Editorial Commentary

Sunvozertinib: shining light on lung cancer's exon 20 fight

Tetsuya Mitsudomi[1,2]^

[1]Izumi City General Hospital, Izumi, Osaka, Japan; [2]Department of Innovative Medicine, Kindai University Faculty of Medicine, Osaka-Sayama, Osaka, Japan

Correspondence to: Tetsuya Mitsudomi, MD, PhD. President, Izumi City General Hospital, 4-5-1 Wake-cho, Izumi, Osaka 594-0073, Japan; Department of Innovative Medicine, Kindai University Faculty of Medicine, Osaka-Sayama, Osaka, Japan. Email: mitsudom@gmail.com.

Comment on: Wang M, Fan Y, Sun M, *et al.* Sunvozertinib for patients in China with platinum-pretreated locally advanced or metastatic non-small-cell lung cancer and EGFR exon 20 insertion mutation (WU-KONG6): single-arm, open-label, multicentre, phase 2 trial. Lancet Respir Med 2024;12:217-224.

Keywords: Non-small cell lung cancer (NSCLC); epidermal growth factor receptor (*EGFR*); exon 20 insertion mutation; targeted therapy

Submitted Oct 03, 2024. Accepted for publication Jan 17, 2025. Published online Feb 27, 2025.
doi: 10.21037/tlcr-24-907
View this article at: https://dx.doi.org/10.21037/tlcr-24-907

Non-small cell lung cancer (NSCLC) harboring mutations in the epidermal growth factor receptor (*EGFR*) gene usually demonstrates significant sensitivity to EGFR tyrosine kinase inhibitors (TKIs), exemplifying a prototype of precision medicine in cancer treatment. The most prevalent *EGFR* mutations are small deletions in exon 19 and leucine to arginine substitution at codon 858 (L858R), which are collectively referred to as classical *EGFR* mutations, accounting for 70–80% of all *EGFR* mutations. However, a range of rarer mutations exists, such as G719X, S768I, L747P/S, E709_T710delinsD, referred to as uncommon *EGFR* mutations and exon 20 insertion mutations (Ex20ins) (1). Ex20ins mutations were originally described by two groups including ours (2,3), and later, it turned out that they account for about 10% of the *EGFR* mutations (1,4,5). Although over 100 distinct Ex20ins have been identified (6), A767_V769 dup[1], S768_D770dup, and N771_H773dup collectively comprise more than 45% of the 636 Ex20ins according to the compilation of the five databases (6). Thus, it is crucial to efficiently diagnose the diverse range of Ex20ins without missing any of them, as polymerase chain reaction (PCR)-based kits may miss as high as 40–50% of Ex20ins (6,7). This is also true for the *EGFR* exon 19 deletion as there are many variants for this subtype, too (8) as well as other driver genes (*ALK/RET/ROS1*, etc.) (9). The timely use of comprehensive genomic testing using a next generation sequencing is shown to prolong overall survival and to avoid ineffective and costly treatment (9) On the other hand, when considering the next-generation sequencing, we have to also be aware of several pitfalls related to tissue sample quality and quantity, or cost and accessibility (10).

Greulich *et al.* were the first to experimentally demonstrate that the Ex20ins, D770_771ins NPG has a strong transforming capacity (11). Yet, it is unresponsive to first-generation EGFR-TKI, such as gefitinib or erlotinib. Yasuda *et al.* characterized specifically Ex20ins for the first time and found that D770_771ins NPG has an unaltered adenosine triphosphate-binding pocket and the inserted residues form a wedge at the end of the C helix that promotes the active kinase conformation without enhancing affinity to EGFR TKI, resulting in insensitivity to the conventional EGFR-TKIs (12). However, there is heterogeneity in the degree of insensitivity within Ex20ins

^ ORCID: 0000-0001-9860-8505.

[1] A767_V769dup, where dup is short for duplication, represents a change in amino acid sequence from …MASVDNPHV… to MASVASVDNP…. Please note that this mutation can also be described either as M766_A767insASV or V769_D770insASV. Be aware that all these three represent the same mutation and the Human Genome Variation Society recommends the first description.

mutations. Although exon 20 of the *EGFR* gene spans from codon 762 to 823, insertion mutations usually occur between codon 762 and 775. These mutations can be classified into three main categories based on the location of the inserted amino acids. Insertion in the αC helix (between codon 762 and 766 such as A763_Y764insFQEA) is known to be very sensitive to all generations of EGFR-TKIs (12). On the other hand, Ex20ins occurring at the loop region between codons 767 and 775 following the αC helix is insensitive. However, Ex20ins at codons between 767 and 772 (near-loop region) show intermediate sensitivity to second-generation or Ex20ins-active TKIs compared with those at codons between 773 and 775 (far loop region) (13). In addition, Ex20 ins such as 767_S768insTLA, D770_N771insG, D770_N771insGT, N771_P772insH, or N771_P772insN are sensitive to osimertinib at least *in vitro* (14). Another study found that Ex20ins mutations that have glycine at position 770, such as D770insGY, are sensitive to second generation EGFR-TKI such as afatinib or dacomitinib (15). Zwierenga *et al.*, have recently reported that computational molecular modeling can predict treatment outcome in patients with NSCLC harboring several *EGFR* exon 20 mutations (16). Furthermore, there may be potential effect of co-occurring mutations such as *TP53* genes on patients' outcome (17) as seen in classical *EGFR* mutations.

Due to their general resistance to EGFR-TKIs, NSCLC patients with Ex20ins have a median survival of 16.2 months, significantly shorter than 25.5 months observed in patients with classical *EGFR* mutations by conventional therapies in the real-world retrospective study (18). To address this unmet medical need, drugs for Ex20ins are being actively developed (*Table 1*).

Notably, amivantamab (EGFR-cMET bispecific antibody) and mobocertinib were the first two drugs that were granted accelerated approval by US Food and Drug Administration (FDA) in 2021 for NSCLC patients with Ex20ins as a second-line treatment. However, because of the failure of the phase 3 study, mobocertinib was withdrawn from the market (34), as discussed later.

Sunvozertinib, an oral, small-molecule, irreversible selective EGFR-TKI, targets Ex20ins as well as *EGFR* classical, T790M, and uncommon mutations (35). Starting with osimertinib scaffold, sunvozertinib was synthesized after extensive optimization by substituting various moieties based on its potency against Ex20ins and *in vitro* drug metabolism and pharmacokinetics parameters (*Figure 1*) (35).

In the March 2024 issue of the *Lancet Respiratory Medicine*, Wang *et al.* reported the results of the WU-KONG 6 phase 2 study of sunvozertinib (DZD9008) conducted in China, demonstrating that among 97 patients evaluable for efficacy analysis, 59 (61%) patients achieved a confirmed objective response rate (ORR) [95% confidence interval (CI): 50–71%] (19). Responses were consistent across various demographics including age, sex, smoking history, *EGFR* exon20ins subtypes, brain metastasis at baseline, number of previous lines of therapy, and history of immunotherapy. Sunvozertinib was well tolerated at a dosage of 300 mg once daily. The most common grade 3 or worse treatment-related adverse events were increased blood creatine phosphokinase (17%), diarrhea (8%), and anemia (6%). Serious treatment-related adverse events included interstitial lung disease (5%), anemia (3%), vomiting (2%), nausea (2%), and pneumonia (2%). The authors concluded that sunvozertinib demonstrated anti-tumor efficacy for patients with Ex20ins following platinum-doublet chemotherapy with acceptable toxicities, leading to breakthrough therapy designations from both US FDA and China National Medical Products Administration (NMPA) in 2022 and approval in China in 2023. In addition, the primary analysis of WU-KONG 1B study, a global pivotal study similarly designed to WU-KONG 6, reported an ORR of 44.9% (95% CI: 34.0–56.1%) with responses regardless of previous amivantamab treatment (20). These results appear more favorable comparing other Ex20ins drugs in development (*Table 1*).

Looking ahead, the PAPILLON study is the first phase 3 trial to demonstrate the superiority of targeted therapy over platinum-based chemotherapy in the first-line setting for patients with *EGFR* Ex20ins (31). The study randomized 308 patients, showing a progression-free survival (PFS) of 11.4 months for the amivantamab plus chemotherapy arm compared to 6.7 months for the chemotherapy-only group [hazard ratio (HR) 0.40, 95% CI: 0.30–0.53]. The ORR was 73% in the combination arm versus 47% in the control group. Notably, 75% of patients in the amivantamab-chemotherapy arm experienced grade 3 or higher adverse events (31). Frequent non-hematologic adverse events observed ≥30% of the patients in the amivantamab-chemotherapy arm include paronychia (all grade 56%/grade 3 ≤7%), rash (54%/11%), infusion-related reaction (42%/1%), hypoalbuminemia (41%/4%), increased glutamic oxaloacetic transaminase (ALT) (33%/4%), increased glutamic pyruvic transaminase (AST) (31%/1%) and peripheral edema (30%/1%) (31). On the other hand,

Table 1 Results of clinical trials for the patients with *EGFR* Ex20ins mutation

Drug	Drug class	Trial	N	N of previous tx ≥1 (%)	ORR (%) [95% CI]	mPFS/mDOR/mOS (months)	Common toxicities, all (%)/≥ grade 3 (%)	Dose reduction/discontinuation (%)	Reference
Sunvozertinib (DZD9008)	Pyrimidine-based TKI	WU-Kong6 (China)	97	100	61 [50–71]	NA	Diarrhea 67/8, rash 54/1, CPK increase 58/17	29/10	(19)
Sunvozertinib (DZD9008)	Pyrimidine-based TKI	Wu-Kong 1B (Global)	107	100	45 [34–56]	NA	Diarrhea 17/–, CPK increase 11/–, rash 4/–, anemia 4/–	36/6	(20)
Second line trial									
Amivantamab	EGFR-cMET bispecific antibody	Chrysalis	81	100	40 [29–51]	8/11/23	Rash 86/4, Infusion reaction 66/3, paronychia 45/1	13/10	(21)
Mobocertinib	Pyrimidine-based TKI	EXCLAIM	114	100	28 [20–37]	7/18/25	Diarrhea 91/21, rash 45/0, paronychia 38/<1, appetite loss 35/<1, nausea 34/4	25/17	(22)
Poziotinib	Qunazoline-based TKI	Zenith 20	88	100	19 [12–29]	4.2/7.4/NA	NA	NA	(23)
Poziotinib	Qunazoline-based TKI	MD Anderson	50	94	32 [21–46]	5.5/8.6/19.2	Diarrhea 92/22, rash 90/34, paronychia 68/10, stomatitis 68/2	72/6	(13)
Osimertinib 80 mg	Pyrimidine-based TKI	No name available	12	83	0	3.8/NA/15.8	Dry skin 50/0, thrombocytopenia 42/0, diarrhea 33/0, nausea 33/0, rash 25/1	17/NR	(24)
Osimertinib 160 mg	Pyrimidine-based TKI	EA5162	17	100	24	10/NA/NA	Diarrhea 76/0, fatigue 67/10, platelet decreased 67/0, anemia 43/10, WBC decreased 43/0, anorexia 43/5	NA/5	(25)
Zipalertinib (CLN-081/TAS6417)	Pyrimidine-based TKI	NCT04036682	73	96	38 [27–49]	10/10/NA	Rash 80/1, paronychia 32/0, diarrhea 30/3	14/8	(26)
Furmonertinib	Small molecule TKI	FAVOUR	56	100	240 mg: 46 [27–67]; 160 mg: 39 [20–59]	NR/13.1/NA; NR/9.7/NA	240 mg cohort; diarrhea 86/0, anemia 25/4, AST increase 25/0, ALT increase 25/0, rash 21/0	240 mg cohort 18/4	(27)
ORIC-114	Pyrimidine-based TKI	NCT05315700	21	100	NR	NR/NR/NR	Rash 54/0, diarrhea 40/6, stomatitis, 30/1, paronychia 28/0	16/4	(28)
JMT101 (Becotarug) + osirmertinib	EGFR antiboy + pyrimidine-based TKI	BECOME	112	100	50 [40–60]	6.9/NA/NA	Rash 80/32, diarrhea 68/10, decreased appetite 64/4, oral mucositis 65/11, weight decreased 59/2	NA/5	(29)
BLU-451	Pyrimidine-based TKI	CONCERTO	48	100	NR	NA/NA/NA	Rash 22/0, fatigue 14/0, diarrhea 12/0	NA	(30)
First line trial									
Amivantamab + chemotherapy	EGFR-cMET bispecific antibody	Papillon	153	0	73 [65–80]	11.4/NA/NR	Neutropenia 59/33, paronychia 56/7, rash 54/11, anemia 50/11, infusion related reaction 42/1, hypoalbuminemia 41/4, constipation 40/0, peripheral edema 30/1	48/24	(31)
Sunvozertinib (DZD9008)	Pyrimidine-based TKI	Wu-Kong 1A+15	28; 200 mg (N=19), 300 mg (N=9)	0	79	200 mg: 10.2/9.2/NA; 300 mg: 12.4/NR/NA	CPK increase –/18, diarrhea –/7, lipase –/5, anemia –/5, QT prolongation –/4, amylase –/4	NA	(32)
Furmonertinib	Small molecule TKI	FAVOUR	28	0	79 [59–92]	NR/15.2/NA	Diarrhea 73/0, anemia 43/0, AST increase 27/0, ALT increase 23/0, rash 23/0	13/0	(27)
YK-029A	Pyrimidine-based TKI	NCT05767866	28	0	73 [52–88]	9.3/7.5/NR	Anemia 51/–, diarrhea 49/–, rash 34/–	9/3	(33)

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CI, confidence interval; CPK, creatine phosphokinase; *EGFR*, epidermal growth factor receptor; mDOR, median duration of response; mOS, median overall survival; mPFS, median progression-free survival; NA, not applicable; NR, not reached; ORR, objective response rate; TKI, tyrosine kinase inhibitor; WBC, white blood cell.

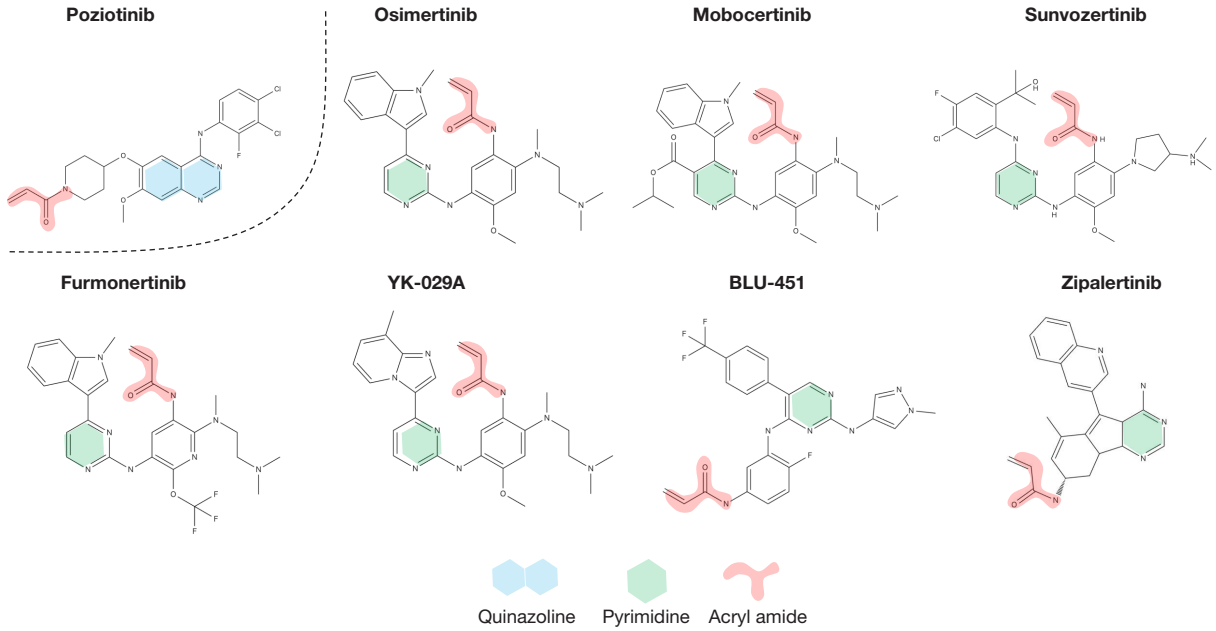

Figure 1 Structures of EGFR-TKIs developed for Ex20ins are compared with osimertinib. Poziotinib features an anilino-quinazoline moiety with an acrylamide group, similar to second-generation EGFR-TKIs such as afatinib and dacomitinib. Other drugs contain a pyrimidine ring and an acrylamide group. Made at MolView website (https://molview.org/). EGFR-TKIs, epidermal growth factor receptor tyrosine kinase inhibitors.

the phase 3 EXCLAIM-2 trial in previously untreated NSCLC patients with *EGFR* exon 20ins showed no superiority of mobocertinib monotherapy over platinum-based chemotherapy, with a median PFS of 9.6 months for both treatment arms (36).

Sunvozertinib monotherapy in the first-line setting demonstrated promising results with an ORR of 79% and a median PFS of 12 months for patients treated at a 300 mg dosage in the combined analysis of WU-KONG 1A and WU-KONG 15 (32). Although the number of patients was small, the FDA granted breakthrough therapy designation to first-line sunvozertinib for Ex20ins NSCLC in April 2024. Similarly, Furmonertinib also showed a promising ORR of 79% in the first-line cohort of the FAVOUR study. WU-KONG28 (NCT05668988), FURVENT (NCT05607550) and REZILENT3 (NCT05973773) are ongoing phase 3 studies evaluating sunvozertinib monotherapy, furmonertinib monotherapy or zipalertinib in combination with pemetrexed plus carboplatin, respectively, against platinum-doublet chemotherapy as a first-line treatment for patients with NSCLC harboring *EGFR* exon20ins.

In summary, the development of treatments for Ex20ins is advancing very rapidly, with many promising agents now available, which was unimaginable a decade ago. However, for the NSCLC patients with classical *EGFR* mutations, median PFS of osimertinib monotherapy in FLAURA (37), osimertinib combined with chemotherapy in FLAURA 2 (38) and lazertinib combined with amivantamab in MARIPOSA (39) are 18.9, 25.5 and 23.7 months, respectively. This level of efficacy could be ideally achieved for Ex20ins as better agents will be developed in the future, considering the high oncogene-dependent nature of Ex20ins in general.

Acknowledgments

None.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Translational Lung Cancer Research*. The article has undergone external peer review.

Peer Review File: Available at https://tlcr.amegroups.com/article/view/10.21037/tlcr-24-907/prf

Funding: None.

Conflicts of Interest: The author has completed the ICMJE uniform disclosure form (available at https://tlcr.amegroups.com/article/view/10.21037/tlcr-24-907/coif). T.M. has received research funding from Boehringer Ingelheim, AstraZeneca, Taiho, Ono Pharmaceuticals, Merck Sharp & Dohme, Eli Lilly, Chugai Pharmaceuticals, and Bridge Biopharma. Additionally, he has received lecture fees from AstraZeneca, Boehringer Ingelheim, Chugai Pharmaceuticals, Pfizer, Bristol-Myers Squibb, Eli Lilly, Merck Sharp & Dohme, Novartis, Merck Biopharma, Ono Pharmaceuticals, Amgen, and Daiichi-Sankyo. He also participated in advisory board of Regeneron, Bristol Myers Squibb, Janssen and Taiho. The author has no other conflicts of interest to declare.

Ethical Statement: The author is accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Robichaux JP, Le X, Vijayan RSK, et al. Structure-based classification predicts drug response in EGFR-mutant NSCLC. Nature 2021;597:732-7.
2. Huang SF, Liu HP, Li LH, et al. High frequency of epidermal growth factor receptor mutations with complex patterns in non-small cell lung cancers related to gefitinib responsiveness in Taiwan. Clin Cancer Res 2004;10:8195-203.
3. Kosaka T, Yatabe Y, Endoh H, et al. Mutations of the epidermal growth factor receptor gene in lung cancer: biological and clinical implications. Cancer Res 2004;64:8919-23.
4. Arcila ME, Nafa K, Chaft JE, et al. EGFR exon 20 insertion mutations in lung adenocarcinomas: prevalence, molecular heterogeneity, and clinicopathologic characteristics. Mol Cancer Ther 2013;12:220-9.
5. 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;13:1560-8.
6. Ou SI, Hong JL, Christopoulos P, et al. Distribution and Detectability of EGFR Exon 20 Insertion Variants in NSCLC. J Thorac Oncol 2023;18:744-54.
7. Viteri S, Minchom A, Bazhenova L, et al. Frequency, underdiagnosis, and heterogeneity of epidermal growth factor receptor exon 20 insertion mutations using real-world genomic datasets. Mol Oncol 2023;17:230-7.
8. Pisapia P, Russo A, De Luca C, et al. The relevance of the reference range for EGFR testing in non-small cell lung cancer patients. Lung Cancer 2024;198:108002.
9. Yorio J, Lofgren KT, Lee JK, et al. Association of Timely Comprehensive Genomic Profiling With Precision Oncology Treatment Use and Patient Outcomes in Advanced Non-Small-Cell Lung Cancer. JCO Precis Oncol 2024;8:e2300292.
10. Zalis M, Viana Veloso GG, Aguiar PN Jr, et al. Next-generation sequencing impact on cancer care: applications, challenges, and future directions. Front Genet 2024;15:1420190.
11. Greulich H, Chen TH, Feng W, et al. Oncogenic transformation by inhibitor-sensitive and -resistant EGFR mutants. PLoS Med 2005;2:e313. Erratum in: PLoS Med 2024;21:e1004470.
12. Yasuda H, Park E, Yun CH, et al. Structural, biochemical, and clinical characterization of epidermal growth factor receptor (EGFR) exon 20 insertion mutations in lung cancer. Sci Transl Med 2013;5:216ra177.
13. Elamin YY, Robichaux JP, Carter BW, et al. Poziotinib for EGFR exon 20-mutant NSCLC: Clinical efficacy, resistance mechanisms, and impact of insertion location on drug sensitivity. Cancer Cell 2022;40:754-767.e6.
14. Hirose T, Ikegami M, Endo M, et al. Extensive functional evaluation of exon 20 insertion mutations of EGFR. Lung Cancer 2021;152:135-42.
15. Kobayashi IS, Viray H, Rangachari D, et al. EGFR-D770>GY and Other Rare EGFR Exon 20 Insertion Mutations with a G770 Equivalence Are Sensitive to Dacomitinib or Afatinib and Responsive to EGFR Exon 20 Insertion Mutant-Active Inhibitors in Preclinical Models and Clinical Scenarios. Cells 2021;10:3561.

16. Zwierenga F, Zhang L, Melcr J, et al. The prediction of treatment outcome in NSCLC patients harboring an EGFR exon 20 mutation using molecular modeling. Lung Cancer 2024;197:107973.
17. Christopoulos P, Kluck K, Kirchner M, et al. The impact of TP53 co-mutations and immunologic microenvironment on outcome of lung cancer with EGFR exon 20 insertions. Eur J Cancer 2022;170:106-18.
18. Bazhenova L, Minchom A, Viteri S, et al. Comparative clinical outcomes for patients with advanced NSCLC harboring EGFR exon 20 insertion mutations and common EGFR mutations. Lung Cancer 2021;162:154-61.
19. Wang M, Fan Y, Sun M, et al. Sunvozertinib for patients in China with platinum-pretreated locally advanced or metastatic non-small-cell lung cancer and EGFR exon 20 insertion mutation (WU-KONG6): single-arm, open-label, multicentre, phase 2 trial. Lancet Respir Med 2024;12:217-24.
20. Yang JCH, Doucet L, Wang M, et al. A Multinational Pivotal Study of Sunvozertinib iin Platinum Pre-treated Non-Small Cell Lung Cancer with EGFR exon 20 insertion mutations: Primary Analysis of WU-KONG1 Study. J Clin Oncol 2024;42:abstr 8513.
21. Park K, Haura EB, Leighl NB, et al. Amivantamab in EGFR Exon 20 Insertion-Mutated Non-Small-Cell Lung Cancer Progressing on Platinum Chemotherapy: Initial Results From the CHRYSALIS Phase I Study. J Clin Oncol 2021;39:3391-402.
22. Zhou C, Ramalingam SS, Kim TM, et al. Treatment Outcomes and Safety of Mobocertinib in Platinum-Pretreated Patients With EGFR Exon 20 Insertion-Positive Metastatic Non-Small Cell Lung Cancer: A Phase 1/2 Open-label Nonrandomized Clinical Trial. JAMA Oncol 2021;7:e214761.
23. Le X, Goldman JW, Clarke JM, et al. Poziotinib shows activity and durability of responses in subgroups of previously treated EGFR exon 20 NSCLC patients. J Clin Oncol 2020;38:abstr 9514.
24. Yasuda H, Ichihara E, Sakakibara-Konishi J, et al. A phase I/II study of osimertinib in EGFR exon 20 insertion mutation-positive non-small cell lung cancer. Lung Cancer 2021;162:140-6.
25. Piotrowska Z, Wang Y, Sequist LV, et al. ECOG-ACRIN EA5162 : A phase Il study of high-dose osimertinib in NSCLC with EGFR exon 20. J Clin Oncol 2020; 38:9513.
26. Piotrowska Z, Tan DS, Smit EF, et al. Safety, Tolerability, and Antitumor Activity of Zipalertinib Among Patients With Non-Small-Cell Lung Cancer Harboring Epidermal Growth Factor Receptor Exon 20 Insertions. J Clin Oncol 2023;41:4218-25.
27. Han B, Zhou C, Zheng W, et al. A Phase 1b Study Of Furmonertinib, an Oral, Brain Penetrant, Selective EGFR Inhibitor, in Patients with Advanced NSCLCwith EGFR Exon 20 Insertions. J Thorac Oncol 2023; 18 suppl 11:S49.
28. Hong MH, Spira AI, Lee KH, et al. A global phase 1b study of ORIC-114, a highly selective, brain penetrant EGFR and HER2 inhibitor, in patients with advanced solid tumors harboring EGFR Exon 20 or HER2 alterations. Ann Oncol 2023;34:abstr 1333P.
29. Zhang L, Fang W, Zhao S, et al. Phase II study of becotarug (JMT101) combined with osimertinib in patients (pts) with locally advanced or metastatic NSCLC harboring EGFR exon 20 insertion (ex20ins) mutations (BECOME study). ESMO Open 2024;9:102724.
30. Nguyen D, Shum E, Baik CS, et al. Emerging phase 1 data of BLU-451 in advanced NSCLC with EGFR exon 20 insertions. J Clin Oncol 2023;41:abstr 9064.
31. Zhou C, Tang KJ, Cho BC, et al. Amivantamab plus Chemotherapy in NSCLC with EGFR Exon 20 Insertions. N Engl J Med 2023;389:2039-51.
32. Yang JCH, Wang M, Chiu C-H, et al. 1325p Sunvozertinib as first-line treatment in NSCLC patients with EGFR exon20 insertion mutations. Ann Oncol 2023:S765.
33. Duan J, Wu L, Yang K, et al. Safety, Tolerability, Pharmacokinetics, and Preliminary Efficacy of YK-029A in Treatment-Naive Patients With Advanced NSCLC Harboring EGFR Exon 20 Insertion Mutations: A Phase 1 Trial. J Thorac Oncol 2024;19:314-24.
34. Takeda Provides Update on EXKIVITY® (mobocertinib) 2023 [updated 2023.10.2. Available online: https://www.takeda.com/newsroom/newsreleases/2023/Takeda-Provides-Update-on-EXKIVITY-mobocertinib/
35. Wang M, Yang JC, Mitchell PL, et al. Sunvozertinib, a Selective EGFR Inhibitor for Previously Treated Non-Small Cell Lung Cancer with EGFR Exon 20 Insertion Mutations. Cancer Discov 2022;12:1676-89.
36. Jänne PA, Wang BC, Cho BC, et al. EXCLAIM-2: Phase III trial of first-line (1L) mobocertinib versus platinum-based chemotherapy in patients (pts) with epidermal growth factor receptor (EGFR) exon 20 insertion (ex20ins)+ locally advanced/metastatic NSCLC. Ann Oncol 2023;34:S1663-4.
37. Soria JC, Ohe Y, Vansteenkiste J, et al. Osimertinib in Untreated EGFR-Mutated Advanced Non-Small-Cell

Lung Cancer. N Engl J Med 2018;378:113-25.
38. Planchard D, Jänne PA, Cheng Y, et al. Osimertinib with or without Chemotherapy in EGFR-Mutated Advanced NSCLC. N Engl J Med 2023;389:1935-48.
39. Cho BC, Lu S, Felip E, et al. Amivantamab plus Lazertinib in Previously Untreated EGFR-Mutated Advanced NSCLC. N Engl J Med 2024;391:1486-98.

Cite this article as: Mitsudomi T. Sunvozertinib: shining light on lung cancer's exon 20 fight. Transl Lung Cancer Res 2025;14(2):334-340. doi: 10.21037/tlcr-24-907