The preliminary safety result of a phase II study of osimertinib in combination with platinum + pemetrexed in patients with previously untreated EGFR-mutated advanced NSCLC (NEJ0332/LOGIK1801: OPAL)


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Background: Based on the result of the FLAURA trial, osimertinib (OSI) is a standard of care in patients with (pts) with previously untreated EGFR-mutated advanced non-small cell lung cancer (NSCLC). One of the promising strategies to further improve pts outcome is a combination therapy with OSI and platinum-doublet chemotherapy. Methods: An ongoing multicenter phase II study is assessing the safety and efficacy of OSI + cisplatin (CDP)/Pemetrexed (P) in previously untreated pts with EGFR-mutated NSCLC. A total of 67 pts were enrolled in arm A (CDP) or arm B (CDP/P) at the discretion of each investigator. In addition to OSI 80 mg administered orally daily, CDP (75 mg/m²) and P (500 mg/m²) were administered intravenously every 3 weeks for up to 4 cycles. Pts without disease progression (PD) after 4 cycles of induction therapy continued OSI + P until PD or unacceptable toxicity. The co-primary endpoints are safety and objective response rate (ORR). Secondary endpoints include complete response rate, disease control rate, and progression-free survival.

Results: As of 25 Feb 2020, 67 pts (34 in arm A; 33 in arm B) were enrolled: [median age 67 [range, 26-75] years; 43 females [64.2%]; 46 ECOG PS 0 [68.7%]; 66 adenocarcinoma [98.5%]; 31 EGFR exon19del/16 (46.3%); 35 ex21 L858R [52.2%], 1 both [1.5%]. At the data cut-off (31 Mar 2020), 11 pts [16.4%] discontinued treatment: 2 (3.0%) due to PD, 6 (9.0%) due to AEs [3 (4.5%) pts’ withdrawal. At least one dose reduction was required in 41.2% [arm A] and in 57.6% [arm B]. Most common (≥5%) Grade 3 > AEs were neutropenia (37.3%), lymphocyte count decreased (29.9%), white blood cell decreased (25.4%), platelet count decreased (19.4%), anemia (17.9%), anorexia (7.5%) and alanine aminotransferase increased (6.0%). One patient in arm B experienced grade 4 QT prolongation and terminated protocol treatment.

Conclusions: This is the first study to explore the efficacy and safety of OSI in combination with platinum-based chemotherapy as the first line treatment. This combination treatment has been well tolerated and follow-up is ongoing.

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1383MO Tepotinib in Asian patients (pts) with advanced NSCLC with MET exon 14 (METex14) skipping


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Background: Tepotinib, an oral, once daily (QD), highly selective, potent MET inhibitor that has shown durable activity in pts with METex14 skipping advanced NSCLC, is approved in Japan. The phase II VISION study showed an overall objective response rate (ORR) of 44.5%–47.4% by independent review (IR) and 54.7%–53.8% by investigator-assessed (inv) response (IRR). The current study was conducted to further evaluate the efficacy and safety of tepotinib in an Asian population with METex14 skipping NSCLC.

Methods: Pts with advanced EGFR/ALK wild-type and METex14 skipping NSCLC, detected by liquid or tissue biopsy, received oral tepotinib 500 mg QD until disease progression, intolerable toxicity, or withdrawal of consent. The primary endpoint was objective response rate (ORR) [confirmed by scans ≥4 weeks apart] by IRR. Secondary endpoints were ORR by inv, duration of response (DOR), progression-free survival (PFS), and safety. Pts evaluable for ORR had ≥2 post-baseline assessments or discontinuation for any reason.

Results: As of data cut-off (Jan 1, 2020), 38 pts evaluable for efficacy were Asian with a median age of 70 years (52-85), 31 female (82%), 31 non-smokers, and 32% treatment-naive (31%) vs 75% (50%) in Korea (26%) and Japan (13%), Spain (3%), and the US (8%). Efficacy of tepotinib in Asian pts was similar to the overall population; ORR (95% CI) was 47.4% (31.0, 64.2) by IR (median DOR [mDOR] was not reached) and 60.5% (43.4, 76.0) by inv (mDOR was 10.9 months [9.7, ne]). Disease control rate (DCR) was 91.4% [90.2, 92.5] [confirmed complete or partial response, or stable disease lasting ≥12 weeks] was 68.4% (51.3, 82.5) by IR and 81.6% (65.7, 92.3) by inv. Although still immature, median PFS (95% CI) was 11.0 months (4.9, ne). Overall, 50 Asian pts received ≥2 dose of tepotinib. The most common adverse events (any cause) were peripheral edema, increased blood creatinine, and diarrhea. Grade ≥3 treatment-related adverse events (TRAEs) were observed in 26% of pts. TRAEs led to dose reductions in 28%, temporary discontinuation in 36%, and permanent discontinuation in 10% of pts.

Conclusions: Tepotinib showed robust, durable clinical activity in Asian pts with METex14 skipping NSCLC. Adverse events were mostly mild and manageable, with few discontinuations. The VISION study will enroll pts at 55 sites in Asia.
Results: BLU-945 activity on EGFR mutants and EGFR wild-type (WT) was tested in biochemical assays and cellular phosphorylation specific EGFR AlphaLISA assays. The in vitro anti-tumor activity of BLU-945 was evaluated in an NCI-H1975 cell line-derived tumor xenograft (CDX) model, as well as in osimertinib-resistant CDX- and patient-derived xenograft (PDX) models of NSCLC.

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Results: BLU-945 inhibits EGFRex19del/C797S, EGFRex19del/C797T, EGFRex19del/C797S, EGFRex19del/C797T, and EGFR L858R/T790M/C797S mutants with sub-nanomolar IC50 values in an enzyme assay. BLU-945 inhibited EGFRex19del/C797S, and Ba/F3 EGFRex19del/C797S cell lines and a large window relative to EGFRex19del/C797S inhibition. Oral administration of BLU-945 to tumor-bearing mice demonstrated potent antitumor activity at well-tolerated doses in the subcutaneous NCI-H1975 CDX model, and osimertinib-resistant CDX and PDX models, as well as in the intracranial luc-H1975 model of NSCLC.

Conclusions: BLU-945 is a potent, selective, and orally available EGFR inhibitor that shows robust anti-tumor activity in osimertinib-resistant EGFR xenograft models. Its pharmaceutical and pharmacological properties make BLU-945 a candidate with the potential to demonstrate activity in osimertinib-resistant EGFR-mutant NSCLC.

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Patient reported outcomes (PROs) analysis for patients with ROS1 fusion-positive (ROS1+) non-small cell lung cancer (NSCLC) receiving entrectinib in the global phase II STARTTRK-2 study


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Background: In the ongoing STARTTRK-2 study (NCT02568267), entrectinib demonstrated a favourable efficacy and safety profile in patients with locally advanced/metastatic ROS1+ NSCLC. We present the results of a pre-specified PRO analysis in an updated dataset with longer follow-up.

Methods: The European Organization for Research and Treatment of Cancer quality of life questionnaire (EORTC QLQ-C30), and lung cancer module (EORTC-LC13) were completed prior to entrectinib dosing on Day 1 of every treatment cycle, and at end of treatment. The safety analysis set (SAS; patients received ≥1 entrectinib dose) was used to assess treatment-related symptoms. The efficacy analysis set (EAS; SAS patients with measurable baseline disease) was used to assess tumor-related symptoms, functioning, and global health status (GHS).