Phase I studies of DZD9008, an oral selective EGFR/HER2 inhibitor for patients with advanced NSCLC and EGFR Exon20 insertion mutations

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DZD9008 is an important drug to add to the growing list of oral compounds for patients diagnosed with EGFR exon20 insertion insertions. This irreversible EGFR inhibitor shows activity across EGFR insertion mutation subtypes. And that matters. Because exon 20 research is a complicated enough field, no one would expect every community oncologist across the world to know what a "near-loop mutation" is versus a "far-loop mutation." So it is welcome news that DZD9008, an irreversible EGFR inhibitor, has shown activity across the mutational spectrum.

The data regarding DZD9008, presented by Pasi A. Jänne, MD, PhD, of Dana-Farber Cancer Institute (DFCI) and director of the Chen-Huang Center for EGFR Mutant Lung Cancers at DFCI, are based on two ongoing phase I studies: WU-KONG1 (NCT03974022 in U.S. sites, Taiwan, Australia, and Korea) and WU-KONG2 (China: CTR20192097). Adverse events associated with DZD9008 are mainly diarrhea and rash. For the 33% of patients with adverse events at or greater than grade 3, dose reductions and dose interruptions are expected. The majorities of each of DZD9008's various adverse events are grade 1 or 2, which is better news for patients; however, six patients out of 102, as of WU-KONG's data cut-off of April 3, 2021, discontinued the drug due to a treatment-related adverse event.

With confirmed overall response rate of 37.5%, a best overall response rate of 41.1%, and disease control rate of 85.7%, the Exon 20 Group looks forward to DZD9008's ongoing phase II study (NCT03974022) and to the drug's continued development. We are also keenly interested in seeing additional data on the drug's CNS penetration. I am hopeful that this drug will join the list of targeted agents that are extending the lives of heavily pretreated patients who have experienced disease progression on either the bispecific antibody amivantamab–now part of our standard arsenal–and/or prior EGFR targeted therapies in the clinical trials pipeline.