1231P

Characterization and Management of Mobocertinib (TAK-788)–Induced Skin Toxicity in Patients With *EGFR* Exon 20 Insertion+ (ex20ins+) Non–Small Cell Lung Cancer (NSCLC) Who Previously Received Platinum Chemotherapy

James Chih-Hsin Yang,[1] Suresh S Ramalingam,[2] Tae Min Kim,[3] Sang-We Kim,[4] Gregory J Riely,[5] Tarek Mekhail,[6] Danny Nguyen,[7] Maria R Garcia Campelo,[8] Enriqueta Felip,[9] Lyudmila Bazhenova,[10] Shu Jin,[11] Celina Griffin,[11] Veronica Bunn,[11] Jianchang Lin,[11] Eric N Churchill,[11] Minal Mehta,[11] Pasi A Jänne,[12] Caicun Zhou[13]

[1]National Taiwan University Cancer Center, Taipei, Taiwan; [2]Emory University, Atlanta, GA, USA; [3]Seoul National University Hospital, Seoul, South Korea; [4]Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea; [5]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [6]AdventHealth Orlando, Orlando, FL, USA; [7]Pacific Shores Medical Group, Long Beach, CA, USA*; [8]University Hospital A Coruña, CHUAC, A Coruña, Spain; [9]Vall d'Hebron University Hospital, Barcelona, Spain; [10]University of California San Diego Moores Cancer Center, La Jolla, CA, USA; [11]Millennium Pharmaceuticals, Inc., Cambridge, MA, USA, a wholly owned subsidiary of Takeda Pharmaceutical Company Limited; [12]Dana-Farber Cancer Institute, Boston, MA, USA; [13]Shanghai Pulmonary Hospital, Shanghai, China

Current affiliation: City of Hope National Medical Center, Los Angeles, CA, USA

Introduction

- Up to 12% of epidermal growth factor receptor gene (*EGFR*)-mutated non–small cell lung cancer (NSCLC) tumors have *EGFR* exon 20 insertion (*EGFR* ex20ins) mutations[1,2]
- Most patients with *EGFR* ex20ins+ metastatic NSCLC receive first-line platinum-based chemotherapy, but typically develop progressive disease (PD) within 6 months[3-5]
- Patients with *EGFR* ex20ins+ NSCLC have a poor prognosis, with median overall survival ranging from 7.1 months to 13.6 months in the second-line treatment setting according to real-world data[6]
- Mobocertinib is an oral EGFR tyrosine kinase inhibitor (TKI) designed to specifically target *EGFR* ex20ins mutations[7,8]
- Mobocertinib demonstrated meaningful clinical benefit in 114 platinum-pretreated patients (PPP) with *EGFR* ex20ins+ NSCLC in a phase 1/2 study (NCT02716116), with confirmed objective responses by independent assessment reported in 28% of patients and median duration of response of 17.5 months[9]

Objective

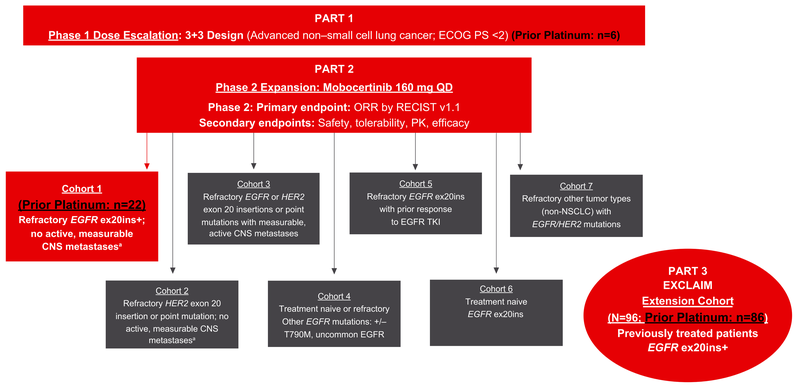
- Because normal functioning in epidermal tissue depends on EGFR signaling, skin-related toxicities are commonly reported with irreversible EGFR TKIs, including skin rash, dry skin, and paronychia[10]
- In light of this, the objective of this analysis was to characterize skin-related toxicities associated with mobocertinib treatment in the PPP cohort of the phase 1/2 study

Methods

Data Sources

- The PPP cohort included patients from Parts 1, 2, and 3 (EXCLAIM) from the phase 1/2 study (N=114) who received mobocertinib 160 mg orally once daily (**Figure 1**)
- Here, we report the incidence of any-Grade and Grade 3/4 skin-related treatment-emergent adverse events (TEAEs), time to onset and resolution, time to resolution by grade, and the pharmaceutical agents used to manage these events (data cutoff date: 1 November 2020)

Figure 1. Study Design



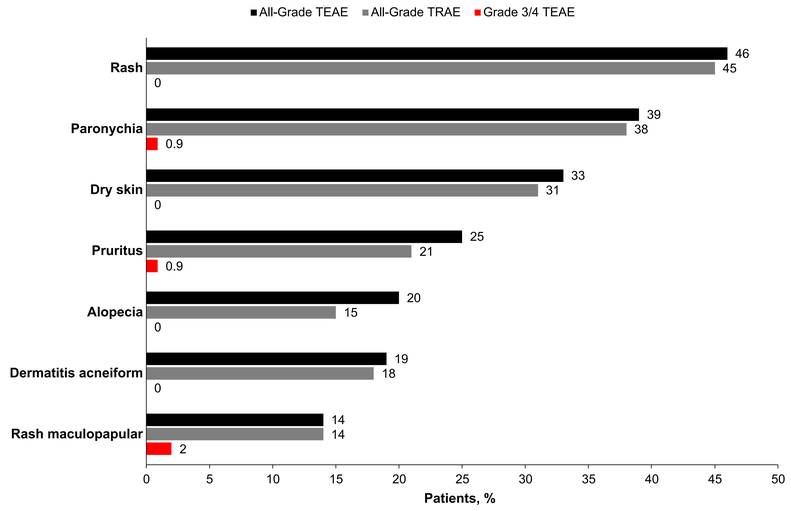
Data cutoff date: 1 November 2020
Locations: United States only for phases 1 and 2; United States, Europe, and Asia for phase 2 extension cohort
[a]Active or measurable (but not both) CNS metastases permitted
Active CNS metastases: Untreated or treated and progressing; measurable CNS metastases: ≥10 mm in longest diameter by contrast-enhanced MRI

Results

Skin-Related Toxicity in the PPP Cohort

- Among 114 patients in the PPP cohort, skin-related toxicity events were observed in 105 patients (92%)
  - Most events were low grade in severity; Grade 3 skin toxicity events occurred in 5 patients (4%)
  - There were no Grade 4 or 5 skin-related TEAEs
  - There were no skin-related serious adverse events (SAEs)
  - One patient discontinued mobocertinib treatment due to skin-related TEAEs of dermatitis and alopecia (Grade 1)
- The most common skin-related TEAEs were rash (n=52, 46%), paronychia (n=44, 39%), and dry skin (n=38, 33%) (**Figure 2**)

Figure 2. Skin-Related AEs Occurring in >10% of Patients (N=114)



Data cutoff date: 1 November 2020
TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event

- Median time to onset and resolution of any-Grade and Grade 3 skin-related TEAEs are shown in **Table 1**

Table 1. Median Time to Onset and Resolution[a] of Skin-Related TEAEs

	All-Grade Skin-Related TEAEs	Grade 3 Skin-Related TEAEs
Median time to onset, d	9.0	–
Median time to resolution[a], d	78	38

Data cutoff date: 1 November 2020
[a] Summary of time from first onset to resolution for individual events. Resolution is defined as event status of resolved/recovered or resolved/recovered with sequelae or return to baseline or lower severity as of the latest assessment for pre-existing events. Number of events: 195 all-Grade events; 3 Grade 3 events

Management of Skin-Related Toxicities

- Topical corticosteroids, most commonly hydrocortisone, and topical antibiotics, most commonly clindamycin, were the most frequent pharmaceutical management of skin-related toxicities (**Table 2**)

Table 2. Most Common Pharmaceutical Management of Skin-Related Toxicities (N=114)

Medication	n (%)
Topical antibiotics	32 (28)
Mupirocin	20 (18)
Clindamycin	25 (22)
Topical corticosteroids	49 (43)
Hydrocortisone	14 (12)

Data cutoff date: 1 November 2020

Conclusions

- Types of skin toxicities observed with mobocertinib were consistent with those previously reported with the class of EGFR TKIs,[10] and characterized by a low frequency of high-grade toxicity
- Most skin-related toxicity events were low grade in severity, and no serious cutaneous AEs have been observed
- Skin-related toxicities started within the first 2 weeks of treatment and resolved in approximately 11 weeks
- Most were managed with skin care and proactive use of topical corticosteroids and/or antibiotics

References

1. Riess JW, Gandara DR, Frampton GM, et al. Diverse EGFR exon 20 insertions and co-occurring molecular alterations identified by comprehensive genomic profiling of NSCLC. *J Thorac Oncol*. 2018;13(10):1560-1568. **2.** Fang W, Huang Y, Hong S, et al. EGFR exon 20 insertion mutations and response to osimertinib in non-small-cell lung cancer. *BMC Cancer*. 2019;19(1):595. **3.** Byeon S, Kim Y, Lim SW, et al. Clinical outcomes of EGFR exon 20 insertion mutations in advanced non-small cell lung cancer in Korea. *Cancer Res Treat*. 2019;51(2):623-631. **4.** Wang Y, Yang G, Li J, et al. Real-world treatment outcome of advanced Chinese NSCLC EGFR exon 20 insertion patients. *J Clin Oncol*. 2019;37(15 suppl):9043. **5.** Udagawa H, Matsumoto S, Ohe Y, et al. Clinical outcome of non-small cell lung cancer with EGFR/HER2 exon 20 insertions identified in the LCSCRUM-Japan. *J Thorac Oncol*. 2019;14(10 suppl):S224. **6.** Ou S-HI, Lin HM, Hong J-L, et al. Real-world response and outcomes in NSCLC patients with EGFR exon 20 insertion mutations. *J Clin Oncol*. 2021;39(suppl 15; abstr 9098). **7.** Riely GJ, Neal JW, Camidge DR, et al. Activity and safety of mobocertinib (TAK-788) in previously treated non–small cell lung cancer with *EGFR* exon 20 insertion mutations from a phase 1/2 trial. *Cancer Discov*. 2021;11(7):1688-1699. **8.** Gonzalvez F, Vincent S, Baker TE, et al. Mobocertinib (TAK-788): A targeted inhibitor of *EGFR* exon 20 insertion mutants in non–small cell lung cancer. *Cancer Discov*. 2021;11(7):1672-1687. **9.** Zhou C, Ramalingam SS, Kim TM, et al. Mobocertinib in platinum-pretreated patients with *EGFR* exon 20 insertion-positive metastatic non-small cell lung cancer: phase 1/2 open-label study. *JAMA Oncol*. 2021. In press. **10.** Lacouture M. Mechanisms of cutaneous toxicities to EGFR inhibitors. *Nat Rev Cancer*. 2006;6:803-812.

Abbreviations

AE, adverse event; CNS, central nervous system; ECOG PS, Eastern Cooperative Oncology Group Performance Status; EGFR, epidermal growth factor receptor; *EGFR*, epidermal growth factor receptor gene; *EGFR* ex20ins, *EGFR* exon 20 insertion; *HER2*, human epidermal growth factor receptor 2 gene; MRI, magnetic resonance imaging; NSCLC, non–small cell lung cancer; ORR, objective response rate; PD, progressive disease; PK, pharmacokinetics; PPP, platinum-pretreated patients; QD, once daily; RECIST v1.1, Response Evaluation Criteria in Solid Tumors, version 1.1; TEAE, treatment-emergent adverse event; TKI, tyrosine kinase inhibitor; TRAE, treatment-related adverse event

Acknowledgments

We thank the patients, their families, and their caregivers. We thank the mobocertinib investigators and their team members at each study site, and colleagues from Millennium Pharmaceuticals, Inc. Medical writing support was provided by Peloton Advantage, LLC, an OPEN Health company, Parsippany, NJ, USA, and funded by Millennium Pharmaceuticals, Inc., with editorial support from Teodor G. Paunescu, PhD, of Millennium Pharmaceuticals, Inc. This study was sponsored by Millennium Pharmaceuticals, Inc., Cambridge, MA, a wholly owned subsidiary of Takeda Pharmaceutical Company Limited.

Disclosures

James CH Yang: Advisory board (Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Daiichi Sankyo, Eli Lilly, GSK, Janssen, Merck Serono, MSD, Novartis, Ono Pharmaceuticals, Pfizer, Puma Pharmaceuticals, Roche/Genentech, Takeda Oncology, Yuhan Pharmaceuticals), invited speaker (AstraZeneca, Boehringer Ingelheim, Novartis), coordinating PI (AstraZeneca, Daiichi Sankyo, Dizal Pharmaceutical, MSD), steering committee (Bayer, Eli Lilly, Ipsen, Janssen, Merck, Novartis, Numab, Takeda Oncology); **Suresh S. Ramalingam:** Honoraria or advisory role (Amgen, AstraZeneca, Bristol Myers Squibb, Merck, Lilly, Genentech/Roche, GlaxoSmithKline, Takeda), research support to institution (Amgen, Advaxis, BMS, Genmab, AstraZeneca, Takeda); **Tae Min Kim:** Honoraria or advisory role (AstraZeneca, Boryung, F. Hoffmann-La Roche Ltd/Genentech, Inc, Novartis, Sanofi, and Takeda), research funding (AstraZeneca-Korea Health Industry Development Institute); **Sang-We Kim:** No relationships to disclose; **Gregory J Riely:** Travel (Merck, Sharp & Dohme), research funding (all to institution: Novartis, Roche/Genentech, Millennium, GSK, Pfizer, Infinity Pharmaceuticals, ARIAD, Mirati Therapeutics, Merck); **Tarek Mekhail:** Speakers bureau (AstraZeneca, BMS, Lilly, Merck, Takeda), advisory role (AstraZeneca, Lilly); **Danny Nguyen:** No relationships to disclose; **Maria R Garcia Campelo:** Consulting/advisory role (Takeda, AstraZeneca, Roche, Pfizer, BMS, Boehringer Ingelheim, Pfizer, Janssen, Eli Lilly, MSD, Sanofi); **Enriqueta Felip:** Consulting/advisory role (AstraZeneca, Boehringer Ingelheim, BMS, Celgene, Eli Lilly, Guardant Health, MSD, Novartis, Pfizer, Roche, Takeda, Merck); **Lyudmila Bazhenova:** Stock and other ownership interests (Epic Sciences), consulting or advisory role (Neuvogen, Janssen, Daiichi Sankyo, Boehringer Ingelheim, Merck, Regeneron, Bristol-Myers Squibb, Novartis), research funding (BeyondSpring); **Shu Jin:** Employment (Takeda); **Celina Griffin:** Employment (Takeda); **Veronica Bunn:** Employment (Takeda); **Jianchang Lin:** Employment (Takeda); **Eric N Churchill:** Employment (Takeda); **Minal Mehta:** Employment (Takeda); **Pasi A Jänne:** Consulting (Araxes Pharmaceuticals, ARIAD/Takeda, AstraZeneca, Boehringer Ingelheim, Chugai, Ignyta, Lilly, Loxo Oncology, Merrimack, Mirati Therapeutics, Pfizer, Roche, Novartis, Voronoi, Daiichi Sankyo, SFJ Pharmaceuticals, Biocartis), research support (Astellas, AstraZeneca, Boehringer Ingelheim, Daiichi Sankyo, Lilly, Puma Biotechnology), stock ownership (Gatekeeper and Loxo Oncology), postmarketing royalties from Dana-Farber Cancer Institute–owned patent on EGFR mutations licensed to LabCorp; **Caicun Zhou:** Honoraria or advisory role (Lilly China, Sanofi, BI, Roche, MSD, Qilu, Hengrui, Innovent Biologics, C-Stone, LUYE Pharma, TopAlliance Biosciences Inc, Amoy Diagnostics)

Email for questions or comments: chihyang@ntu.edu.tw

For an e-Print, scan this QR code.

Copies of this poster obtained through Quick Response (QR) Code are for personal use only and may not be reproduced without permission from the authors of this poster.

Presented at ESMO 2021 (European Society for Medical Oncology) 16–21 September 2021 (Virtual)