Acalabrutinib, and Acalabrutinib Metabolite M27

Zanubrutinib is a next-generation BTK inhibitor caused by off-target kinase binding many patients discontinue therapy because they intolerant of ibrutinib and/or acalabrutinib. This phase 2 study (BGB-3111-215; NCT04116437) (Figure 1)

OBJECTIVE
To assess the longer-term safety and efficacy of zanubrutinib in patients intolerant of brutinib and/or acalabrutinib

METHODS
Methodological details have been published and are summarized in Figure 2

Recurrence of AEs that led to intolerance of prior BTK inhibitors and other treatment-emergent AEs were assessed based on Common Terminology Criteria for Adverse Events v5.0

The investigator-assessed responses using disease parameters at study entry as baseline were assessed every third 28-day cycle using standard response criteria

On study entry, patients were required to not have PD, and hence some patients could not achieve PR or PR-L on study

Safety was assessed in all patients who received at least one dose of zanubrutinib

RESULTS
Of 82 patients, 24 (29.3%) discontinued treatment (Table 2) (means: AE, n=7; myalgia, stomatitis, perioptic neuritis, COVID-19 pneumonia, and esophageal stricture). Recurrence of AEs that led to intolerance of prior BTK inhibitors and other treatment-emergent AEs were assessed based on Common Terminology Criteria for Adverse Events v5.0

While receiving zanubrutinib, 84 of 124 (67.7%) Acalabrutinib-intolerance events did not recur

Safety
The safety profile observed during the longer follow-up was consistent with what has been previously reported for zanubrutinib

A total of 37 patients (45.1%) experienced grade 3/4 intolerance grade 3/4 intolerance events did not recur

The most common AEs are shown in Table 2

The most common AEs are shown in Table 3

CONCLUSIONS
The median exposure to zanubrutinib was longer than the median exposure to the prior BTK inhibitor before discontinuation

In this longer-term analysis, 67.7% of zanubrutinib-intolerance events and 73.0% of acalabrutinib-intolerance events did not recur

Zanubrutinib provided disease control in ≥65% of efficacy-evaluable patients who were responding to, but intolerant of, prior treatment with brutinib and/or acalabrutinib

These longer-term safety and efficacy outcomes suggest that patients who are intolerant of other BTK inhibitors can attain clinical benefit by switching to zanubrutinib

Study enrollment and follow-up are ongoing

Efficacy
Among the 76 efficacy-evaluable patients receiving zanubrutinib, ≥65% of patients across cohorts had controlled disease and ≥65% achieved a PR, thereby maintaining or improving response (Table 5)

DISCLOSURES
No disclosures.

ACKNOWLEDGMENTS
Center of Excellence for Cancer Research at the Norwegian Radium Hospital and the Norwegian Cancer Society

REFERENCES


