Association of $STK11/LKB1$ genomic alterations with lack of benefit from the addition of pembrolizumab to platinum doublet chemotherapy in non-squamous non-small cell lung cancer

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Study characteristics/Inclusion criteria

- Retrospective multi-center international study
- Two distinct cohorts:
  1. Metastatic non-squamous NSCLC treated with 1st line PCP with available genomic profiling INCLUDING STK11 (Cohort 1)
  2. Metastatic STK11 and/or KEAP1-mutant non-squamous NSCLC treated with 1st line PC prior to regulatory approval of PCP (Cohort 2)
- Alive ≥ 14 days after C1D1
- All non-synonymous STK11 and KEAP1 mutations and bi-allelic deletions included
- Sensitizing EGFR mutations and ALK translocations excluded
- Prior chemotherapy allowed only if adjuvant or as part of definitive chemoRT
- Prior immunotherapy not allowed
- Concurrent bevacizumab not allowed
- Patients with brain metastases eligible (treated of untreated)
- Date cutoff: 12/31/2018
STK11 genomic alterations are associated with inferior clinical outcomes with PCP in non-squamous NSCLC

HR 1.58 (95% CI 1.20-2.08)  
P=0.0012, log-rank test

HR 1.57 (95% CI 1.11-2.21)  
P=0.0113, log-rank test
Lack of benefit from addition of pembrolizumab to CP chemotherapy in STK11 and/or KEAP1-mutant non-squamous NSCLC
Conclusions

- **STK11** and **KEAP1** genomic alterations are associated with poor clinical outcomes with PCP chemo-immunotherapy and lack of apparent benefit from addition of pembrolizumab to carbo(cis)platin and pemetrexed in non-squamous NSCLC.

- The negative impact of **STK11** and **KEAP1** genomic alterations on clinical outcomes with PCP is most prominent in TMB-High and PD-L1 positive tumors.

- TMB and PD-L1 TPS don't impact outcomes with PCP in **STK11** and/or **KEAP1**-mutant tumors.

- 76.5% of PCP-primary refractory patients harbor **STK11** and/or **KEAP1** alterations.

- **STK11** and/or **KEAP1** alterations define a prevalent (~25%) subgroup of NSCLC patients with an unmet need for novel strategies to establish effective antitumor immunity.