12810 Atezolizumab (atezo) vs platinum-based chemo in blood-based tumour mutational burden-positive (bTMB+) patients (pts) with first-line (1L) advanced/metastatic (m)NSCLC: Results of the Blood First Assay Screening Trial (BFAST) phase III cohort C

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Background: Adding bevacizumab to erlotinib prolonged PFS in NEJ026 and CTONG 1500. NEJ026 and CTONG 1500 are available in non-squamous patients (pts). BEV alone or Italian no-profit, randomized, open-label, multicenter phase III trial of bevacizumab (BEV) plus erlotinib (E) vs E alone as first-line treatment for EGFR-mutated advanced NSCLC.

Methods: Eligible pts were randomized 1:1 to E (150mg daily) alone or combined with BEV (15mg/kg iv q2wk) until disease progression or unacceptable toxicity. Centers ECOG PS and type of mutation (exon 19 deletion vs ex21 L858R vs others) were stratification variables. Co-primary endpoints were investigator-assessed PFS (IA-PFS) and blinded-independent centrally-reviewed PFS (BIRC-PFS). Secondary endpoints were OS, QoL, IA- and BIRC objective response rate (ORR) and safety; biomarker analysis are planned. 126 pts were required to detect a PFS prolongation with BEV from 10 to 16.7 mos (HR 0.60), with 2-sided power.

Results: From Apr 11, 2016 to Feb 27, 2019, 160 pts were randomized to BEV+E (80) or E alone (80). Pts were mainly female (63.8%), never smokers (51.9%), ECOG PS 0-1 (98.1%), mean age 66 (IQR 59-73); 55% of pts had ex19del and 41% L858R mutation. At a median follow-up of 31 mos, 130/160 (81.3%) pts had a PFS event (progression death) and 84/160 (52.5%) died. BEV significantly prolonged IA-PFS over E alone with a median of 15.4 vs 9.7 mos (HR 0.60; 95%CI 0.42-0.85, log-rank P=0.0039). Median OS was 28.4 vs 23.0 mos in BEV+E vs E arms, respectively (HR 0.70; 95%CI 0.46-1.10, log-rank P=0.012). One toxic death was reported, due to intracranial hemorrhage with BEV+E. Hypertension (any grade: 49% vs 18%; grade 3/4: 22% vs 7%) and proteinuria (any grade: 23% vs 6%) were more frequent with the experimental combination treatment.

Conclusions: The addition of BEV to E significantly prolonged IA-PFS compared with E alone as first-line treatment in Italian EGFR-mutated NSCLC patients, with no unexpected safety issues. Blinded radiologic revision of PFS and ORR is ongoing and will be presented at the meeting.

Clinical trial identification: NCT02633189; EudraCT 2015-002235-17.

Legal entity responsible for the study: Clinical Trial Unit, Istituto Nazionale Tumori, IRCCS, Fondazione G. Pascale.

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Disclosure: M.C. Piccirillo, F. De Marinis, L. Crinò, F. Morgillo, F. Ciardiello, N. Normanno, C. Gallo, C. Gridelli, A. Morabito

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Results of the Blood First Assay Screening Trial (BFAST) phase III cohort C


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References: BFAST (NCT03178552). A global, open-label, multi-center trial, evaluated safety and efficacy of targeted therapies, or immunotherapy in biomarker-selected pts with unresectable mNSCLC. Here we present results from Cohort C of 1L atezolizumab vs platinum-based chemo in pts with TMB+ mNSCLC.

Methods: We planned to randomise n=440 pts with 1L mNSCLC with measurable disease per RECIST 1.1 and TMB >10 (9.1 mut/mb; MFI TMB assay) 1:1 to aLBEV and chemotherapy (chemo) for 2 cycles every 3 weeks or 2 cycles of aLBEV atezolizumab vs chemo (n=220 per arm). The primary endpoint was OS from TMB+ pts to 16 pts was not met. OS was 23.4 mos vs 16 mos in BEV+E vs E arms, respectively (HR 0.60; 95%CI 0.42-0.85, log-rank P=0.0039). Median OS was 28.4 vs 23.0 mos in BEV+E vs E arms, respectively (HR 0.70; 95%CI 0.46-1.10, log-rank P=0.012). One toxic death was reported, due to intracranial hemorrhage with BEV+E. Hypertension (any grade: 49% vs 18%; grade 3/4: 22% vs 7%) and proteinuria (any grade: 23% vs 6%) were more frequent with the experimental combination treatment.

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Legal entity responsible for the study: F. Hoffmann-La Roche, Ltd.

Background: Amivantamab (am), an epidermal growth factor receptor (EGFR)-MET bисpecific antibody, has demonstrated efficacy in EGFR mutant non-small cell lung cancer (NSCLC) that progressed on osimertinib (osi), both as monotherapy and in combination with lazertinib (laz), a 3rd-generation tyrosine kinase inhibitor. Clinical outcomes of patients (pts) treated with ami monotherapy (mono) and ami in combination with laz (combo) are presented here.

Methods: CHRYSLIS is an ongoing study of ami in pts with advanced EGFR mutant NSCLC (NCT02609776). Pts who progressed on osi were pooled to form the mono group, a majority of whom were preselected for C797S/other resistance mutations or acquired resistance. For the combo group, all pts were preselected for C797S/other resistance mutations or acquired resistance. Response was assessed by the investigator per RECIST v1.1.

Results: As of 19 Apr 2021, 121 pts in the mono group (85% with EGFR/MET-based resistance) and 45 in the combo group (38% with EGFR/MET-based resistance) were efficacy-evaluable, with median follow-up of 6.9 and 11.1 months, respectively. Antitumor activity was observed in both groups. In the mono group, a majority of whom were preselected for C797S/other resistance mutations or acquired resistance, antitumor activity of ami was observed in 33 pts (27% of the total mono population), with 38% of pts achieving partial or complete response (PRs were observed, all of which continued, for an overall response rate (ORR) of 19% (95% CI, 12–57) 64% (49–85). In the combo group, a majority of whom were preselected for C797S/other resistance mutations or acquired resistance, antitumor activity (PRs were observed, all of which continued, for an overall response rate (ORR) of 19% (95% CI, 12–27)–57) 64% (49–85). In the combo group, a majority of whom were preselected for C797S/other resistance mutations or acquired resistance, antitumor activity of ami was observed in 33 pts (27% of the total combo population), with 38% of pts achieving partial or complete response (PRs were observed, all of which continued, for an overall response rate (ORR) of 19% (95% CI, 12–27). In the combo group, 1 complete response and 15 PRs were observed, all of which continued, for an ORR of 36% (95% CI, 22–51). Median duration of response was 5.9 months with mono, 9.6 months with combo (Table). The safety profile for both mono and combo was consistent with previously-reported safety. No new safety signals were identified.

Table: 1192MO Efficacy of amivantamab monotherapy and in combination with lazertinib among efficacy-evaluable* patients

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<th>Endpoint</th>
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<th>Chemo*</th>
<th>HR (95% CI)</th>
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<td>MONO (n=121)</td>
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| Involved patients | 1192MO Amivantamab monotherapy and in combination with lazertinib in post-osimertinib EGFR-mutant NSCLC: Analysis from the CHRYSLIS study |

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Methods: CHRYSLIS is an ongoing study of ami in pts with advanced EGFR mutant NSCLC (NCT02609776). Pts who progressed on osi were pooled to form the mono group, a majority of whom were preselected for C797S/other resistance mutations or MET amplification. The combo group comprised unselected pts who had progressed on osi but were chemotherapy-naive. Response was assessed by the investigator per RECIST v1.1.

Results: As of 19 Apr 2021, 121 pts in the mono group (85% with EGFR/MET-based resistance) and 45 in the combo group (38% with EGFR/MET-based resistance) were efficacy-evaluable, with median follow-up of 6.9 and 11.1 months, respectively. Antitumor activity was observed in both groups. In the mono group, a majority of whom were preselected for C797S/other resistance mutations or acquired resistance, antitumor activity of ami was observed in 33 pts (27% of the total mono population), with 38% of pts achieving partial or complete response (PRs were observed, all of which continued, for an overall response rate (ORR) of 19% (95% CI, 12–27)–57) 64% (49–85). In the combo group, a majority of whom were preselected for C797S/other resistance mutations or acquired resistance, antitumor activity of ami was observed in 33 pts (27% of the total combo population), with 38% of pts achieving partial or complete response (PRs were observed, all of which continued, for an overall response rate (ORR) of 19% (95% CI, 12–27). In the combo group, 1 complete response and 15 PRs were observed, all of which continued, for an ORR of 36% (95% CI, 22–51). Median duration of response was 5.9 months with mono, 9.6 months with combo (Table). The safety profile for both mono and combo was consistent with previously-reported safety. No new safety signals were identified.