KEYNOTE-189: Updated OS and progression after the next line of therapy (PFS2) with pembrolizumab (pembro) plus chemo with pemetrexed and platinum vs placebo plus chemo for metastatic nonsquamous NSCLC.

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Background:
Pembro + chemo significantly improved OS and PFS over chemo alone and had manageable safety as 1L therapy for metastatic nonsquamous NSCLC in the KEYNOTE-189 study (NCT02578680). The benefit was observed irrespective of PD-L1 TPS. We present updated OS based on longer follow-up and, for the first time, PFS2.

Methods:
Eligible pts were randomized 2:1 to pembro (n = 410) or placebo (n = 206) + pemetrexed and carboplatin or cisplatin for 4 cycles followed by pembro or placebo for up to 35 cycles + maintenance pemetrexed. Pts in the chemo arm could crossover to pembro alone upon PD. Poststudy anticancer therapy and outcomes were collected. PFS2 was defined as time from randomization to PD per investigator after start of 2L therapy or death, whichever occurred first. There was no multiplicity adjustment, and all P values are nominal. Data cutoff was 21 Sep 2018. Results: With 18.7-mo median follow-up, pembro + chemo continued to provide longer OS (HR 0.56 [95% CI 0.45-0.70], P< .00001; median 22.0 mo vs 10.7 mo) and PFS (HR 0.48 [95% CI 0.40-0.58], P< .00001). Benefit was seen in all PD-L1 TPS groups (Table). 2L+ therapy was received by 45% in the pembro + chemo arm and 59% (54% 2L+ immunotherapy) in the placebo + chemo arm. PFS2 was longer for 1L pembro + chemo (HR 0.49 [95% CI 0.40-0.59], P< .00001; median 17.0 mo vs 9.0 mo), with no difference by TPS (Table).

Conclusions:
1L pembro + pemetrexed/platinum continued to show substantial OS benefit in metastatic nonsquamous NSCLC, regardless of PD-L1 TPS and despite 54% of pts in the placebo + chemo arm receiving subsequent immunotherapy. Median OS, PFS and PFS2 were approximately doubled with pembro + chemo. These data confirm that pembro should be given as part of 1L therapy to maximize outcomes in both PD-L1 expressing and PD-L1 non-expressing NSCLC. Clinical trial information: NCT02578680
<table>
<thead>
<tr>
<th></th>
<th>PD-L1 TPS ≥50% n = 202</th>
<th>PD-L1 TPS 1-49% n = 186</th>
<th>PD-L1 TPS &lt; 1% n = 190</th>
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<tbody>
<tr>
<td><strong>OS, HR (95% CI)</strong></td>
<td>0.59 (0.39-0.88)</td>
<td>0.62 (0.42-0.92)</td>
<td>0.52 (0.36-0.74)</td>
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<tr>
<td><strong>PFS, HR (95% CI)</strong></td>
<td>0.36 (0.26-0.51)</td>
<td>0.51 (0.36-0.73)</td>
<td>0.64 (0.47-0.89)</td>
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<tr>
<td><strong>PFS2, HR (95% CI)</strong></td>
<td>0.47 (0.33-0.69)</td>
<td>0.59 (0.41-0.86)</td>
<td>0.46 (0.33-0.66)</td>
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