Table: LBA53			
N (%)	**Baseline (N = 46)**	**Progression (N = 46)**	**Acquired* (N = 46)**
MET amp	2 (4)	9 (20)	**8 (17)**
CDKN2A del	10 (22)	11 (24)	**7 (15)**
CDKN2B del	9 (20)	11 (24)	**7 (15)**
MTAP del	7 (15)	10 (22)	**7 (15)**
EGFR C797S	0 (0)	7 (15)	**7 (15)**
NKX2.1 amp	4 (9)	9 (20)	**5 (11)**
EGFR amp	13 (28)	11 (24)	**5 (11)**
CCNE1 amp	3 (7)	6 (13)	**3 (7)**
ARAF amp	0 (0)	2 (4)	**2 (4)**
ALK fusion	0 (0)	1 (2)	**1 (2)**

*Defined as mutations detectable at PD that were not detectable at baseline (for an individual patient) Genetic alterations shown were selected based on high-frequency of detection and/or prior knowledge of involvement in osimertinib resistance.

Conclusions: Efficacy and safety of 1L osimertinib were consistent with FLAURA. MET amp was the main acquired resistance mechanism to osimertinib, consistent with previous data. NKX2.1 amp was identified as a potential new resistance marker. Paired biopsies were obtained in only 39% of pts, highlighting the challenges of obtaining post-PD tissue biopsies and the need for more comprehensive non-invasive testing methods. See table.

Clinical trial identification: NCT03239340.

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LBA54 Three years survival outcome and continued cemiplimab (CEMI) beyond progression with the addition of chemotherapy (chemo) for patients (pts) with advanced non-small cell lung cancer (NSCLC): The EMPOWER-Lung 1 trial

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Background: In the EMPOWER-Lung 1 trial, CEMI monotherapy provided a significantly improved overall survival (OS) and an acceptable safety profile vs chemo in pts with newly diagnosed advanced NSCLC. We are reporting the 3-year survival data of the trial. Also, we are presenting the first efficacy data of pts who continued CEMI at progression (PD) with addition of histology-specific chemo.

Methods: Pts were randomized 1:1 to CEMI 350 mg IV every 3 weeks for 2 years or investigator's choice of chemo. Pts randomized to CEMI with PD, confirmed by a blinded independent review committee (BIRC), were allowed to continue CEMI with the addition of up to 4 cycles of chemo. To be included in the post PD analysis, pts had to receive at least one dose of chemo and have at least one scan following PD on CEMI. Response to continued CEMI + chemo was assessed by BIRC against a new baseline, defined as the last scan prior to the initial dose of chemo.

Results: At median follow-up of 37.1 months (m; range: 24.0 : 56.5), median OS (mOS) was 23.4 m (19.4, 27.4) for CEMI pts (N=357) vs 13.7 m (11.2, 16.2) for chemo pts (N=355), with hazard ratio (HR) of 0.634 (0.524, 0.768); median progression free survival (mPFS) was 6.3 m (4.6, 8.3) vs 5.3 m (4.3, 6.0), HR 0.560 (0.470, 0.666). 64 pts continued CEMI + chemo as 2L therapy. Continued CEMI + chemo as 2L therapy resulted in a 31.3% objective response rate and a mOS of 15.1 m (11.3, 18.7), and was generally tolerated, with 19 pts (29.7%) experiencing serious treatment-emergent adverse event (TEAE), and 3 pts each with TEAE resulting in discontinuation of study treatment or death.

Conclusions: At 3 year follow-up, HRs of CEMI vs. chemo improved (vs at 13 m follow-up) for both PFS and OS despite 76% crossover rate, an exceptional finding in the NSCLC field. Continued CEMI + chemo as 2L therapy provided meaningful and durable ORR and OS benefits and these results compare favorably to historical data of pts receiving chemo alone as 2L therapy (after immune-checkpoint inhibitor monotherapy). This data is the first report from a Phase 3 study providing therapeutic advantage to pts who progress after 1L PD1 monotherapy.

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