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THORACIC TUMOURS, LOCALLY ADVANCED

466O ASTRIS real world study of osimertinib in patients (pts) with EGFR T790M NSCLC: Efficacy analysis by tissue or plasma T790M test

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Background: Osimertinib, a third-generation, CNS-active EGFR-TKI, potently and selectively inhibits both EGFR-TKI sensitizing and EGFR T790M resistance mutations. We report results from a second planned interim analysis of the ongoing ASTRIS study (NCT02474355), including analysis of outcomes by specimen source (tissue, plasma or others) used for determining T790M status.

Methods: Pts with T790M-positive advanced NSCLC, assessed by any approved molecular testing method from any specimen, treated with prior EGFR-TKI therapy, with WHO performance status (PS) 0–2 were included. Asymptomatic, stable CNS metastases were permitted. Eligible pts received osimertinib 80 mg once daily. Efficacy outcomes include investigator assessed response, progression-free survival and overall survival.

Results: From 18 Sep 2015 to 20 Oct 2017 data cut-off (DCO), 3014 pts across 16 countries had received ≥1 dose of osimertinib, 2870 had ≥1 investigator-assessed response documented at DCO: median follow-up 7.9 months (range <1–24), median age 62 years (27–92), 13% age ≥75, 64% female, 69% Asian. Samples were assessed for T790M status in tissue (n = 1611, 53%), plasma (n = 1242, 41%) and other specimens (fine needle aspirate, fluid cytology, bone marrow; n = 160, 5%). T790M was tested by cobas® EGFR Mutation Test v2 (n = 1593, 53%), PNA-clamp (n = 371, 12%), Qiagen therascreen (n = 322, 11%) ddPCR (n = 134, 4%). Overall clinical response was reported in 1611/2870 pts (56.1%; 95% CI 54.3, 58.0); 978/1565 pts by tissue (62.5%; 95% CI 60.0, 64.9), 539/1147 pts by plasma (47.0%; 95% CI 44.1, 49.9) and 94/158 pts by other specimens (59.5%; 95% CI 51.4, 67.2). Clinical results in the table.

Table: 466O Efficacy outcomes in FAS and by tissue and plasma T790M test

	Overall (FAS; n = 3014)	Tissue (n = 1611)	Plasma (n = 1242)
Median PFS, months[i] (95% CI)	11.0 (10.6, 11.1)	12. (11.0, 12.5)	9.0 (8.4, 10.3)
Median TTD, months[i] (95% CI)	12.6 (12.2, 13.7)	15.1 (13.8, 15.7)	10.4 (9.7, 11.5)
Deaths, n (%) Estimated 1-year OS rate[ii], % (95% CI)	593 (19.7) 75.8 (73.7, 77.8)	252 (15.6) 80.9 (78.2, 83.3)	304 (24.5) 67.1 (63.2, 70.7)

FAS, full analysis set; NC, not calculable; OS, overall survival; PFS, progression-free survival; TTD, time to treatment discontinuation. [i]95% CI for OS/PFS/TTD calculated using the log-log transformation. [ii]1-yr OS rate calculated using the KM estimate.

Conclusions: ASTRIS, the largest real-world study of osimertinib in T790M-positive NSCLC, showed clinical activity consistent with the osimertinib clinical trial program. Clinical outcomes were better in pts T790M positive by tissue compared with pts T790M positive by plasma.

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