First line (1L) durvalumab in patients with PD-L1 positive, advanced non-small cell lung cancer (NSCLC) with a performance status of 2 (PS2). Primary analysis of the multicenter, single-arm phase II trial SAKK 19/17

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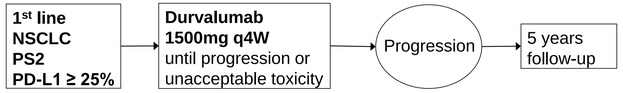
Abstract: 9088

Background

- The safety and efficacy of 1L durvalumab in PS2 patients (pts) with advanced NSCLC is unknown.
- Important safety data leading to exclusion of pts with relevant respiratory symptoms have been published as an interim report (1).
- Here we present the primary analysis of 1L durvalumab in PS2 PD-L1 positive pts, unsuitable for combination chemotherapy.

Methods

- Trial design: single-arm, multicenter, phase II.
- Inclusion criteria: pts with PS2, PD-L1 positive (tumor proportion score, TPS ≥25%), unresectable, advanced NSCLC, treatment-naïve, unsuitable for combination chemotherapy according to investigator, absence of dyspnea ≥G3 (based on an amendment after 21 pts), EGFR-, ALK- and ROS1-wild type.
- Treatment: fixed dose of durvalumab 1500 mg every four weeks.
- Primary endpoint: Overall survival (OS) at 6 months.
- Secondary endpoints: ORR, Duration of response (DOR), PFS, OS, Adverse events (AEs) according to National Cancer Institute Common Terminology Criteria for AEs (NCI CTCAE) version 5.0, Quality of life (QoL) measured with the EORTC QLQ-C30 and QLQ-LC13 (range 0-100).
- Statistics hypothesis: To improve OS at 6 months from ≤35% to ≥53%.



Results

- Forty-eight pts were enrolled at 10 Swiss centers from 12/2018 to 04/2022 (Table 1).
- OS at 6 months was 60% (95% CI: 45-74%).
- OS at 6 months after the exclusion of pts with initially relevant respiratory symptoms was 67% (95% CI: 46-84%, n=27) compared to the subgroup of pts without this exclusion criteria who were recruited before the amendment (52%, 95% CI: 30-74%, n=21) (Figure 1).
- Median OS was 8.5 months (95% CI: 4.4-16.7).
- ORR, median DOR and median PFS were 17% (95% CI: 8-30%), 22.8 months (95% CI: 3.8-NR) and 2.5 months (95% CI: 1.8-7.1).

Table 1: Patient characteristics

Variable	N = 48 (100%)
Age (years), median (range)	76 (37–87)
Sex	
female	19 (40%)
male	29 (60%)
Stage	
IV	41 (85%)
III	7 (15%)
Previous radiotherapy and/or surgery	17 (39%)
Subtype of NSCLC	
Adenocarcinoma	28 (59%)
Squamous cell carcinoma	17 (35%)
NSCLC not otherwise specified	3 (6%)
Extent of metastatic disease	
Lymph nodes	32 (67%)
Lung	25 (52%)
Bone	11 (23%)
Brain	7 (15%)
Liver	7 (15%)

- Thirty-three deaths (69%) were observed so far.
- Seven early fatal events considered not treatment-related occurred during the first 5 weeks of treatment before the protocol amendment.
- Four out of the first 7 early fatal events (4/7; 57%) were respiratory failures in pts with advanced symptomatic primary lung tumors.
- Only 3 more not treatment-related early fatal events occurred after the protocol amendment excluding pts with severe respiratory symptoms.
- Global health status/ QoL (Figure 2), symptom and single item QoL scales remained stable or even improved over time for patients who remained on treatment.
- AEs ≥ G3 are shown in Table 2.

Figure 1: OS of pts according to respiratory symptoms

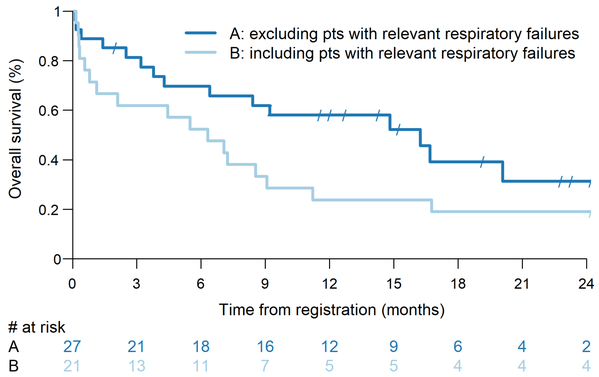
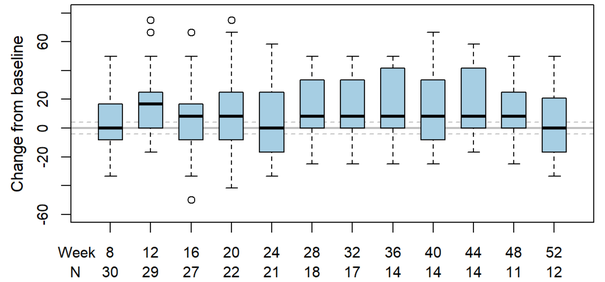


Figure 2: Changes from baseline in global health status/QoL



Note: Horizontal lines: median values; solid boxes: 25th–75th percentile; whisher bars: lowest and highest value (without outliers); circles: outliers; horizontal dashed lines: minimally important change ≥ 4 points (2); positive changes represent improvement

Table 2: Adverse events

	N = 48 (100%)
Patients with AE ≥G3	39 (81%)
Most frequent AEs ≥G3	
Lung infection	9 (19%)
Dyspnea	7 (15%)
Hypertension	5 (10%)
Respiratory failure	5 (10%)
Treatment-related AEs ≥G3 included	
Colonic perforation	1 (2%)
Colitis	5 (10%)
Hepatitis	3 (6%)
Increased lipase	3 (6%)

Conclusion

For PS2 pts without severe pulmonary symptoms diagnosed with PD-L1 positive (TPS ≥25%) advanced/metastatic NSCLC unsuitable for standard combination chemotherapy, monotherapy with durvalumab is effective and can result in prolonged tumor control.

References:
(1) Mark et al., Cancer Immunol Immunother, 2021 (70):1255-1262.
(2) Maringwa, J.T., et al., Support Care Cancer, 2011. 19(11): p. 1753-60.

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