

1050 Osimertinib for patients (pts) with leptomeningeal metastases (LM) associated with EGFRm advanced NSCLC: The AURA LM study

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Background: Osimertinib, a 3rd-generation EGFR-TKI selective for both sensitising and EGFR T790M resistance mutations, has shown efficacy in pts with CNS metastases; encouraging activity has been reported in pts with LM at 160 mg once daily (QD)

(BLOOM; NCT02228369). We report LM activity with osimertinib 80 mg QD in pts with LM from studies across the AURA program (NCT01802632; NCT02094261; NCT02442349; NCT02151981).

Methods: Pts with EGFR T790M positive advanced NSCLC and progression on EGFR-TKI received osimertinib 80 mg QD. Patients with LM and CNS metastases were eligible if asymptomatic and stable. Baseline brain scans were mandated in pts with known or treated CNS metastases at study entry; pts with evidence of LM by neuroradiological blinded independent review (BICR) were included for retrospective analysis. Follow-up brain scans were assessed for radiologic LM response by LM BICR per Response Assessment in Neuro-Oncology LM criteria. LM objective response rate (ORR), LM duration of response (DoR), LM progression-free survival (PFS) and overall survival (OS) were assessed retrospectively. Results are based on individual data cutoffs for each study. A longitudinal analysis overlaid changes from baseline non-CNS tumour size with LM responses at each visit for AURA LM and BLOOM LM pts.

Results: 22 LM pts from the AURA studies were included for analysis. Median treatment exposure was 7.3 mo (range 2.3–16.5). Baseline characteristics were broadly consistent with the overall AURA study population: median age 58 yrs; female 59%; Asian 82%; WHO PS 1 82%. LM ORR was 55% (95% CI 32, 76); complete or partial LM response reported in 6 pts (27%) each. Median LM DoR was not reached (95% CI 2.8, not calculable [NC]). Median LM PFS was 11.1 mo (95% CI 4.6, NC). OS was 18.8 mo (95% CI 6.3, NC). Graphical assessment of longitudinal analysis showed similar non-CNS and LM responses in AURA LM and BLOOM LM pts.

Conclusions: Consistent with early efficacy outputs from BLOOM (160mg QD), osimertinib 80 mg QD showed a clinically meaningful benefit in pts with T790M-positive NSCLC and radiographically-detected LM. Additional studies are needed to further evaluate the CNS efficacy of osimertinib 80 mg QD in pts with EGFRm NSCLC and LM.

Clinical trial identification: AURA extension (NCT01802632), AURA2 (NCT02094261), AURA3 (NCT02151981), AURA17 (NCT02442349).

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