line crizotinib with or without subsequent ALK TKIs, 133 had crizotinib followed by alectinib and/or ceritinib, 62 had only crizotinib, 99 had only alectinib, and 80 had no observed ALK TKI. 167 (40.4%) brigatinib patients discontinued or switched to another ALK TKI. Median (95% confidence interval [CI]) brigatinib TTD was 10.3 (8.2-15.0) months. Among patients who discontinued brigatinib, 100 (59.9%) received subsequent ALK-TKIs. Lorlatinib was the most common next ALK TKI (57.0%), followed by brigatinib retreatment (16.0%), alectinib (13.0%), ceritinib (10.0%), and crizotinib (4.0%). The median (95% CI) TTD of the post-brigatinib ALK TKI was 7.2 (3.9-13.8) months. In patients who received crizotinib then brigatinib, the median (95% CI) TTD of the post-brigatinib ALK TKI was 6.7 (3.7-22.2) months. In patients who received lorlatinib after brigatinib was discontinued, median (95% CI) lorlartinib TTD was 8.0 (3.9-not reached) months.

Conclusions: These results indicate that brigatinib has real-world durable clinical effects for patients. Treatment with subsequent TKIs, can still bring benefit to patients after discontinuing brigatinib. More formalized prospective data are needed to establish sequencing recommendations.

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1206P UNcommon EGFR mutations: International Case series on efficacy of Osimertinib in Real-life practice in first-liNe setting (UNICORN)

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Background: About 10% of EGFR mutations (EGFRmut) are 'uncommon mutations' (ucEGFRmut), correlating with lower response to 1st & 2nd generation EGFR inhibitors (EGFRi) compared to common mutations. Osimertinib is a 3rd generation EGFRi, active against common EGFRmut. Efficacy data of osimertinib in ucEGFRmut are scarce. We aimed to collect real-world data of the usage of osimertinib as the 1st EGFRi for ucEGFRmut.

Methods: This is a multi-center, international, academic-initiated retrospective study of mNSCLC with ucEGFRmut treated with osimertinib prior to any other EGFRi. RECIST response was evaluated by investigators. PFS and OS were calculated by Kaplan-Meier method from initiation of Osimertinib, duration of response (DOR) was calculated for responders.

Results: 46 patients were identified in 18 centers from 8 countries (Austria, Belgium, France, Germany, Italy, Israel, Spain, Switzerland). Median age was 64 (range 37-91) years, 72% females, 89% Caucasian, never/former/current smokers were 50%/33%/15% respectively, ECOG PS was 0-1/2/3-4 in 78%/13%/6.5%. G719X was the most frequent mutation (16 pts, 34.8%), followed by de novo T790M (9 pts, 22%, 5 of them compound with common mutations) and L861Q (7 pts, 15.2%). Compound EGFR mutations were found in 16 pts (34.8%), TP53 mutations in 13 pts (28.3%). Most frequent metastatic sites were brain/bone/lung in 47%/47%/36% respectively. For 37 pts (80.4%), osimertinib was the 1st treatment given for advanced disease. Most frequent toxicities were gastrointestinal (24 pts, 52%) and skin (16 pts, 35%); 5 patients had grade 3-4 AEs. RECIST response (RR) was available for 44 pts, CR for 2 (4.5%), PR for 20 (45.5%), SD for 17 (38.6%), and PD for 5 (11.4%). Median DOR was 17.4 months (95% CI 9.1-NA). RR for G719X was 43.8%, 33.3% for T790M, and 71.4% for L861Q. Median PFS was 9.1 months (95% CI 8.1—19.2). Median OS was 18.4 months (95% CI 13.5-NR).

Conclusions: Osimertinib showed activity in ucEGFRmut with 85% disease control rate and encouraging PFS and DOR. This report comprises, to the best of our knowledge, the largest dataset of osimertinib as the first EGFRi for ucEGFRmut. UNICORN continues to recruit patients, to expand our knowledge on efficacy of osimertinib for these patients.

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1208P Final results of APOLLO study: Overall survival (OS) of aumolertinib in patients with pretreated EGFR T790M-positive locally advanced or metastatic non-small cell lung cancer (NSCLC)

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Background: Aumolertinib is a novel, irreversible third generation epidermal growth factor receptor tyrosine kinase inhibitor (EGFR TKI). APOLLO, a pivotal phase II single-arm study (NCT02981108), has demonstrated progression-free survival (PFS) benefit with a favorable safety profile in pretreated EGFR T790M positive NSCLC patients.

Methods: Adult pts received aumolertinib 110 mg once daily until disease progression. Treatment beyond progression was allowed if clinical benefit was expected. The primary endpoint was objective response rate by independent central review. Secondary endpoints included PFS, OS and safety. Explore endpoints included the drug resistance mechanism.

Table: 1208P

	mOS (95% CI), mo
EGFR mutation	
Ex19del	30.2 (23.8, NA)
L858R	28.5 (22.7, NA)
Brain metastases at baseline	
Yes	19.1 (16.0, 23.7)
No	36.4 (31.5, NA)
Sex	
Male	25.2 (20.4, 32.5)
Female	34.7 (25.9, NA)
Age	
<65yr	34.1 (23.9, NA)
≥65yr	28.4 (22.9, 34.7)
Smoking history	
Yes	23.9 (18.2, 34.1)
No	32.5 (25.6, NA)
WHO PS	
0	34.1 (27.9, NA)
1	27.0 (20.2, 36.4)

Results: At data cutoff (Jul 20, 2021), 126 (51.6%) pts had died among 244 pts. The median follow-up time was 34.5 mo (95%CI 34.0-35.4). The median OS was 30.2 mo (95% CI, 24.2-36.4), and the OS rate at 24 mo was 57.5% (95% CI, 50.8-63.6). OS analyses across pts subgroups was summarized in the table. A total of 82 (33.6%) pts continued aumolertinib treatment beyond disease progression. Forty-two pts had molecular profiling using tumor tissue or blood samples upon first progression on aumolertinib. Seven pts had acquired EGFR C797S in cis with T790M. EGFR L718Q mutation was found in 1 pt. Aberrations in bypass tracks including PIK3CA, JAK2, BRAF and KRAS mutation, HER2 amplification and FGFR3-TACC3 fusion were found in 8 pts. The safety profile of aumolertinib remained consistent with previous data.

Conclusions: Clinical benefit in OS was observed in pts with pretreated EGFR T790M-positive advanced NSCLC receiving aumolertinib. The common mechanisms of resistance to aumolertinib were EGFR C797S mutation and aberrations in bypass tracks.

Clinical trial identification: NCT02981108.

Legal entity responsible for the study: Jiangsu Hansoh Pharmaceutical Group Co. Ltd.

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1209P RELAY, ramucirumab plus erlotinib (RAM+ERL) in untreated metastatic EGFR-mutant NSCLC (EGFR+NSCLC): Association between TP53 status and clinical outcome

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Background: Tumour Protein 53 (TP53) plays a role in angiogenesis by regulating vascular endothelial growth factor A (VEGFA) and VEGF receptor 2 (VEGFR2). In patients (pts) with EGFR+ NSCLC, TP53 mutations, notably on exon 8, are associated with poorer outcomes of EGFR tyrosine kinase inhibitor treatment and may be involved in primary resistance. We evaluated the relationship between TP53 status and outcomes in RELAY.

Methods: Pts with untreated metastatic EGFR+ NSCLC received oral ERL (150 mg/day) with either intravenous RAM (10 mg/kg) or placebo (P+ERL) every 2 weeks. This exploratory analysis consisted of 386 pts with any mutation detected at baseline by Guardant 360 next-generation sequencing. The primary endpoint was PFS. Secondary and exploratory endpoints included overall response rate (ORR), disease control rate (DCR), DoR, overall survival (OS), safety, and biomarker analysis. TP53 status was assessed in relation to outcomes and treatment-emergent gene alterations at progression.

Results: TP53 mutations were detected in 46% of White and 42% of Asian pts and was similar for EGFR exon 19 and exon 21 mutations (~43%). Other pt and disease characteristics and concurrent gene alterations were comparable between TP53 mutant (mt) and wildtype (wt) tumors. Irrespective of treatment, pts with TP53 mutations, notably on exon 8, had worse outcomes than pts with TP53wt. In all pts, RAM+ERL improved PFS and DoR, while ORR (78% to 82%) and DCR (95% to 97%) were similar. OS data were immature. Safety was comparable between TP53mt and wt subgroups. Treatment-emergent T790M mutation rates at progression were higher in TP53mt (33% to 39%) than TP53wt tumors (19% to 21%) regardless of treatment.

Conclusions: The addition of RAM to ERL showed consistent benefit in both TP53wt and TP53mt EGFR+ NSCLC, suggesting that the RELAY regimen is a suitable first-line treatment option for pts with EGFR+ NSCLC irrespective of TP53 status.

Clinical trial identification: NCT02411448.

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