Hî nonhematologic toxicities for >7 days (with or without šŒ šu v š • U nonhematologic toxicity of any duration, grade 3 neutropenia with infection or fever, or grade 4 hematologic toxicity that persists to the point that the INV chose to stop therapy due to toxicity and not disease progression (nPD). All enrolled patients must not have documented PD during prior BTKi therapy. Response assessment was evaluated by INV for CLL per modified International Workshop on CLL criteria (Hallek et al, Blood 2008;131:2745; Chesonet al, J Clin Oncol 2012;30:2820), for SLL, MCL, and marginal zone lymphoma per Lugano criteria (Chesonet al, J Clin Oncol 2014;32:3059), and for WM per modified 6th International Workshop on WM criteria (Owenet al, Br J Haematol 2013;160:171). Disease parameters (imaging and laboratory parameters) performed at study entry were used as the baseline for response assessment.

Results: As of 01 June 2020 (data cutoff), 17 patients with CLL/SLL were enrolled, Œ] À H í dose of zanubrutinib, and were analyzed for safety. Median age was 70 years (range, 49-91) and median duration of treatment exposure was 3.02 mo (range, 0.5-6.9). The median number of prior regimens was 1 (range, 1-3). All patients had received ibrutinib. At data cutoff, no patients had received acalabrutinib. At data cutoff, 16 patients remained on zanubrutinib treatment. One patient withdrew herself from the study following an AE (grade 3 syncope) unrelated, as per INV, to study treatment. Of the 31 BTKi-related AEs associated with intolerance (Table 1), 30 (96.8%) did not recur, and 1 event (3.2%, atrial fibrillation) recurred at a lower grade (grade 3 vs 2) and for a shorter duration (14 vs 3 days) vs the initial ibrutinib-intolerant event. Ten patients (58.8%) reported ≥1 AE. AEs reported in ≥10% of patients on zanubrutinib included dizziness (n=3; 17.6%) and cough (n=2; 11.8%). Grade 3+ AEs were reported in 2 patients (11.8%): neutropenia and syncope (n=1 each; 5.9%). AEs of interest included hemorrhage and infections (n=3 each; 17.6%) and anemia, neutropenia, and atrial fibrillation (n=1 each; 5.9%). No AEs led to dose modification or treatment discontinuation. No serious AEs or deaths were reported. As of data cutoff, 10 patients were evaluable for efficacy with ≥1 response assessment. All 10 patients achieved at least stable disease, and 60% of these patients achieved a deepening of response since initiating zanubrutinib. Enrollment is ongoing and the presentation will include additional patients.

Conclusions: Zanubrutinib demonstrated efficacy and tolerability in CLL/SLL patients who were intolerant to previous BTKi. These data suggest that zanubrutinib may provide a potential option after intolerance to other BTKi.

Table 1: Reoccurrence and Severity Change of Ibrutinib/Acalabrutinib-Intolerant Events

	Intolerant to Prior Ibrutinib/Acalabrutinib*		Reoccurrence on Zanubrutinib	
AEs	No. of AEs	Severity Grade, Median (Range)	No. of AEs	Severity Grade, Median (Range)
Any AE	31	2 (2-4)	1	2 (2)
Atrial fibrillation/flutter	5	3 (2-3)	1	2 (2)
Transaminases increased	3	4 (3-4)	0	—
Hypertension	3	3 (2-3)	0	—
Fatigue	3	2 (2-3)	0	—

Nausea	2	2.5 (2-3)	0	—
Arthralgia	2	2 (2-2)	0	—
Muscle spasm	2	2 (2-2)	0	—
Neutropenia	1	4 (4)	0	—
Headache, synovial rupture, vertigo, vomiting	1 each	3 (3) each	0	—
Bone pain, contusion, edema, myalgia, rash pustular, subcutaneous abscess	1 each	2 (2) each	0	—

*All patients received prior ibrutinib.
AE, adverse event.