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P1104 A PHASE 1 STUDY EVALUATING SAFETY AND EFFICACY OF PARSACLISIB IN COMBINATION WITH BENDAMUSTINE + OBINUTUZUMAB IN PATIENTS WITH RELAPSED OR REFRACTORY FOLLICULAR LYMPHOMA (CITADEL-102)

Topic: 18. Indolent and mantle-cell non-Hodgkin lymphoma - Clinical

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Background: Patients (pts) with follicular lymphoma (FL) generally respond well to first-line CD20-targeted therapies, such as obinutuzumab or rituximab-based regimens. However, many pts relapse and studies suggest that each subsequent relapse is associated with shorter durations of response to the next treatment. Parsaclisib is a potent and highly selective next generation PI3Kδ inhibitor. The combination of bendamustine + obinutuzumab is approved for pts with relapsed/refractory (R/R) FL. We hypothesized that adding parsaclisib may improve clinical benefit with a manageable safety profile in this pt population.

Aims: CITADEL-102 (NCT03039114) is an open-label, phase 1, dose-finding study that investigated safety and efficacy of parsaclisib in combination with bendamustine + obinutuzumab in pts with R/R FL following rituximab-containing regimens.

Methods: Pts enrolled were ≥18 years with histologically confirmed CD20-positive FL, R/R to any prior rituximab-containing regimen, ECOG PS 0–2, ≥1 measurable lesion, and ≤4 prior therapies. Pts received parsaclisib 20 mg orally once daily (QD) for 8 weeks then 20 mg once weekly (QW); bendamustine 90 mg/m^2 infusion on days 1 and 2 of cycles 1–6; and obinutuzumab 1000 mg infusion on days 1, 8, and 15 of cycle 1, and day 1 of cycles 2–6, and on every second cycle of cycles 8–30 in pts having complete response/complete metabolic response (CR/CMR), partial response/partial metabolic response (PR/PMR), or stable disease/no metabolic response. Part 1 (safety run-in) used a 3+3 design with dose de-escalation to identify the maximum tolerated dose (MTD) of parsaclisib in combination with bendamustine + obinutuzumab. In Part 2 (dose expansion), the safety and efficacy of this combination were further evaluated. The primary study endpoint was safety and tolerability; secondary endpoints included efficacy outcomes (ORR, DOR, PFS, and OS).

Results: A total of 26 pts were enrolled and treated; median (range) age was 65.0 (44–80) years, 25 (96.2%) had ECOG PS ≤1, 11 (42.3%) had ≥2 prior systemic therapies, and 6 (23.1%) had received prior bendamustine. Median (range) parsaclisib exposure was 10.6 (0.4–32.8) months. Main reasons for treatment discontinuation included adverse events (AEs) (8 pts, 30.8%) and progressive disease (6 pts, 23.1%). All pts experienced treatment-emergent AEs (TEAEs); most common any-grade TEAEs (≥10 pts) were pyrexia (53.8%), neutropenia (50%), diarrhea (46.2%), thrombocytopenia, and nausea (each 38.5%). Grade ≥3 TEAEs were experienced by 88.5% of pts; most common grade ≥3 TEAEs (≥2 pts) were neutropenia (34.6%), febrile neutropenia (23.1%), thrombocytopenia (19.2%), ALT and AST increase (each 11.5%), and diarrhea, neutrophil count decreased, and rash maculopapular (each 7.7%). One of 6 evaluable pts in Part 1 had a DLT of grade 4 QTc elongation. The MTD was not reached, and parsaclisib 20 mg QD for 8 weeks then 20 mg QW was the selected dosage for dose expansion in Part 2. Treatment discontinuation due

to TEAEs was 30.8%, 7.7%, and 15.4% for parsaclisib, bendamustine, and obinutuzumab, respectively. One fatal TEAE (COVID-19 pneumonia) occurred. ORR (95% CI) as reported by the investigator was 76.9% (56.4–91.0), with 17 pts (65.4%) achieving CR/CMR and 3 pts (11.5%) achieving PR/PMR as the best overall response. Median DOR, PFS, and OS were not reached.

Summary/Conclusion: Parsaclisib in combination with bendamustine + obinutuzumab appears to have a manageable safety profile and demonstrated promising efficacy in pts with R/R FL.