Immune checkpoint inhibitors in non-small cell lung cancer

Rolf Stahel
University Hospital of Zürich

Siena, 4.7.2016
### PD-1/PD-L1 immune checkpoint inhibitors in phase III studies

<table>
<thead>
<tr>
<th></th>
<th>Name</th>
<th>Type</th>
<th>Company</th>
<th>Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PD-1</strong></td>
<td></td>
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<tr>
<td></td>
<td>Nivolumab</td>
<td>Fully human IgG4 mAb</td>
<td>Bristol-Myers Squibb</td>
<td>Phase III</td>
</tr>
<tr>
<td></td>
<td>BMS-936558</td>
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</tr>
<tr>
<td></td>
<td>Pembrolizumab</td>
<td>Humanized IgG4 mAb</td>
<td>Merck</td>
<td>Phase III</td>
</tr>
<tr>
<td></td>
<td>MK-3475</td>
<td></td>
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</tr>
<tr>
<td><strong>PD-L1</strong></td>
<td></td>
<td>Engineered human IgG1 mAb</td>
<td>AstraZeneca</td>
<td>Phase III</td>
</tr>
<tr>
<td></td>
<td>Durvalumab</td>
<td></td>
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<tr>
<td></td>
<td>Medl-4736</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Atezolizumab</td>
<td>Engineered human IgG1 mAb</td>
<td>Genentech</td>
<td>Phase III</td>
</tr>
<tr>
<td></td>
<td>MPDL-3280A</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Avelumab</td>
<td>Engineered human IgG1 mAb</td>
<td>Merck Serono/Pfizer</td>
<td>Phase III</td>
</tr>
<tr>
<td></td>
<td>MSB0010718C</td>
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</tr>
<tr>
<td><strong>CTLA-4</strong></td>
<td></td>
<td></td>
<td>Bristol-Myers Squibb</td>
<td>Combination studies</td>
</tr>
<tr>
<td></td>
<td>Ipilimumab</td>
<td></td>
<td>AstraZeneca</td>
<td>Combination studies</td>
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</tr>
<tr>
<td></td>
<td>Temelilimab</td>
<td></td>
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</tr>
</tbody>
</table>
Immune checkpoint inhibitors in thoracic malignancies

- Advanced NSCLC
  - Activity in pretreated patients
  - PD-L1 and other potential biomarkers
  - Activity in first line
- Earlier stages NSCLC
  - Consolidation after chemoradiotherapy
  - Neoadjuvant window of opportunity
  - Adjuvant after section
Evolution of second line therapy for NSCLC: Key studies

- Docetaxel > BSC
  - Shepherd, JCO 2000

- Non-inferiority of pemetrexed to docetaxel
  - Hanna, JCO 2004

- Erlotinib > placebo (2nd or 3rd line)
  - Shepherd, NEJM 2005
Docetaxel plus nintedanib (LUME-Lung 1) or docetaxel plus ramucirumab (REVEL) versus docetaxel plus placebo for second-line treatment of stage IV NSCLC

LUME-Lung 1: Adenocarcinoma

OS 12.6 vs 10.3 ms

REVEL: 25% squamous cell carcinoma

OS 10.5 vs 9.1 ms

Reck, Lancet Oncol 2014; Garon, Lancet Oncol 2014
Nivolumab in second or further line advanced NSCLC

- 54% pretreated with 3-5 therapies
- 17% confirmed responses, 5% unconventional iR

Gettinger, JCO 2015
Randomized phase II study comparing atezolizumab (vs docetaxel in 2L/3L NSCLC (POPLAR), no biomarker selection

**Graphical Representation:**

- **Overall Survival** vs **Time (mo)**
  - Median 9.7 mo (8.6, 12.0) for Atezolizumab
  - Median 12.6 mo (9.7, 16.4) for Docetaxel

**HR**

\[ HR^a = 0.73 \ (0.53, \ 0.99) \]

**P value**

\[ P = 0.040 \]

**Legend:**

- Atezolizumab
- Docetaxel
- Censored

**Table:**

<table>
<thead>
<tr>
<th></th>
<th>Atezolizumab</th>
<th>Docetaxel</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Patients at Risk</td>
<td>144 139 131 123 117 110 106 95 90 84 78 73 69 64 42 33 20 12 7 4</td>
<td>143 130 123 118 106 97 92 87 82 73 65 61 54 46 39 24 17 9 3</td>
</tr>
</tbody>
</table>

*Vansteenkiste, ECCO-ESMO 2015*
Durvalumab monotherapy phase 1 dose escalation and expansion in advanced solid tumors: NSCLC cohort: Response according to PD-L1 status

Best change in tumour size from baseline by PD-L1 status (n=152)

\[\text{PD-L1 +} \quad \text{PD-L1 -}\]

\[\text{Best Change from Baseline (\%)}\]

\[\text{Includes all patients with baseline and \geq 1 follow-up scan}\]

Rizvi. ASCO 2015
Checkmate 017 and 057: 2-years update of OAS,

* No biomarker selection

Borghael, ASCO 2016
Checkmate 017 and 057: 2-years update, no biomarker selection

### CheckMate 017 (SQ NSCLC)

<table>
<thead>
<tr>
<th></th>
<th>Nivolumab (n = 135)</th>
<th>Docetaxel (n = 137)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events, n (%)</td>
<td>109 (81)</td>
<td>123 (90)</td>
</tr>
<tr>
<td>Median PFS, mo (95% CI)</td>
<td>3.5 (2.1, 5.1)</td>
<td>2.8 (2.1, 3.5)</td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>0.63 (0.48, 0.83)</td>
<td></td>
</tr>
</tbody>
</table>

### CheckMate 057 (non-SQ NSCLC)

<table>
<thead>
<tr>
<th></th>
<th>Nivolumab (n = 292)</th>
<th>Docetaxel (n = 290)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events, n (%)</td>
<td>240 (82)</td>
<td>249 (86)</td>
</tr>
<tr>
<td>Median PFS, mo (95% CI)</td>
<td>2.3 (2.2, 3.4)</td>
<td>4.3 (3.4, 4.9)</td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>0.89 (0.75, 1.07)</td>
<td></td>
</tr>
</tbody>
</table>

*Investigator-assessed; \(^{a}\)NC = not calculable because no patients remained in follow-up for progression at this time point; the PFS rate at the time of the last event was 3%, and the last observation at 2 years was not an event.

Borghael, ASCO 2016
EQ-5D Utility Index: Mean Scores Over Time While on Treatment

Higher scores indicate better health status. Only time points that had PRO data available for ≥5 patients in either treatment arm are plotted on the graph.

Reck, ECCO-ESMO 2015
Pembrolizumab versus doxetaxel in second line NSCLC (KEYNOTE 10), at least 1% of tumor cells PD-L1 positive.
Less toxicity with immune checkpoint inhibitors in second line comparative studies

<table>
<thead>
<tr>
<th>Toxicity Grade</th>
<th>% of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Check-mate 17</td>
</tr>
<tr>
<td>N</td>
<td>59</td>
</tr>
<tr>
<td>Doc</td>
<td>87</td>
</tr>
<tr>
<td>All</td>
<td>63</td>
</tr>
<tr>
<td>3-5</td>
<td>13</td>
</tr>
</tbody>
</table>
CheckMate 17: Time to onset of first treatment-related select AE with nivolumab by category

The majority of patients who experienced treatment-related select AEs with nivolumab experienced their first event within the first 3 months of treatment.
EQ-5D Utility Index:
Mean Scores Over Time While on Treatment

Higher scores indicate better health status.
Only time points that had PRO data available for ≥5 patients in either treatment arm are plotted on the graph.

Nivolumab (n = 97)
- Week 0: 0.9
- Week 12: 0.8
- Week 24: 0.7
- Week 36: 0.6
- Week 48: 0.5
- Week 60: 0.4

Docetaxel (n = 89)
- Week 0: 0.9
- Week 12: 0.8
- Week 24: 0.7
- Week 36: 0.6
- Week 48: 0.5
- Week 60: 0.4

Reck, ECCO-ESMO 2015
Case study, R.M. 1952

06/15
Diagnosis: Pleomorphic carcinoma right upper lobe
Initial stage cT3 cN1-2 cM-1 (bone)

07/15 - 0815
3 cycles of cisplatin and gemcitabine

28.08.2015
Re-Staging: Primary stable disease, nodal regression, bone progression
Case study, R.M. 1952

06/15  Diagnosis: Pleomorphic carcinoma right upper lobe
        Initial stage cT3 cN1-2 cM-1 (bone)
07/15 - 08/15 3 cycles of cisplatin and gemcitabine
28.08.2015 Re-Staging: Primary stable disease, nodal regression, bone progression
29.09.2015 Right upper lobe resection ypT3 ypN1 (1/8)
# Case study, R.M. 1952

<table>
<thead>
<tr>
<th>Date</th>
<th>Event Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>06/15</td>
<td>Diagnosis: Pleomorphic carcinoma right upper lobe</td>
</tr>
<tr>
<td></td>
<td>Initial stage cT3 cN1-2 cM-1 (bone)</td>
</tr>
<tr>
<td>07/15 - 0815</td>
<td>3 cycles of cisplatin and gemcitabine</td>
</tr>
<tr>
<td>28.08.2015</td>
<td>Re-Staging: Primary stable disease, nodal regression, bone progression</td>
</tr>
<tr>
<td>29.09.2015</td>
<td>Right upper lobe resection ypT3 ypN1 (1/8)</td>
</tr>
<tr>
<td>06.11.2015</td>
<td>Re-Staging: progression bone, LN</td>
</tr>
</tbody>
</table>
Progression Bone and LN

→ Radiotherapy sacrum and parvertebral upper thoracic spine
Case study, R.M. 1952

06/15 Diagnosis Pleomorphic Carcinoma right upperlobe
   Initial Stage cT3 cN1-2 cM0-1
07/15 - 09/15 Cisplatin/Gemcitabine 3 cycles
28.08.2015 Re-Staging: SD lung partial response LN, PD bone (oligo)
29.09.2015 UL resection with LAD ypT3 ypN1 (1/8)
06.11.2015 Re-Staging: progression bone, LN
09.11.2015 RT Sacrum, paravertebral, Os

Emergency hospitalisation 05.01.2016

- PiO2 67%; no fever, ECOG 3-4
- CRP 115, LDH 680; Leucocytes 11 G/l

- Methyprodnisolon 250mg iv (1d)
- Prednison 200mg (2d), 100mg (2d), 50mg (3d), 25mg (3d), 20mg (3d), 10mg (2d), 5mg (2d)
- Tazobac +Bactrim
Re-Staging after resolution of symptoms

11/15

02/16 and 6/2016
Should I rechallenge the patient in case of progression?
Immune checkpoint inhibitors in second line NSCLC

- Immune checkpoint inhibition provide a survival benefit as compared to second line chemotherapy
- Their safety profile is superior to the safety profile of chemotherapy
- Patient-reported outcomes suggest a stable or improved health status while on treatment
- The optimal duration of therapy is an important in need to be addressed
Companion PD-L1 tests developed by different pharmaceutical companies

<table>
<thead>
<tr>
<th>PD-1</th>
<th>PD-L1</th>
<th>Keytruda pembrolizumab</th>
<th>Opdivo nivolumab</th>
<th>Atezolizumab MPDL3280a</th>
<th>Durvalumab MEDI-4736</th>
</tr>
</thead>
<tbody>
<tr>
<td>Merck</td>
<td>Dako</td>
<td>BMS (Roche)</td>
<td>Ventana (AZ)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **22C3**
  - 1% or 50%
  - Tumor only
  - Only validated cut-off in a prospective clinical study

- **28-8**
  - Retrospective analysis of 1, 5 and 10%

- **SP142**
  - IHC 3: ≥ 10% tumor immune cells positive for PD-L1 (IC+); IHC 2 and 3: ≥ 5% tumor immune cells positive for PD-L1 (IC+); IHC 1/2/3: ≥ 1% tumor immune cells positive for PD-L1 (IC+); IHC 0/1/2/3: all patients with evaluable PD-L1 tumor IC status

- **SP263**
  - Cut-off 25% tumor cells in NSCLC

- Developing PD-L1+ IHC CDx with Dako
- Label for PD-L1 positive 2L NSCLC
- No need for PD-L1+ testing in 2L NSCLC
- Developing PD-L1+ IHC CDx with Dako
- CDx platform (Ventana) for development and to validate commercial PD-L1+ CDx
- Developing CDx for PD-L1+ with Ventana
KEYNOTE 01: NSCLC previously treated, results according to PD-L1 expression.
Analytical Evaluation Results: Mean Tumor Proportion Score (TPS) per case based on three readers

- Analytical comparison of % tumor cell staining (Tumor Proportion Score), by case, for each assay
- Data points represent the mean score from three pathologists for each assay on each case
- Superimposed lines / points indicate identical TPS values
- No clinical diagnostic cut-off applied

**Conclusion:** 3 of 4 assays are analytically similar for tumor cell staining.

*Hirsch, AACR 2016*
Blueprint projects: comparing PD-L1 immunohistochemistry diagnostics for immune checkpoint inhibitors

Analytical Evaluation Results: Mean Immune Cell Proportion Score (ICPS) per case based on three readers

- Analytical comparison of % immune cell staining (Immune Cell Proportion Score), by case, for each assay
- Data points represent the mean score for each assay on each case from three pathologists
- Superimposed lines / points indicate identical ICPS values
- No clinical diagnostic cut-off applied

**Conclusion:** Each assay stains immune cells, but the quantification is more variable than for tumor cells. *This is maybe due to no training or alignment on*

*Hirsch, AACR 2016*
Checkmate 57: OS by PD-L1 Expression

<table>
<thead>
<tr>
<th>≥1% PD-L1 expression level</th>
<th>≥5% PD-L1 expression level</th>
<th>≥10% PD-L1 expression level</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>mOS (mos)</strong></td>
<td><strong>mOS (mos)</strong></td>
<td><strong>mOS (mos)</strong></td>
</tr>
<tr>
<td>Nivo: 17.7</td>
<td>Nivo: 19.4</td>
<td>Nivo: 19.9</td>
</tr>
<tr>
<td>Doc: 9.0</td>
<td>Doc: 8.1</td>
<td>Doc: 8.0</td>
</tr>
</tbody>
</table>

Based on a July 2, 2015 DBL. Symbols represent censored observations
Limitations in defining PD-L1 as the biomarker

Expression of PD-L1 in NSCLC is heterogeneous and varies with antibody used.

Immunofluorescence shows stroma and epithelial staining are often concordant and adjacent.

Green = Cytokeratin  
Blue = Nuclei  
Red = PD-L1 (SP142)
High tumoral IFNγ mRNA, PD-L1 protein, and combined IFNγ mRNA/PD-L1 protein expression associates with response to durvalumab monotherapy in NSCLC patients

Higgs, ESMO 2015
Mutational landscape determines sensitivity of PD-1 blockade in NSCLC: Candidate neoantigens, response and PFS
Are we ready to use biomarkers for selection of patients for treatment with immune checkpoint inhibitors?

- PD-L1 expression is a – albeit imperfect - biomarker. It represents a continuous variable and needs further prospective clinical validation in addition to laboratory validation.

- Other evolving biomarkers not yet suitable for clinical routine include:
  - Co-localization with tumor infiltrating lymphocytes
  - Immunologic signatures
  - The neoantigen load
BIRCH: Atezolizumab in TC2/3 and/or IC2/3 NSCLC

- BIRCH met its primary endpoint in all predefined subgroups per protocol-specified criteria
- Majority of responses were ongoing (> 61% in TC3 or IC3)
- Median DOR was 7 mo in 3L+, NR in 1L/2L in TC3 or IC3, although follow-up is limited
- IRF- and INV-assessed ORRs (per RECIST v1.1) were similar. In TC3 or IC3, eg, 27% vs 29% in 3L+; 24% vs 25% in 2L; and 26% vs 31% in 1L, respectively

Besse, ECCO-ESMO 2015
Intensity and duration of therapy?
A case of a 70-year old man with stage IV adenocarcinoma of the lung treated with two doses of atezolizumab

April 2014: Pretreatment

September 2014: After 2 doses of therapy in June 2014

March 2015: Hilar progression
Immune checkpoint inhibitors in first line therapy: Results of treatment naive cohort in KEYNOTE 1

Median PFS was 6.1 months in all treated patients and 12.5 months with >50% PD-L1 staining.

OS was not reached in all treated patients or in patients with ≥50% staining, and was 16.2 months and 10.4 months in patients with staining in 1%–49% and <1% of cells, respectively.

Rizvi, ASCO 2015
KEYNOTE-024: Merck Presse Release

- **KEYNOTE-024 Studied Patients Whose Tumors Expressed High Levels of PD-L1**
- KENILWORTH, N.J.--(BUSINESS WIRE)--Merck (NYSE:MRK), known as MSD outside the United States and Canada, today announced that the KEYNOTE-024 trial investigating the use of KEYTRUDA® (pembrolizumab), in patients with previously untreated advanced non-small cell lung cancer (NSCLC) whose tumors expressed high levels of PD-L1 (tumor proportion score of 50 percent or more), met its primary endpoint. In this trial, KEYTRUDA was superior compared to chemotherapy for both the primary endpoint of progression-free survival (PFS), and the secondary endpoint of overall survival (OS). Based on these results, an independent Data Monitoring Committee (DMC) has recommended that the trial be stopped, and that patients receiving chemotherapy in KEYNOTE-024 be offered the opportunity to receive KEYTRUDA.
### Chemotherapy combination trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Phase</th>
<th>Drug Combination</th>
<th>ORR, %</th>
<th>Grade 3–4 treatment-related AEs, %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GP28328</strong></td>
<td>PhII</td>
<td>PhII 1L NSCLC</td>
<td>69%</td>
<td>71%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Plcembo + chemo (n=58)</td>
<td>32%</td>
<td>25%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N10 + gem/cis</td>
<td>47%</td>
<td>47%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N10 + pem/cis</td>
<td>43%</td>
<td>29%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N5 + carbo/pac</td>
<td>29%</td>
<td>28%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N1 q3w + l1 q3w</td>
<td>35%</td>
<td>31%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N1 q2w + l1 q6w</td>
<td>29%</td>
<td>29%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N3 q2w + l1 q12w</td>
<td>25%</td>
<td>28%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N3 q2w + l1 q6w</td>
<td>25%</td>
<td>28%</td>
</tr>
</tbody>
</table>

**References:**
- Camidge, et al. WCLC 2015
- Giaccone, et al. ECC 2015
- Papadimitrakopoulous, et al. ASCO 2015
- Gettinger, et al. ESMO 2014
- Rizvi, et al. WCLC 2015
Safety and antitumour activity of durvalumab plus tremelimumab in non-small-cell lung cancer: a multicentre, phase 1b study

Tumour shrinkage observed irrespective of PD-L1 tumour status

Antonia, Lancet Oncol 2016
### Phase 1 CheckMate 012: Efficacy summary

<table>
<thead>
<tr>
<th></th>
<th>Nivo 3 Q2W + Ipi 1 Q12W (n = 38)</th>
<th>Nivo 3 Q2W + Ipi 1 Q6W (n = 39)</th>
<th>Nivo 3 Q2W (n = 52)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confirmed ORR, % (95% CI)</td>
<td>47 (31, 64)</td>
<td>39 (23, 55)</td>
<td>23 (13, 37)</td>
</tr>
<tr>
<td>Median duration of response, mo (95% CI)</td>
<td>NR (11.3, NR)</td>
<td>NR (8.4, NR)</td>
<td>NR (5.7, NR)</td>
</tr>
<tr>
<td>Median length of follow-up, mo (range)</td>
<td>12.9 (0.9–18.0)</td>
<td>11.8 (1.1–18.2)</td>
<td>14.3 (0.2–30.1)</td>
</tr>
<tr>
<td>Best overall response, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete response</td>
<td>0</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>Partial response</td>
<td>47</td>
<td>39</td>
<td>15</td>
</tr>
<tr>
<td>Stable disease</td>
<td>32</td>
<td>18</td>
<td>27</td>
</tr>
<tr>
<td>Progressive disease</td>
<td>13</td>
<td>28</td>
<td>38</td>
</tr>
<tr>
<td>Unable to determine</td>
<td>8</td>
<td>15</td>
<td>12</td>
</tr>
<tr>
<td>Median PFS, mo (95% CI)</td>
<td>8.1 (5.6, 13.6)</td>
<td>3.9 (2.6, 13.2)</td>
<td>3.6 (2.3, 6.6)</td>
</tr>
<tr>
<td>1-year OS rate, % (95% CI)</td>
<td>NC</td>
<td>69 (52, 81)</td>
<td>73 (59, 83)</td>
</tr>
</tbody>
</table>

NC = not calculated (when >25% of patients are censored); NR = not reached

Combination data based on a February 2016 database lock; monotherapy data based on a March 2015 database lock except for OS data, which are based on an August 2015 database lock.

Hellmann, ASCO 2016
Phase 1 CheckMate 012: Efficacy across all tumor PD-L1 expression levels

Combination data based on a February 2016 database lock; monotherapy data based on a March 2015 database lock
Phase 3 PD1/PD-L1 combination in 1L advanced NSCLC

**Nivolumab**
- **CHECKMATE 227**: Treatment-naïve or recurrent NSCLC, N=1980
  - Primary endpoints: OS, PFS
  - Treatment: Nivolumab
  - SOC chemotherapy

**Pembrolizumab**
- **KEYNOTE-189**: Treatment-naïve non-squamous NSCLC, N=580
  - Primary endpoints: PFS
  - Treatment: Pembrolizumab, Pemetrexed/platinum

**Nivolumab**
- **CHECKMATE 026**: Treatment-naïve non-squamous NSCLC PD-L1-positive NSCLC, N=495
  - Primary endpoint: PFS
  - Treatment: Nivolumab 3 mg/kg Q2W
  - ICC with potential for crossover

**Pembrolizumab**
- **KEYNOTE-042**: Treatment-naïve non-squamous NSCLC PD-L1-positive NSCLC, N=1240
  - Primary endpoint: OS
  - Treatment: Pembrolizumab 200 mg IV Q3W
  - SOC chemotherapy

**Durvalumab**
- **Mystic**: Advanced NSCLC, N=675
  - Primary endpoint: PFS
  - Treatment: Durvalumab
  - SOC chemotherapy

**Durvalumab**
- **Neptune**: First-line metastatic NSCLC, N=800
  - Primary endpoint: OS
  - Treatment: Durvalumab + Tremelimumab
  - SOC chemotherapy

**Atezolizumab**
- **Impower 110**: Stage IV non-squamous PD-L1+ NSCLC, N=400
  - Primary endpoint: PFS
  - Treatment: Atezolizumab
  - Carboplatin or carboplatin + pemetrexed

**Atezolizumab**
- **Impower 111**: Stage IV squamous PD-L1+ NSCLC, N=400
  - Primary endpoint: PFS
  - Treatment: Atezolizumab
  - Gemcitabine + cisplatin or carboplatin
  - Atezolizumab + carboplatin + nab-paclitaxel

**Atezolizumab**
- **Impower 130**: Stage IV non-squamous NSCLC, N=550
  - Primary endpoint: PFS
  - Treatment: Carbo + nab-paclitaxel
  - Atezolizumab + carboplatin + nab-paclitaxel

**Atezolizumab**
- **Impower 131**: Stage IV squamous NSCLC, N=1200
  - Primary endpoint: PFS
  - Treatment: Carbo + nab-paclitaxel
  - Atezolizumab + carboplatin + paclitaxel

**Atezolizumab**
- **Impower 150**: Stage IV non-squamous NSCLC, N=1200
  - Primary endpoint: PFS
  - Treatment: Atezolizumab + bevacizumab + paclitaxel + carboplatin
  - Bevac + paclitaxel + carboplatin

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Peters, WCLC 2015
What are other developments of immune checkpoint inhibitors in thoracic malignancies?

- The combination between PD-1/PD-L1 antibodies with CTLA-4 antibodies or with chemotherapy is under investigation.

- Over 12 large randomized studies of immune checkpoint inhibitors in first line, generally either selected for PD-L1 positive patients or else used in combination are ongoing. First results are expected 2016.

- Consolidation trials for stage III NSCLC and neoadjuvant adjuvant trials have been initiated.