (fresh biopsy or archived tissue); §PD on ICI > 24 weeks (fresh biopsy or archived tissue). ATM, ataxia-telangiectasia mutated; ATRi, ataxia-telangiectasia receptor inhibitor; CD73, cluster of differentiation 73; HER2, human epidermal growth factor receptor 2; HRR, homologous recombination repair; NSCLC, non-small-cell lung cancer; PARPi, poly ADP ribose polymerase inhibitor; PD, progression of disease; STAT3i, Signal transducer and activator of transcription 3 inhibitor; STK11, Serine/threonine kinase 11 (also known as LKB1)
<table>
<thead>
<tr>
<th>Biomarker Selected</th>
<th>N</th>
<th>Age (%)</th>
<th>Female (%)</th>
<th>Lesions (%)</th>
<th>M+ at entry (%)</th>
<th>Histology type (%)</th>
<th>Smoking status</th>
<th>Previous therapies (%)</th>
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<td>Liver</td>
<td>Smoker†</td>
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<td>69.6</td>
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<th>Biomarker Selected</th>
<th>N</th>
<th>Age (%)</th>
<th>Female (%)</th>
<th>Lesions (%)</th>
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<th>Histology type (%)</th>
<th>Smoking status</th>
<th>Previous therapies (%)</th>
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<td>≥65 y</td>
<td>1-2</td>
<td>≥3</td>
<td>CNS</td>
<td>Liver</td>
<td>Smoker†</td>
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<td>Olaparib HRR</td>
<td>23</td>
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<td>52.2</td>
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<td>4.5</td>
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<td>58.3</td>
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†Current and former smokers; 73H, signal transducer and activator of transcription 3-73H; ATM, ataxia-telangiectasia mutated; CNS, central nervous system; HRR, homologous recombination repair; M+, metastasis confirmed; STK11, Serine/threonine kinase 11 (also known as LKB1); y, years
HUDSON – ORR and median PFS

<table>
<thead>
<tr>
<th>Biomarker selected</th>
<th>N</th>
<th>mF/U m</th>
<th>ORR n (%)</th>
<th>Median PFS m (80% CI)</th>
<th>PFS rate (%) 6, 9 and 12 m</th>
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<td><strong>Durvalumab</strong></td>
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<tr>
<td>Olaparib HRR</td>
<td>21</td>
<td>2.8</td>
<td>2 (9.5)</td>
<td>2.79 (1.48 – 5.26)</td>
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<tr>
<td>Olaparib STK11</td>
<td>21</td>
<td>1.4</td>
<td>1 (4.8)</td>
<td>1.41 (1.38 – 1.81)</td>
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<tr>
<td>Ceralasertib ATM</td>
<td>18</td>
<td>5.0</td>
<td>2 (11.1)</td>
<td>7.43 (3.45 – 9.46)</td>
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<tr>
<td>Oleclumab 73H</td>
<td>23</td>
<td>1.5</td>
<td>0 (0)</td>
<td>1.58 (1.41 – 2.76)</td>
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<tr>
<td><strong>Primary resistance</strong></td>
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<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Olaparib</td>
<td>22</td>
<td>2.8</td>
<td>0 (0)</td>
<td>3.38 (2.10 – 4.93)</td>
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<tr>
<td>Danvatirsen</td>
<td>23</td>
<td>1.7</td>
<td>0 (0)</td>
<td>1.68 (1.64 – 2.99)</td>
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<tr>
<td>Ceralasertib</td>
<td>20</td>
<td>2.6</td>
<td>2 (10.5)</td>
<td>4.24 (1.94 – 6.77)</td>
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<tr>
<td>Oleclumab</td>
<td>9</td>
<td>1.4</td>
<td>0 (0)</td>
<td>1.41 (1.35 – 1.81)</td>
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<tr>
<td><strong>Acquired resistance</strong></td>
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<tr>
<td>Olaparib</td>
<td>23</td>
<td>4.2</td>
<td>1 (4.3)</td>
<td>4.17 (2.69 – 4.37)</td>
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<tr>
<td>Danvatirsen</td>
<td>22</td>
<td>2.8</td>
<td>0 (0)</td>
<td>3.09 (2.83 – 6.14)</td>
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<tr>
<td>Ceralasertib</td>
<td>24</td>
<td>4.6</td>
<td>2 (8.3)</td>
<td>4.96 (3.55 – 5.98)</td>
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<tr>
<td>Oleclumab</td>
<td>25</td>
<td>2.6</td>
<td>1 (4.2)</td>
<td>2.63 (1.64 – 2.79)</td>
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</tbody>
</table>

Data in italics are not yet mature; treatment modules include the biomarker selected, primary resistance and acquired resistance cohorts for each drug combination

73H, signal transducer and activator of transcription 3-73H; ATM, ataxia-telangiectasia mutated; CI, confidence interval; HRR, homologous recombination repair; m, months; mF/U, median follow-up; NC, not calculated; ORR, objective response rate; PFS, progression-free survival; STK11, Serine/threonine kinase 11 (also known as LKB1)
## HUDSON – median OS

<table>
<thead>
<tr>
<th>Durvalumab combination</th>
<th>N</th>
<th>mF/U m</th>
<th>Median OS m (80% CI)</th>
<th>OS rate (%) 6, 9 and 12 m</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olaparib HRR</td>
<td>21</td>
<td>9.6</td>
<td>9.63 (5.26 – 15.97)</td>
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<tr>
<td>Olaparib STK11</td>
<td>21</td>
<td>5.6</td>
<td>5.75 (5.29 – 10.84)</td>
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<tr>
<td>Ceralasertib ATM</td>
<td>18</td>
<td>10.5</td>
<td>15.80 (11.01 – NC)</td>
<td>21</td>
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<tr>
<td>Oleclumab 73H</td>
<td>23</td>
<td>7.6</td>
<td>9.49 (7.49 – NC)</td>
<td>9</td>
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</tbody>
</table>

### Biomarker selected

- **Olaparib HRR**
  - N: 21
  - mF/U m: 9.6
  - Median OS m (80% CI): 9.63 (5.26 – 15.97)
  - OS rate (%) 6, 9 and 12 m: 21

- **Olaparib STK11**
  - N: 21
  - mF/U m: 5.6
  - Median OS m (80% CI): 5.75 (5.29 – 10.84)
  - OS rate (%) 6, 9 and 12 m: 9

- **Ceralasertib ATM**
  - N: 18
  - mF/U m: 10.5
  - Median OS m (80% CI): 15.80 (11.01 – NC)
  - OS rate (%) 6, 9 and 12 m: 21

- **Oleclumab 73H**
  - N: 23
  - mF/U m: 7.6
  - Median OS m (80% CI): 9.49 (7.49 – NC)
  - OS rate (%) 6, 9 and 12 m: 9

### Primary resistance

- **Olaparib**
  - N: 22
  - mF/U m: 7.2
  - Median OS m (80% CI): 7.16 (4.93 – 10.28)
  - OS rate (%) 6, 9 and 12 m: 22

- **Danvatirsen**
  - N: 23
  - mF/U m: 6.0
  - Median OS m (80% CI): 6.01 (3.55 – 6.51)
  - OS rate (%) 6, 9 and 12 m: 23

- **Ceralasertib**
  - N: 20
  - mF/U m: 6.7
  - Median OS m (80% CI): 11.60 (10.45 – NC)
  - OS rate (%) 6, 9 and 12 m: 20

- **Oleclumab**
  - N: 9
  - mF/U m: 2.8
  - Median OS m (80% CI): 7.06 (4.90 – 7.06)
  - OS rate (%) 6, 9 and 12 m: 9

### Acquired resistance

- **Olaparib**
  - N: 23
  - mF/U m: 11.6
  - Median OS m (80% CI): 15.51 (8.80 – 19.75)
  - OS rate (%) 6, 9 and 12 m: 23

- **Danvatirsen**
  - N: 22
  - mF/U m: 10.8
  - Median OS m (80% CI): 11.20 (9.72 – 12.55)
  - OS rate (%) 6, 9 and 12 m: 22

- **Ceralasertib**
  - N: 24
  - mF/U m: 12.7
  - Median OS m (80% CI): 17.38 (14.06 – NC)
  - OS rate (%) 6, 9 and 12 m: 24

- **Oleclumab**
  - N: 25
  - mF/U m: 6.1
  - Median OS m (80% CI): 12.78 (6.14 – 12.78)
  - OS rate (%) 6, 9 and 12 m: 25

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73H, signal transducer and activator of transcription 3-73H; ATM, ataxia-telangiectasia mutated; CI, confidence interval; HRR, homologous recombination repair; m, months; mF/U, median follow-up; NC, not calculated; OS, overall survival; STK11, Serine/threonine kinase 11 (also known as LKB1).
HUDSON demonstrates that molecularly stratified enrolment in the immune therapy failed setting is feasible: 617 patients were screened, and >270 have been treated to date.

Preliminary efficacy signals were observed in patients who received ceralasertib + durvalumab. Potentially more pronounced in ATM selected patients (ATR low or mutated).

Patients in the STK11 mut selected arm had the poorest outcomes, as previously reported.

The safety profile of the drug combinations was in line with the individual drugs investigated.

Additional translational medicine findings are reported in abstract #3491.