Results of the PI3Kδ inhibitor ME-401 alone or with rituximab in relapsed/refractory (R/R) follicular lymphoma (FL).

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Abstract Disclosures

Background:
ME-401, a potent and selective oral PI3kδ inhibitor, is being evaluated in a Phase 1b study in patients (pts) with R/R B-cell malignancies (NCT02914938). 70 pts were treated; we report here results in FL.

Methods:
Pts with ECOG ≤2, no prior PI3K therapy and progression of disease (POD) after ≥1 prior therapy were initially enrolled in a dose escalation phase (60-180 mg) then in 60 mg expansion cohorts as monotherapy or in combination with rituximab. ME-401 was given initially on a daily continuous schedule (CS) until POD or unacceptable toxicity. An intermittent schedule (IS) on days 1-7 of a 28-day cycle was then evaluated after 2 cycles (n = 18) or ≥3 cycles (n = 9) of CS. Toxicity on CS managed by switch to IS. POD on IS managed by switch to CS.

Results:
48 FL pts received ME-401 alone (n = 39) or with rituximab (n = 9). Median age 64.5 yrs. (range 38-81), median prior therapies 2 (range 1-10), 30 had ≥3 prior therapies and 25 were POD24. 28 pts remain on therapy with median follow-up of 9.3 months (range 0.5-22.5) and 20 discontinued: 9 POD, 4

adverse events (AEs), 4 withdrew consent, and 3 for stem cell transplant. Delayed (> Cycle 2) grade 3 immune related AEs (irAEs), primarily diarrhea/colitis and rash, reported in 9/30 (30%) on CS and 2/18 (11%) switched to IS after 2 cycles, with irAEs noted 15 and 18 days after switch. 4 pts with grade 3 irAEs had a drug holiday and corticosteroids then resumed ME-401 on IS without AE recurrence. Objective responses in 34/43 pts (79%) with follow-up disease assessment: 79% with ME-401 alone (including 26% morphologic/metabolic CR), 78% with ME-401 plus rituximab, 91% in POD24, and 75% in ≥3rd line therapy. 24/27 (89%) IS pts continue therapy, 20 on IS and 4 who switched to CS due to POD on IS, and 3 pts discontinued due to persistent POD after switch to CS.

Conclusions:

ME-401 achieves a high rate of durable responses in R/R FL. IS appears to reduce the incidence of irAEs and maintains responses. POD on IS can be salvaged by reverting to CS. A randomized study to evaluate ME-401 given by IS or CS is enrolling pts with R/R FL, with switch to IS for irAEs and switch to CS if POD on IS. Clinical trial information: NCT02914938

Schedule	No. Pts	irAEs	Evaluable Pts	CR+PR
CS only or CS ⇒ IS in Cycles ≥4	30	9 (30%)	25	20
CS ⇒ IS in Cycle 3	18	2 (11%)	18	14 (78%)