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Updated results from a phase I/II study of mobocertinib (TAK-788) in NSCLC with EGFR exon 20 insertions (exon20ins)

G.J. Riely[1], J.W. Neal[2], D.R. Camidge[3], A. Spira[4], Z. Piotrowska[5], L. Horn[6], D.B. Costa[7], A. Tsao[8], J. Patel[9], S. Gadgeel[10], L. Bazhenova[11], V.W. Zhu[12], H. West[13], T. Mekhail[14], R. Gentzler[15], D. Nguyen[16], V. Bunn[17], S. Jin[18], Z. Feng[18], P.A. Jänne[19]

[1] Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA, [2] Stanford Cancer Institute, Stanford University, Stanford, CA, USA, [3] Medical Oncology, University of Colorado Cancer Center, Aurora, CO, USA, [4] Research Institute, Virginia Cancer Specialists and US Oncology Research, The Woodlands, TX, USA, [5] Hematology/Oncology, Massachusetts General Hospital, Boston, MA, USA, [6] Hematology Oncology, Vanderbilt - Ingram Cancer Center, Nashville, TN, USA, [7] Hematology-Oncology, Beth Israel Deaconess Medical Center, Boston, MA, USA, [8] Department of Thoracic/Head & Neck Medical Oncology, University of Texas M.D. Anderson Cancer Center, Houston, TX, USA, [9] Lurie Cancer Center, Northwestern University Feinberg School of Medicine, Chicago, IL, USA, [10] Department of Internal Medicine, Division of Hematology/Oncology, University of Michigan, Ann Arbor, MI, USA, [11] Medicine, Moores Cancer Center - UC San Diego Health, La Jolla, CA, USA, [12] School of Medicine, University of California - Irvine, Orange, CA, USA, [13] Thoracic Oncology, City of Hope Comprehensive Cancer Center, Los Angeles, CA, USA, [14] Oncology and Hematology, AdventHealth Orlando, Orlando, FL, USA, [15] Cancer Center, University of Virginia Cancer Center, Charlottesville, VA, USA, [16] Medical Oncology, Pacific Shores Medical Group, Long Beach, CA, USA, [17] Biostatistics, Millennium Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited, Cambridge, MA, USA, [18] Clinical Science, Millennium Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited, Cambridge, MA, USA[19] Lowe Center for Thoracic Oncology, Dana Farber Cancer Institute, Boston, MA, USA

Background

EGFR exon20ins occur in ⊠1%–2% of patients (pts) with NSCLC. Currently approved EGFR TKIs have not shown efficacy in most of these mutations. Mobocertinib is an investigational oral EGFR/HER2 inhibitor under evaluation in pts with metastatic NSCLC with *EGFR* exon20ins. We previously reported dose escalation and establishment of 160 mg qd as RP2D. We report updated antitumor activity and safety results from an open-label, multicenter study of mobocertinib (NCT02716116).

Methods

Antitumor activity by investigator-assessed radiographic response (RECIST 1.1) and toxicity (NCI CTCAE) were determined for pts with advanced, previously treated NSCLC with *EGFR* exon20ins who received mobocertinib 160 mg qd. Safety data were collected for all pts treated at 160 mg qd.

Results

As of 27 Jan 2020, 28 pts with previously treated NSCLC and *EGFR* exon20ins were treated in dose escalation/expansion at 160 mg qd. In these pts: median age, 62 y (range 28– 84); women, 75%; ECOG 0/1, 21%/79%; ≥2 prior anticancer therapies, 86%; brain metastases, 43%. Median time on treatment was 12 mo (13 treatment cycles) and 7 pts remain on treatment. Confirmed ORR (PR) was 43% (12/28; 95% CI 24–63). The disease control rate was 86% (24/28; 95% CI 67–96). Two pts had best response of PD; 2 pts were not evaluable. Median duration of response in the 12 pts with confirmed PR was 14 mo (95% CI 5–not reached). The median PFS was 7.3 mo (95% CI 4.4–15.6); 12-mo PFS was 33% (15–52). Response to mobocertinib was observed in diverse *EGFR* exon20ins variants. Among these 28 pts, most common any grade treatment-related AEs (TRAEs; >25%) as assessed by investigator: diarrhea (82%), rash (46%), nausea (39%), decreased appetite (39%), vomiting (36%), paronychia (29%); grade ≥3 TRAEs (≥5%): diarrhea (32%), nausea (11%), increased lipase (7%), increased amylase (7%), stomatitis (7%), vomiting (7%). In all 136 pts treated with ≥1 dose of 160 mg, most common TRAEs: diarrhea (83%), nausea (43%), rash (33%), vomiting (27%); grade ≥3 TRAEs: diarrhea (21%) and increased lipase (5%).

Conclusions

Mobocertinib demonstrated antitumor activity in pts with advanced NSCLC with *EGFR* exon20ins. The safety profile for mobocertinib was consistent with other EGFR TKIs.

Clinical trial identification

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