Table: 111P

	ROS1-fp		NTRK-fp	
	Overall (N=38)	Intracranial (n=8)†	Overall (N=21)	Intracranial (n=5)†
ORR*, n (%)	24 (63)	3 (38)	17 (81)	5 (100)
95% CI	46.0–78.2	8.5–75.5	58.1–94.6	47.8–100.0
CR	4 (11)	1 (13)	1 (5)	5 (100)
PR	20 (53)	2 (25)	16 (76)	0
SD	5 (13)	0	1 (5)	0
PD	3 (8)	0	1 (5)	0
Non-CR/non-PD	4 (11)	4 (50)	1 (5)	0
Missing/unevaluable	2 (5)	1 (13)	1 (5)	0
Median time to event, months (95% CI)				
Duration of response*	11.1 (7.5–21.5)	30.9 (22.5–NE)	NE (11.1–NE)‡	NE (5.8–NE)‡
Progression-free survival*	17.7 (9.6–22.9)	13.6 (2.8–NE)	30.3 (13.7–NE)‡	NE (6.7–NE)‡
Overall survival	40.2 (21.4–NE)	–	NE (NE)‡	–

ORR for NTRK-fp NSCLC patients was 82%
*BICR assessed; †Baseline CNS metastases by BICR; ‡Data are not yet mature
NE, not estimable

67.1%; 1 May 2019 cutoff) and NTRK-fp solid tumours (ORR 61.2%; 31 Aug 2020 cutoff). We report primary results for the subset of Chinese (mainland China, HK, Taiwan) pts from STARTRK-2 (17 Jun 2021 cutoff).

Methods: Adult Chinese pts with ROS1- and TRK- TKI-naïve, ROS1-fp locally advanced/metastatic NSCLC or NTRK-fp solid tumours were enrolled. Tumour responses were assessed by blinded independent central review (BICR) per RECIST v1.1 after 4 wks and every 8 wks thereafter. ORR, duration of response, intracranial (IC) efficacy, time-to-event outcomes, and safety were assessed.

Results: The efficacy-evaluable analysis set included 38 pts with ROS1-fp NSCLC and 21 pts with NTRK-fp tumours (NSCLC, 11; sarcoma, 5; colon, 2; breast, 1; salivary, 1; thyroid, 1) with ≥6 mos follow-up. Median survival follow-up was 28.5 mos for pts with ROS1-fp NSCLC and 10.6 mos for pts with NTRK-fp tumours. ORR was 63% (ROS1-fp NSCLC) and 81% (NTRK-fp tumours); overall and IC outcomes (Table) are consistent with the overall study population. In pts with/without investigator-assessed baseline CNS metastases, overall ORR was 58.3%/65.4% (ROS1-fp NSCLC) and 100%/76.5% (NTRK-fp tumours). In the safety-evaluable analysis set, most treatment-related adverse events (TRAE) were grade 1/2 and non-serious. Discontinuation rates due to TRAEs were 5.6% (ROS1-fp NSCLC) and 0% (NTRK-fp tumours) and no deaths due to TRAEs occurred.

Conclusions: In Chinese pts with locally advanced/metastatic ROS1-fp NSCLC or NTRK-fp solid tumours, with or without baseline CNS metastases, entrectinib induced deep and durable responses.

Clinical trial identification: STARTRK-2 (NCT02568267).

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112P Patient-reported outcomes (PROs) with first-line (1L) cemiplimab in patients with locally advanced non-small cell lung cancer (laNSCLC): EMPOWER-Lung 1 subpopulation

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Background: Previously reported post hoc exploratory subgroup analysis of the phase 3 EMPOWER-Lung 1 study (NCT03088540) demonstrated improvement with cemiplimab (n=45) versus chemotherapy (chemo) (n=42) in overall survival (12-month OS, 78.5% vs 57.8%; hazard ratio [HR], 0.48; 95% confidence interval [CI], 0.20, 1.14; P=0.09) and progression-free survival (median, 8.4 vs 6.2 months; HR, 0.49; 95% CI, 0.27, 0.88; P=0.02), in patients with laNSCLC (IIIB–IIIC) and programmed cell death-ligand 1 (PD-L1) ≥50% who were not candidates for definitive chemoradiation. Post hoc exploratory analyses evaluated PROs in this subgroup.

Methods: PROs were assessed at baseline (BL) and Day 1 of each treatment cycle for the first 6 cycles, then on Day 1 of every third cycle using European Organisation for Research and Treatment of Cancer Quality of Life-Core 30 (QLQ-C30) and Lung Cancer module (QLQ-LC13) questionnaires. Higher scores indicate better functioning, improved global health status (GHS)/quality of life (QoL), or worse symptom severity. Mixed model for repeated measures analyses compared overall change from BL scores between the two treatment arms, while controlling for BL characteristics.

Results: PRO scores at BL were broadly similar between the cemiplimab and chemo arms. A significant overall change from BL in GHS/QoL favouring cemiplimab (6.27; 95% CI, 0.62, 11.93; P=0.0302) was observed. Cemiplimab led to significant favourable overall change from BL versus chemo in nausea/vomiting (-6.06; 95% CI, -9.07, -3.06; P=0.0002), dyspnoea (-11.82; 95% CI, -21.71, -1.92; P=0.0201), appetite loss (-9.39; 95% CI, -15.76, -3.02; P=0.0047), peripheral neuropathy (-7.54; 95% CI, -13.40, -1.68; P=0.0125) and alopecia (-22.03; 95% CI, -31.37, -12.68; P<0.0001). No analyses yielded significant PRO results favouring chemo for any scale.

Conclusions: In this post hoc analysis of patients with laNSCLC and PD-L1 ≥50%, cemiplimab resulted in significant favourable overall change from BL in GHS/QoL and important cancer-related and lung cancer–specific symptoms versus chemo. PRO results further support the favourable benefit-risk profile of 1L cemiplimab versus chemo in laNSCLC with PD-L1 ≥50%.

Clinical trial identification: NCT03088540.

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113P Proton-therapy and concurrent chemotherapy in stage III NSCLC: Effects on durvalumab eligibility and safety profile

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Background: Concurrent chemo-radiotherapy (CCRT) followed by adjuvant Durvalumab (D) represents standard of care for patients (pts) with unresectable stage III NSCLC. The RT can be delivered with both protons and photons. An earlier start of adjuvant D after CCRT may lead to better outcome. Little is known about the effects of protons on adjuvant D efficacy and safety. We assessed whether intensity modulated proton therapy (IMPT), compared to intensity modulated photon therapy (IMRT) affects eligibility for D (primary endpoint) and immune related adverse events (IRAEs) (secondary endpoint) in pts with stage III NSCLC treated with CCRT and adjuvant D.

Methods: Retrospective data completion and analysis of a 2-center prospectively collected series of pts with stage III NSCLC, receiving CCRT between 06.16 and 02.21, staged with FDG-PET and brain imaging. Main exclusion criteria were previous cancer diagnosis-within 2 years- and thoracic RT.

Results: A list of 226 pts was collected, 67 pts received adjuvant D and were included (IMPT: n=28, IMRT: n=39). Median age was 66 years, 52% were male, 33% had a squamous NSCLC and 42% had a WHO Performance Status (PS) of 0 before CCRT. All pts received 60-64 Gy of RT. Programmed death-ligand 1 (PDL-1) level was available for 76% of pts and 39% had a PDL-1 $\geq$ 50% (no significant differences between IMPT and IMRT). At day 21 after CCRT, 93% (IMPT) vs 72% (IMRT) treated pts had a PS$\leq$1 (Odds Ratio 0.8, 95% CI: 0.67-0.95, p=0.03). The median time from the end of CCRT and start of D was 32 vs 38 days respectively (Not Significant (NS)). IRAEs of any grade were reported in 21% versus 31% of pts treated with IMPT versus IMRT, respectively (NS). Hypothyroidism accounted for 44% of IRAEs. Any grade (grade 3) pneumonitis during D was reported in 25% (7%) of IMPT and 23% (5%) of IMRT (NS). Median follow-up was 19.5 months and 9.5 months for IMRT and IMPT, respectively. 90% of pts were still alive and 73% were disease free. IMPT vs IMRT treated pts received a significantly lower RT dose to bone marrow, heart and lungs.

Conclusions: PS at day 21 after CCRT was better in IMPT treated pts, potentially increasing eligibility for adjuvant D. The lower RT dose delivered with IMPT might explain our findings. IMPT appears to be as safe as IMRT regarding IRAEs during D.

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114P Preliminary results of the "Blue Sky Radiomics" study on stage III NSCLC patients treated with chemo-radiation and consolidation immunotherapy

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Background: One of the primary endpoints of this study is to assess the prognostic power of Signature 0, a radiomics signature originally developed for predicting survival in patients undergoing chemoradiotherapy (CRT), in patients receiving consolidation immunotherapy after CRT. Here we present a preliminary analysis on the discriminative power of radiomics features for the potential implementation of Signature 0 in immunotherapy.

Methods: We analysed the clinical and imaging data of 58 stage III unresectable NSCLC patients treated with CRT followed by durvalumab (Blue Sky Radiomics study, NCT04364776). Two sets of CT images were available for each patient, before and after CRT. According to study inclusion criteria all patients were PD-L1 positive (>1%), received at least one dose of durvalumab, and were in stable disease at least after CRT. The CT scans were manually segmented by the radiologist for the primary tumor and the mediastinal lymphadenopathies. Handcrafted radiomics features were extracted from baseline CT scans and correlated with PFS at 18, 24 and 30 months. The univariate discriminating power was calculated for each radiomics feature (n =171) and expressed in term of AUC with an inclusion threshold of 0.75.

Results: Among the analyzed features, six were found to be predictive for PFS at 18, 24, and 30 months. Two features linked to tumor heterogeneity were found to be highly predictive of PFS at 18 months (LocInt_PeakGlobal – AUC =0.94; LocInt_PeakLocal – AUC =0.86) and very good at both 24 and 30 months (AUC of 0.88 and 0.83 and AUC 0.77 and 0.75, respectively). The other four features showed good discriminant power both at 24 and 30 months (AUCs 0.69 to 0.78). As a preliminary test Signature 0 was applied in the cohort on both baseline and follow-up CT scans. No statistically significant discriminative power based on prognosis was observed, with the possible limit of the small sample size.

Conclusions: The six promising radiomics features identified will be used to expand the predictive power of Signature-0, after the application of the same model in the extended cohort of 100 patients. Along with these new features, radiomics of lymphadenopathies will also deserve further investigation.

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