There is currently an unmet need for effective targeted therapy against aberrations that are present in 2–4% of cases; these are ex20ins mutations.

Historically, HER2-ex20ins mutations have responded poorly to TKIs. However, TKIs that inhibit both EGFR and HER2 are typically targeted by toxicities associated with inhibition of wild-type EGFR.

BI 181031 is a novel TKI that selectively and competitively binds to the TKD of HER2, and is under investigation as an oral treatment for NSCLC tumors harboring HER2/TKD mutations, including ex20ins mutations. It was well tolerated across all treatment cohorts.

Mechanism of action of BI 181031, a novel TKI

BI 181031 binds to the TKD of HER2 receptors, inhibiting wild-type and mutant HER2, including ex20ins.

- Avoids toxicity associated with inhibition of wild-type EGFR
- Possible better safety and efficacy than TKIs that bind to both HER2 and EGFR receptors

Key points and conclusions

- As of March 8, 2023, 43 patients had been treated; median number of cycles: 4 (range 1–15).
- Only four DLTs have been observed to date: grade 3 anemia, grade 3 ALT increased, grade 2 edema, and grade 2 diarrhea.
- BI 181031 was well tolerated; 28 patients (65%) experienced TRAEs (mostly grade 1 or 2). The most common TRAE was diarrhea (n=14; 33%).

Data were originally presented: European Lung Cancer Congress, March 29–April 2, 2017; NSCLC, non-small cell lung cancer; TKI, tyrosine kinase inhibitors

References

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