OA15.06
Pooled Analysis of Outcomes with Second-Course Pembrolizumab Across 5 Phase 3 Studies of Non- Small-Cell Lung Cancer

Background

- Pembrolizumab as monotherapy and in combination with chemotherapy substantially prolongs OS and PFS compared with chemotherapy alone in patients with advanced or metastatic NSCLC without driver mutation.
- Generally immunotherapy is given for 35 cycles in case of continued disease response.
- Can IO be rechallanged after initial response or in case of progression beyond 2 years
- In the clinical trial setting, patients whose disease progressed after completing 35 cycles (~2 years) of pembrolizumab were eligible to receive a second course of pembrolizumab.

Introduction

- This analysis pooled patients with advanced or metastatic NSCLC treated with 1)pembrolizumab monotherapy (cohort 1) in the KEYNOTE-024, KEYNOTE-042, and KEYNOTE-598 studies
- 2) pembrolizumab plus chemotherapy (cohort 2) in the KEYNOTE-189 and KEYNOTE-407 studies
- Patients included in this analysis received second-course pembrolizumab (up to 17 cycles) following PD after either completing 35 cycles of pembrolizumab (with/without chemotherapy) with SD or better or stopping pembrolizumab before 35 cycles due to CR.
- Efficacy was analyzed in the ITT population and safety in the as-treated population.

Results

- In cohort 1, among 148 patients who completed 35 cycles of pembrolizumab and experienced PD, 58 patients received second-course pembrolizumab and were included in this analysis.
- Cohort 2 included 16 of 55 patients who completed 35 cycles of pembrolizumab (as part of pembrolizumab plus chemotherapy), experienced PD, and received second course pembrolizumab.
- 18/58 patients (31%) in cohort 1 and 7/16 (44%) in cohort 2 had squamous histology
- 47/58 (81%) and 7/16 (44%), respectively, had PD-L1 TPS !50%.

- Median (range) time from stopping first-course pembrolizumab to starting second course was 11.7 (3.8-35.6) months in cohort 1 and 6.3 (0.9-18.2) months in cohort 2.
- Median duration on second course was 8.3 months in cohort 1 and 7.6 months in cohort 2, with an estimated 62% and 59%, respectively, remaining on second course at 6 months.
- ORR by investigator review during second-course pem- brolizumab was 19% in cohort 1 and 6% in cohort 2
- 14 patients (24%) in cohort 1 and 4 (25%) in cohort 2 experienced treatment-related AEs on or after second course, of which 3 (5%) and 1 (6%) were grade 3-4, respectively; none were grade 5.

Table.

	Cohort 1	Cohort 2
	Pembrolizumab Monotherapy	**Pembrolizumab + Chemotherapy**
	n = 58	**n = 16**
OS, median (95% CI), mo[a]	27.5 (21.7-NR)	NR (NR-NR)
6-mo OS rate, % (95% CI)	*85.4 (72.9-92.4)*	*86.2 (55.0-96.4)*
PFS,[a,b] median (95% CI), mo	8.2 (5.3-14.0)	7.7 (1.8-NR)
6-mo PFS[b] rate, % (95% CI)	*59.6 (45.0-71.5)*	*58.3 (27.0-80.1)*
ORR,[b] % (95% CI)	19.0 (9.9-31.4)	6.3 (0.2-30.2)
SD, n (%)	31 (53.4)	7 (43.8)

Conclusions

- A second course of pembrolizumab monotherapy was feasible, associated with antitumor activity and clinically meaningful benefit, with manageable safety in patients with advanced or meta- static NSCLC who experienced PD after completing first-course pem- brolizumab with/without chemotherapy.
- These data support pembrolizumab retreatment upon PD.

Summarise…..

- ICI free interval is seen to be a predictive factor of PFS
- For most patients who have experienced progression after ICI, chemotherapy is generally preferred.
- However if progression occurs at least 6 mo. after the last dose of ICI, rechallange can be attempted.
- Trials with Nivo rechallange also showed ORR of 8.5% and median PFS of 2.6 mo. ICI free interval was the only predictive factor of PFS, while prior efficacy or h/o irAE was not.
- Even in patients who initially responded to prior ICI and had ICI free interval, once resistance occurred, re treatment with Nivo had limited efficacy

Take home

- Typical approach——- chemotherapy
- Long TFI—— Rechallenge may be attempted
- Reasonable time period- ?? 6 mo.
- Oligoprogression- local therapy + continue ICI
- Other investigational approaches——
- 1) ramucirumab+ pembrolizumab
- 2) cabozantinib +/- atezolizumab

Thank you