Immune checkpoint inhibitors in advanced NSCLC

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University Hospital of Zürich

Zürich, November 2, 2018
Disclosures

Consultant or Advisory Role in the last two years
I have received honoraria as a consultant at advisory boards from Abbvie, Astra Zeneca, Boehringer Ingelheim, MSD, Pfizer, Roche and Takeda.

Speaker Honoraria in the last two years
I have received honoraria as a speaker from Astra Zeneca, Boehringer Ingelheim, MSD and Roche.

DMC in the last two years
Roche and Takeda
Long-term survival with PD-1 checkpoint inhibition

Nivolumab second or later line

<table>
<thead>
<tr>
<th>Median OS (95% CI), months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall (N = 129)</td>
</tr>
<tr>
<td>9.9 (7.8, 12.4)</td>
</tr>
</tbody>
</table>

Pembrolizumab second or later line

Events, n/N | Median, mo (95% CI) | 24-mo Rate, % | 36-mo Rate, % | 48-mo Rate, % |
<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>36/3449</td>
<td>10.5 (8.6 to 13.2)</td>
<td>29.9</td>
<td>20.5</td>
</tr>
</tbody>
</table>

Overall Survival, %

Brahmer, AACR 2017; Felip, ASCO 2018
Five-year follow-up from the CA209-003 study of nivolumab in previously treated advanced NSCLC: Outcome and subsequent treatment of the 16 long term survivors

- 12/16 patients remain without evidence of disease progression
- 4 patients had subsequent therapy
  - 1 had surgical resection alone (and remains with no evidence of disease)
  - 1 had surgery followed by systemic therapies
  - 2 had systemic therapies

Brahmer, JCO 2018
Five-year follow-up from the CA209-003 study of nivolumab in previously treated advanced NSCLC:
KN-001: 4-year overall survival

Felip, ASCO 2018
Safety and clinical activity of atezolizumab monotherapy in metastatic non-small-cell lung cancer: final results from a phase I study

Horn, RJC 2018
Systemic therapy of advanced NSCLC without oncogenic driver mutation: Immunotherapy is the new standard second line therapy

Nivolumab

Pembrolizumab

Atezolizumab

Bramer, NEJM 2015; Borghai, NEJM 2015; Horn, JCO 2017

Herbst, Lancet 2016

Rittmeyer, Lancet 2017
9 | Relationship of PD-L1 expression and outcome

KN-010: Pembrolizumab versus doxetaxel in 2nd line NSCLC (≥1% of tumor cells PD-L1 positive)

Baas, ASCO 2016
ARCTIC: Durvalumab + tremelimumab and durvalumab monotherapy vs soc in ≥3L advanced NSCLC treatment
ARCTIC: Durvalumab + tremelimumab and durvalumab monotherapy vs soc in ≥3L advanced NSCLC treatment
Safety and clinical activity of adoptive cell transfer using tumor infiltrating lymphocytes combined with nivolumab in NSCLC

- Many patients had rapid progression on nivolumab
- Decreases in tumor size were observed after Cy/Flu+TIL+IL2

Antonia, WCLC 2018
Phase 3 studies of immune checkpoint inhibitors alone as first line therapy of advanced NSCLC

All studies biomarker selected

**Pembrolizumab**

KEYNOTE-024

- Treatment-naïve non-squamous NSCLC
- PD-L1–positive NSCLC
- N=305

Primary endpoint: OS

- Pembrolizumab 200 mg IV Q3W
- Platin-based chemotherapy

TPS ≥ 50%:
- Pos. PFS and OS
- Pembrolizumab as standard of Care

≥ 5% PD-L1:
- Neg. PFS and OS
- Importance of TMB

**Nivolumab**

CHECKMATE 026

- Treatment-naïve non-squamous NSCLC
- PD-L1–positive NSCLC
- N=495

Primary endpoint: PFS

- Nivolumab 3 mg/kg IV Q2W
- ICC* with potential for crossover

**Pembrolizumab**

KEYNOTE-042

- Treatment-naïve non-squamous NSCLC
- PD-L1–positive NSCLC
- N=1240

Primary endpoint: OS

- Pembrolizumab 200 mg IV Q3W
- ICC* with potential for crossover

TPS ≥ 1%:
- Pos OS
- No change in standard of care
KN-024: Pembrolizumab vs platinum-based chemotherapy as first-Line therapy for advanced NSCLC with a PD-L1 TPS ≥50%

**KEYNOTE-024 Study Design (NCT02142738)**

**Key Eligibility Criteria**
- Untreated stage IV NSCLC
- PD-L1 TPS ≥50%
- ECOG PS 0-1
- No activating EGFR mutation or ALK translocation
- No untreated brain metastases
- No active autoimmune disease requiring systemic therapy

**Key End Points**
- Primary: PFS (RECIST v1.1 per blinded, independent central review)
- Secondary: OS, ORR, safety
- Exploratory: DOR

**PROGRESSION-FREE SURVIVAL**

<table>
<thead>
<tr>
<th></th>
<th>Events, n</th>
<th>Median, mo</th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pembro</td>
<td>73</td>
<td>10.3</td>
<td>0.50</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Chemo</td>
<td>116</td>
<td>6.0</td>
<td>0.37-0.68</td>
<td></td>
</tr>
</tbody>
</table>

Reck, ESMO 2016
KN-024: Pembrolizumab vs platinum-based chemotherapy as for advanced NSCLC: Updated survival results

**Disposition of Study Treatment**
- 305 patients randomly allocated
  - Pembrolizumab: 154 allocated (ITT), 144 treated (median [range] treatment duration: 7.9 mo [1.6 to 23.7 mo]), 114 discontinued
  - Chemotherapy: 151 allocated (ITT), 150 treated (median [range] treatment duration: 3.9 mo [1.6 to 30.0 mo]), 121 discontinued

Median follow-up: 25.2 mo

**Overall Survival: Updated Analysis**
- Pembrolizumab: 73 events, HR (95% CI): 0.63 (0.47–0.86), P = 0.002
- Chemotherapy: 96 events, HR (95% CI): Not reached

Median (95% CI):
- Pembrolizumab: 30.0 mo (18.3 mo–NR)
- Chemotherapy: 14.2 mo (9.8 mo–19.0 mo)

*Events considered irreversible by the investigator.*
*Data cut-off: July 10, 2017.*

Brahmer, WCLC 2017
CM-024: Impact of tumor mutation burden on the efficacy of first-line nivolumab in advanced NSCLC: PFS by mutation burden tertile

Nivolumab Arm

<table>
<thead>
<tr>
<th>Mutation Burden</th>
<th>N (n)</th>
<th>Median PFS, months</th>
<th>(95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>62</td>
<td>4.2</td>
<td>(1.5, 5.6)</td>
</tr>
<tr>
<td>Medium</td>
<td>49</td>
<td>3.6</td>
<td>(2.7, 6.9)</td>
</tr>
<tr>
<td>High</td>
<td>47</td>
<td>9.7</td>
<td>(5.1, NR)</td>
</tr>
</tbody>
</table>

Chemotherapy Arm

<table>
<thead>
<tr>
<th>Mutation Burden</th>
<th>N (n)</th>
<th>Median PFS, months</th>
<th>(95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>41</td>
<td>6.9</td>
<td>(5.4, NR)</td>
</tr>
<tr>
<td>Medium</td>
<td>53</td>
<td>6.5</td>
<td>(4.3, 8.6)</td>
</tr>
<tr>
<td>High</td>
<td>60</td>
<td>5.8</td>
<td>(4.2, 8.5)</td>
</tr>
</tbody>
</table>

- Data for patients with low and medium TMB were pooled in subsequent analyses.

Peters, AACR 2017
KN-042: Pembrolizumab vs platin-based chemotherapy as first line therapy for advanced NSCLC with a PD-L1 TPS ≥ 1%
KN-042: Pembrolizumab vs platin-based chemotherapy as first line therapy for advanced NSCLC with a PD-L1 TPS ≥ 1%
Phase 3 studies of immune checkpoint inhibitors combined with chemotherapy as first line therapy of advanced non-squamous NSCLC

**Atezolizumab**

- **Impower 150**
  - Stage IV non-squamous NSCLC
  - N=1200
  - Treatments: Atezolizumab + carboplatin + paclitaxel, Bevacizumab + paclitaxel + carboplatin
  - Primary endpoint: PFS and OS
  - **Pos. PFS and OS**
  - Atezo Quadruplet as new option (mEGFR, liver metastases)

- **Impower 130**
  - Stage IV non-squamous NSCLC
  - N=578
  - Treatments: Atezolizumab + carboplatin + nab-paclitaxel, Carboplatin + nab-paclitaxel
  - Primary endpoint: PFS and OS
  - **Pos. PFS and OS**
  - Atezo/Carbo/nabPacli as new option

- **Impower 132**
  - Stage IV non-squamous NSCLC
  - N=68
  - Treatments: Atezolizumab + carboplatin + Pemetrexed, Carboplatin + pemetrexed
  - Primary endpoint: PFS and OS
  - **Pos. PFS, OS pending**

**Pembrolizumab**

- **KEYNOTE-189**
  - Treatment-naive non-squamous NSCLC
  - N=580
  - Treatments: Pembrolizumab + pemetrexed/platinum, Pemetrexed/platinum
  - Primary endpoints: PFS and OS
  - **Pos. PFS and OS**
  - TPS < 50%: Pembro/Carbo/Pem as one new standard of care
Impower 150: Primary PFS analyses of a randomized phase III study of carboplatin and paclitaxel +/- bevacizumab, with or without atezolizumab in 1L non-squamous metastatic NSCLC

INV-assessed PFS in ITT-WT (Arm B vs Arm C)

The principal question is to assess whether the addition of atezolizumab to Arm C provides clinical benefit.
Impower 150: OAS analyses of a randomized phase III study of carboplatin and paclitaxel +/- bevacizumab, with or without atezolizumab in 1L non-squamous metastatic NSCLC

OS in Key Subgroups (Arm B vs Arm C)

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>n (%)</th>
<th>Median OS, mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD-L1–High (TC3 or IC3) WT</td>
<td>136 (20%)</td>
<td>0.70</td>
</tr>
<tr>
<td>PD-L1–Low (TC1/2 or IC1/2) WT</td>
<td>226 (32%)</td>
<td>0.80</td>
</tr>
<tr>
<td>PD-L1–Negative (TC0 and IC0) WT</td>
<td>339 (49%)</td>
<td>0.82</td>
</tr>
<tr>
<td>Liver Metastases WT</td>
<td>94 (14%)</td>
<td>0.54</td>
</tr>
<tr>
<td>No Liver Metastases WT</td>
<td>602 (86%)</td>
<td>0.83</td>
</tr>
<tr>
<td>ITT (including EGFR/ALK+)</td>
<td>800 (100%)</td>
<td>0.76</td>
</tr>
<tr>
<td>EGFR/ALK+ only</td>
<td>104b (13%)</td>
<td>0.54</td>
</tr>
<tr>
<td>ITT-WT</td>
<td>696 (87%)</td>
<td>0.78</td>
</tr>
</tbody>
</table>

Hazard Ratio:
- In favor of Arm B: atezo + bev + CP
- In favor of Arm C: bev + CP

NE: not estimable.

* Prevalence % for PD-L1 IHC and liver metastases subgroups out of ITT-WT (n=896); prevalence of ITT, EGFR/ALK+, and ITT-WT out of ITT (n=800).
* One patient had EGFR exon 19 deletion and also tested ALK positive per central lab.
* Stratified HR for ITT and ITT-WT; unstratified HR for all other subgroups. Data cutoff: January 22, 2018

Socinski, ASCO 2018
Impower 150: OAS analyses of a randomized phase III study of carboplatin and paclitaxel +/- bevacizumab, with or without atezolizumab in 1L non-squamous metastatic NSCLC: Patients with EGFR/ALK+ tumors

Arm $B^b$ vs Arm $C$
- Atezo+Bev+CP
- Bev+CP

HR$^{c}$ 0.54
(95% CI: 0.29, 1.03)

17.5 mo | NE

Arm $A$ vs Arm $C$
- Atezo+CP
- Bev+CP

HR$^{c}$ 0.82
(95% CI: 0.49, 1.37)

17.5 mo | 21.2 mo

Socinski, ASCO 2018
IMpower130: efficacy and safety from a randomized phase 3 study of carboplatin and nab-paclitaxel with or without atezolizumab in 1L advanced non-squamous NSCLC

Cappuzzo, ESMO 2018
IMpower130: efficacy and safety from a randomised phase 3 study of carboplatin and nab-paclitaxel with or without atezolizumab in 1L advanced non-squamous NSCLC

Cappuzzo, ESMO 2018
IMpower132: PFS and safety results with 1st line atezolizumab + carboplatin/cisplatin and pemetrexed in stage IV non-squamous NSCLC

Final investigator assessed PFS

Papadimitrakopoulou, WCLC 2018
KN-189: Randomized double blind phase 3 study of pembrolizumab or placebo plus pemetrexed and platinum as 1L for metastatic non-squamous NSCLC

**Key Eligibility Criteria**
- Untreated stage II nonsquamous NSCLC
- No sensitizing EGFR or ALK alteration
- ECOG PS 0 or 1
- Provision of a sample for PD-L1 assessment
- No symptomatic brain metastases
- No previous or ongoing systemic steroids

**Stratification Factors**
- PD-L1 expression (TPS<1% vs 21%)
- Platinum (cisplatin vs carboplatin)
- Smoking history (never vs former/current)

**Overall Survival, ITT**

Ghandi, AACR 2018
KN-189: Randomized double blind phase 3 study of pembrolizumab or placebo plus pemetrexed and platinum as 1L for metastatic non-squamous NSCLC: OS
Phase 3 studies of immune checkpoint inhibitors combined with chemotherapy as first line therapy of advanced squamous NSCLC

**Pembrolizumab**
*KEYNOTE-407*
- Treatment-naive squamous NSCLC
  - Pembrolizumab + Carbo/Pacl or Nab-Pacl
  - Primary endpoint: PFS and OS
- Primary endpoint: Pos. PFS and OS
- Pembrolizumab/Carbo/Pacl as one new standard of care

**Atezolizumab**
*Impower 131*
- Stage IV squamous NSCLC
  - Atezolizumab + carboplatin + nab-paclitaxel
  - Carboplatin + nab-paclitaxel
  - Primary endpoint: PFS and OS
- Primary endpoint: Pos. PFS, preliminary OS neg
KN-407: Phase 3 study of carboplatin-paclitaxel/nab-paclitaxel with or without pembrolizumab for metastatic squamous NSCLC

**Overall Survival at IA2, ITT**

<table>
<thead>
<tr>
<th>Events</th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pembro + Chemo</td>
<td>30.6%</td>
<td>0.64 (0.49-0.85)</td>
</tr>
<tr>
<td>Placebo + Chemo</td>
<td>42.7%</td>
<td></td>
</tr>
</tbody>
</table>

Median (95% CI): 15.9 mo (13.2-NE) vs 11.3 mo (9.5-14.8)
IMpower131: Primary PFS and safety analysis of a randomized phase III study of atezolizumab + carboplatin + paclitaxel or nab-paclitaxel vs chemotherapy alone as 1L therapy in advanced squamous NSCLC

Jotte, ASCO 2018
Phase 3 studies of CTLA-4 and PD-1 or PD-L1 combinations as first line therapy for advanced NSCLC

All studies biomarker selected

**Nivolumab**

**CHECKMATE 227**
- Treatment-naïve or recurrent NSCLC
  - N=1980
  - Primary endpoints: PFS in TMB high
  - Alternative option, particular in PD-L1 low

**Durvalumab**

**MYSTIC**
- Advanced NSCLC
  - N=675
  - Primary endpoint: PFS and OS

**Nivolumab (PD-L1 ≥ 1%) or nivo/chemotherapy (PD-L1 < %)**
- Nivolumab + ipilimumab
- Platinum-based chemotherapy

**Durvalumab**
- Durvalumab + tremelimumab
- SOC chemotherapy

**Primary endpoints:**
- Pos. PFS and OS
- Neg. PFS, OS pending

**TMB high:**
- PD-L1 ≥ 25%

**TMB high:**
- Pos. PFS and OS
- Alternative option, particular in PD-L1 low

**TMB high:**
- Neg. PFS, OS pending
CM-227: Nivolumab + ipilimumab vs platinum-doublet chemotherapy as 1L treatment for advanced NSCLC: TMB high

CheckMate 227 Part 1 Study Design

Key Eligibility Criteria
- Stage IV or recurrent NSCLC
- No prior systemic therapy
- No known sensitizing EGF/RA/LK alterations
- ECOG PS 0–1

Stratified by SQ vs NSQ

N = 1189
≥1% PD-L1 expression
R 1:1:1

Nivolumab 3 mg/kg Q2W
Ipilimumab 1 mg/kg Q6W
n = 396

Histology-based chemotherapy
n = 397

Nivolumab 240 mg Q2W
n = 396

Patients for PD-L1 co-primary analysis
Nivolumab + Ipilimumab
n = 396
Chemotherapy
n = 397

N = 550
<1% PD-L1 expression
R 1:1:1

Nivolumab 3 mg/kg Q2W
Ipilimumab 1 mg/kg Q6W
n = 167

Histology-based chemotherapy
n = 169

Nivolumab 360 mg Q3W +
histology-based chemotherapy
n = 177

Nivolumab + Ipilimumab
n = 139
Chemotherapy
n = 160

Co-primary endpoints: Nivolumab + ipilimumab vs chemotherapy
- OS in PD-L1-selected populations
- PFS in TMB-selected populations

Hellmann, AACR 2018
• Part 1a: Opdivo plus low-dose Yervoy or Opdivo monotherapy versus chemotherapy in patients whose tumors express PD-L1: Primary endpoint OS in patients with PD-L1 positive tumors
• Part 1b: Opdivo plus low-dose Yervoy or Opdivo plus chemotherapy versus chemotherapy in patients whose tumors do not express PD-L1: Primary endpoint PFS in patients with a TMB ≥10 mut/Mb
• Part 2: Opdivo plus chemotherapy versus chemotherapy, regardless of PD-L1 or tumor mutational burden status (TMB): Primary endpoint OS
• An updated descriptive analysis showed that the HR for OS with Opdivo plus low-dose Yervoy versus chemotherapy in patients with TMB ≥10 mut/Mb was 0.77 (95% CI: 0.56 to 1.06).

• New exploratory analysis in patients with TMB <10 mut/Mb showed that the HR for OS with Opdivo plus low-dose Yervoy versus chemotherapy was 0.78 (95% CI: 0.61 to 1.00), comparable to that observed in patients with TMB ≥10 mut/Mb.

• The median OS in patients with TMB ≥10 mut/Mb was 23.03 months on the Opdivo plus low-dose Yervoy arm and was 16.72 months on the chemotherapy arm.

• In patients with TMB <10 mut/Mb the median OS was 16.20 months and was 12.42 months on the combination and chemotherapy arms, respectively.

BMS press release 19.10.2018
Checkmate-227: Nivolumab + ipilimumab vs platinum-doublet chemotherapy as 1L treatment for advanced NSCLC

Selection of TMB ≥10 mut/Mb Cutoff for Nivolumab + Ipilimumab Using FoundationOne CDx™

- Retrospective testing from CheckMate 026, 012, and 568 informed selection of the TMB cutoff (≥10 mut/Mb)\(^1\)\(^3\)
- ORR increased in patients with higher TMB, and plateaued at TMB ≥10 mut/Mb

CheckMate 568:
Phase 2 study of nivolumab + ipilimumab in 1L NSCLC
Tumor Mutational Burden (TMB) as a Biomarker for Clinical Benefit From Dual Immune Checkpoint Blockade With Nivolumab + Ipilimumab in First-line Non-Small Cell Lung Cancer: Identification of TMB Cutoff From CheckMate 568
Ramalingam S, et al.
Date: April 16, 2018  Time: 12:05 – 12:25pm

CheckMate 568: ROC for TMB by ORR irrespective of tumor PD-L1 expression (n = 98)

AUC = 0.73
Checkmate-227: Nivolumab + ipilimumab vs platinum-doublet chemotherapy as 1L treatment for advanced NSCLC

TMB and Tumor PD-L1 Expression Identify Distinct and Independent Populations of NSCLC

Hellmann, AACR 2018
Checkmate-227: Nivolumab + ipilimumab vs platinum-doublet chemotherapy as 1L treatment for advanced NSCLC

Co-primary endpoint: PFS with nivolumab and ipilimumab in patients with high TMB (≥ 10 mut/Mb)

- In patients with TMB <10 mut/Mb treated with nivo + ipi vs chemo, the HR was 1.07 (95% CI: 0.85, 1.35)
Checkmate-227: Nivolumab + ipilimumab vs platinum-doublet chemotherapy as 1L treatment for advanced NSCLC

Preliminary Overall Survival With Nivolumab + Ipilimumab vs Chemotherapy in Patients With High TMB (≥10 mut/Mb)

- Database lock: March 15, 2018; minimum follow-up: 14.2 months; 53% of patients were censored
- In the chemotherapy arm, 31.3% received subsequent immunotherapy (38.3% among those with disease progression)

Hellmann, AACR 2018
• An updated descriptive analysis showed that the HR for OS with Opdivo plus low-dose Yervoy versus chemotherapy in patients with TMB ≥10 mut/Mb was 0.77 (95% CI: 0.56 to 1.06).

• New exploratory analysis in patients with TMB <10 mut/Mb showed that the HR for OS with Opdivo plus low-dose Yervoy versus chemotherapy was 0.78 (95% CI: 0.61 to 1.00), comparable to that observed in patients with TMB ≥10 mut/Mb.

• The median OS in patients with TMB ≥10 mut/Mb was 23.03 months on the Opdivo plus low-dose Yervoy arm and was 16.72 months on the chemotherapy arm.

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BMS press release 19.10.2018
After ESMO IO, AACR and ASCO

**Non-Squamous**

- **No Targetable Alterations**
  - PD-L1 <1 % TPS
    - Pembrolizumab
  - PD-L1 1-49 % TPS
    - Atezolizumab
    - Carboplatin Pemetrexed
    - Atezolizumab Bevacizumab
    - Carboplatin Paclitaxel *
  - PD-L1 ≥50% TPS
    - Pembrolizumab

- TMB <10/MB
- TMB ≥10/MB
  - Platinum Doublet?
  - Nivolumab Iplilimumab

**Squamous**

- **PD-L1 <1 % TPS**
  - Pembrolizumab
- **PD-L1 1-49 % TPS**
  - Nivolumab Iplilimumab
- **PD-L1 ≥50% TPS**
  - Pembrolizumab

**EGFR, ALK, BRAF, ROS-1**

- **No Targetable Alterations**
  - PD-L1 ≥50% TPS
    - Pembrolizumab
  - PD-L1 1-49 % TPS
    - Carboplatin Paclitaxel or nab-Paclitaxel
  - PD-L1 <1 % TPS
    - Atezolizumab Carboplatin Paclitaxel

- **TMB <10/MB**
- **TMB ≥10/MB**
  - Platinum Doublet?

* First choice In case of TKI-resistant EGFR mutation
Randomized phase III comparison of standard-dose versus high-dose chemo-radiotherapy ± cetuximab for stage III NSCLC

One-sided log-rank $p=0.0042$

Median PFS 11 months

One-sided log-rank, $p=0.2938$

*Carboplatin and paclitaxel
**PACIFIC: Consolidation durvalumab for 1 year after chemoradiotherapy of stage III NSCLC: Progression-free survival**

<table>
<thead>
<tr>
<th>Durvalumab</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Events/Total No. of Patients</td>
<td>214/476</td>
</tr>
<tr>
<td>Median PFS (95% CI) mo</td>
<td>16.8 (13.0–18.1)</td>
</tr>
<tr>
<td>12-Mo PFS (95% CI)</td>
<td>55.9 (51.0–60.4)</td>
</tr>
<tr>
<td>18-Mo PFS (95% CI)</td>
<td>44.2 (37.7–50.5)</td>
</tr>
</tbody>
</table>

Median PFS from start of therapy @ 20 months
Overall survival with durvalumab after chemoradiotherapy in stage III NSCLC

Antonia, NEJM 2018
Exploratory analyses of overall survival in PACIFIC
Exploratory analyses of overall survival in PACIFIC

<table>
<thead>
<tr>
<th>PFS (BICR)</th>
<th>OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (95% CI)</td>
<td>Durvalumab</td>
</tr>
<tr>
<td>ITT&lt;sup&gt;1,2&lt;/sup&gt;</td>
<td>214/476 (45.0)</td>
</tr>
<tr>
<td>Time from last radiotherapy to randomisation</td>
<td>50/120 (41.7)</td>
</tr>
<tr>
<td>&lt;14 days</td>
<td>164/356 (46.1)</td>
</tr>
</tbody>
</table>

Faivre-Finn, ESMO 2018
NICOLAS – A phase II trial evaluating the safety and efficacy of the addition of concurrent anti-PD-1 nivolumab to standard first-line chemotherapy and radiotherapy in locally advanced stage IIIA/B NSCLC (Amendment 2)

**Primary Endpoint:**
Grade ≥3 pneumonitis

**Key secondary endpoint:**
1-year PFS

**Sample Size:**
43 patients → extended to 78 patients under amendment 2

**Countries:**
Belgium, Germany, Netherland, Spain, Switzerland
Neoadjuvant PD-1 blockade in resectable lung cancer with two infusions of nivolumab 2 weeks apart

Forde, ESMO 2016 and NEJM 2018