

## Zanubrutinib in B-cell malignancies

In patients with chronic lymphocytic leukaemia or small lymphocytic lymphoma, zanubrutinib (a selective Bruton tyrosine kinase [BTK] inhibitor) showed positive anticancer activity with manageable toxicity, according to a new study by Constantine Si Lun Tam (Peter MacCallum Cancer Centre, Melbourne, VIC, Australia) and colleagues.

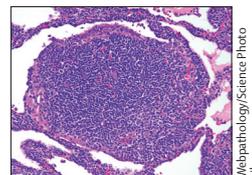
The multicentre, phase 1 trial of zanubrutinib included 17 patients with relapsed or refractory B-cell malignancies (part 1 dose-escalation study). The activity and safety of zanubrutinib was also assessed in 94 patients with treatment-naïve, relapsed, or refractory chronic lymphocytic leukaemia or small lymphocytic lymphoma (part 2 cohort-expansion study). In the dose-escalation phase, zanubrutinib was given orally once per day at doses of 40 mg (n=3), 80 mg (n=4), 160 mg (n=5), and 320 mg

(n=1), and 160 mg twice per day (n=4). The primary endpoints were safety and determination of the maximum tolerated dose; additional endpoints included preliminary activity, pharmacokinetics, and pharmacodynamics. The drug was quickly absorbed, and no dose-limiting toxicities were reported. The maximally administered dose (either 320 mg once daily or 160 mg twice daily) was chosen for part 2 of the study. In these 94 patients, adverse events were predominantly grade 1 or 2. The most common grade 3 or 4 adverse events were neutropenia (six patients [6%]), hypertension (two [2%]), anaemia (two [2%]), and pneumonia (two [2%]). At a median follow-up of 13.7 months (range 0.4–30.5), 75 (96%; 95% CI 89–99) of 78 patients assessable for activity had an overall response; two (3%) had a complete response, 63 (81%) had

a partial response and ten had a partial response with lymphocytosis.

Tam said, “We have a novel BTK inhibitor that allows dosing at drug exposures 6–10 times higher than that of ibrutinib, resulting in continuous deep tissue BTK inhibition as proven by biopsies.” Matthew Davids (Dana-Farber Cancer Institute, Boston, MA, USA) commented, “BTK inhibition with ibrutinib has become a mainstay of chronic lymphocytic leukaemia therapy over the last few years, but particularly in older patients with chronic lymphocytic leukaemia there are a number of toxicities that can make it difficult for patients to stay on long-term therapy.” “Further trials with these agents (eg, zanubrutinib) should follow the early phase study,” added Leo Gordon (Northwestern University Feinberg School of Medicine, Chicago, IL, USA).

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For the study by Tam and colleagues see *Blood* 2019; published online July 24.  
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