Table: 1182P

Characteristics	1L (N=108)	2L (n=57)	BM (n=23)
Age, years			
Median (range)	75 (46–85)	73 (46–85)	72 (48–85)
Sex, n (%)			
Female	59 (54.6)	34 (59.6)	13 (56.5)
Race, n (%)			
White	77 (71.3)	39 (68.4)	14 (60.9)
BMI			
Mean (SD)	26.8 (5.2)	26.5 (5.2)	28.6 (6.4)
Smoking history, n (%)			
Yes	68 (63.0)	34 (59.6)	17 (73.9)
NSCLC diagnosis to treatment, days			
Mean (SD)	241.7 (576.6)	366.1 (359.2)	207.7 (698.4)
Histology, n (%)			
Non-squamous	94 (87.0)	47 (82.5)	22 (95.7)
Squamous	8 (7.4)	8 (14.0)	0
Sites of metastases, n (%)			
Bone	44 (40.7)	27 (47.4)	12 (52.2)
Brain	23 (21.3)	12 (21.1)	23 (100)
Liver	15 (13.9)	7 (12.3)	5 (21.7)
ECOG PS, n (%)			
0	21 (19.4)	9 (15.8)	3 (13.0)
1	37 (34.3)	20 (35.1)	8 (34.8)
2	13 (12.0)	11 (19.3)	3 (13.0)

Conclusions: Real-world pt demographics and clinical characteristics of the Flatiron cohort confirm pts with *MET*ex14 skipping as a distinct population of aNSCLC; older, with/without smoking history, with squamous/non-squamous histology, exclusive of *KRAS*, *ROS-1* or *BRAF* mutations, and with high PD-L1 but low TMB. Analyses indicate a need for routine testing practices to identify pts prior to systemic therapy, since targeted MET TKI therapies are now available for use.

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1183P Patient-reported outcomes (PROs) of cemiplimab vs chemotherapy in advanced non-small cell lung cancer (aNSCLC): EMPOWER-Lung 1 histology subgroups

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Background: In Phase 3 EMPOWER-Lung 1 study of aNSCLC with PD-L1 ≥50% (NCT03088540), improvement in overall survival was observed with cemiplimab monotherapy vs platinum-doublet chemotherapy by histology subgroups (squamous: HR 0.48, 95% CI [0.30,0.77]; non-squamous: HR 0.64, 95% CI [0.43,0.96]). Post-hoc exploratory PROs analyses were conducted in both subgroups.

Methods: PROs were assessed at baseline and Day 1 of each treatment cycle for the 1st 6 cycles, and then on Day 1 of every 3rd cycle using the EORTC QLQ-C30 and LC-13 questionnaires. Higher scores indicate better functioning and global health status/quality of life (GHS/QoL), or worse symptom severity. Repeated-measures analyses were performed to compare overall change from baseline scores between treatment arms, while controlling for baseline characteristics. Time to definitive clinically meaningful deterioration (TTDD) was analysed using a stratified log-rank test and a Cox proportional hazards model.

Results: A statistically significant difference in overall change from baseline in GHS/QoL favouring cemiplimab vs chemotherapy was observed in the two histology subgroups (squamous: 4.32, 95% CI [0.55,8.08], P=0.0247; non-squamous: 5.12, 95% CI [1.39,8.86], P=0.0073). In both histology subgroups, a statistically significant overall change from baseline favouring cemiplimab was found in physical and social functioning; fatigue, nausea/vomiting and appetite loss (QLQ-C30); and peripheral neuropathy and alopecia (QLQ-LC13). In both subgroups, a statistically significant delay in TTDD favouring cemiplimab was observed in social functioning, nausea/vomiting and appetite loss (QLQ-C30), peripheral neuropathy and alopecia (QLQ-LC13). When comparing between arms, no analyses yielded statistically significant PRO favouring chemotherapy for any QLQ-C30 or QLQ-LC13 scale.

Conclusions: In aNSCLC with PD-L1 ≥50%, cemiplimab resulted in significant benefits over chemotherapy in overall change from baseline and delayed TTDD across multiple cancer-related and lung cancer-specific PROs across both histology subgroups. PRO results further support the favourable benefit-risk profile of cemiplimab across both subgroups.

Clinical trial identification: NCT03088540.

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1184P Improving the tolerability of osimertinib by identifying its toxic limit

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Background: Osimertinib is the cornerstone in the treatment of epidermal growth factor receptor-mutated non-small cell lung cancer (NSCLC). Nonetheless, ±25% of patients experience severe treatment-related toxicities. Currently, it is impossible to identify patients at risk of severe toxicity beforehand. We hence aimed to study the relationship between osimertinib exposure and severe toxicity, and to identify a safe toxic limit for a preventive dose reduction.

Methods: In this real-life prospective cohort study, patients with NSCLC treated with osimertinib were followed for severe toxicity (grade ≥3 toxicity, dose reduction or discontinuation, hospital admission, or treatment termination). Blood for pharmacokinetic analyses was withdrawn during every out-patient visit. To quantify individual exposure to osimertinib, a population-pharmacokinetic model was developed. Primary endpoint was the correlation between osimertinib clearance (exposure) and severe toxicity. Secondary endpoint was the exposure-efficacy relationship, defined as progression-free (PFS) and overall survival (OS).

Results: In total, 819 samples from 159 patients were included in the analysis. Multivariate competing risk analysis showed osimertinib clearance (*c.q.* exposure) to be significantly correlated with severe toxicity (hazard ratio (HR) 0.93, 95% CI 0.88 – 0.99). An ROC-curve showed the optimal toxic limit to be 259 ng/mL osimertinib. This target concentration divides the cohort in two groups: the risk of severe toxicity in the >259 ng/mL group is 34% versus 14% in the <259 ng/mL group. A 50% dose reduction in the high-exposure group - *i.e.* 25.8% of the total cohort - would reduce the risk of severe toxicity by 53%. Correlation of the first plasma trough concentrations in collected in the first two months of treatment revealed a similar difference in severe toxicity (31% versus 17%), when dividing the cohort in two by the toxic limit of 259 ng/mL osimertinib. Osimertinib exposure was not significantly associated with PFS nor OS.

Conclusions: Osimertinib exposure is highly correlated with occurrence of severe toxicity. To optimize tolerability, patients above the toxic limit concentration of 259