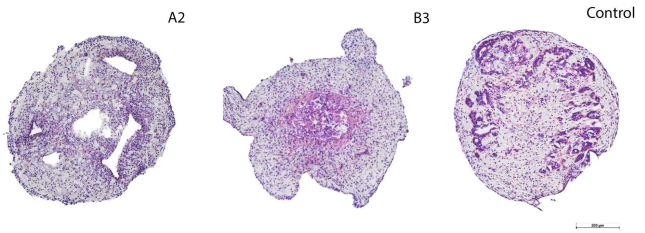

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4615-C | FAT-SOLUBLE VITAMIN LEVELS IN PATIENTS WITH ALAGILLE SYNDROME TREATED WITH ODEVIXIBAT IN THE PHASE 3 ASSERT STUDY

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Background: Alagille syndrome (ALGS) is a rare, genetic, multisystem disease that affects the liver and can lead to cholestasis, with resultant impairments in lipid absorption and subsequent fat-soluble vitamin (FSV) deficiency. In the 24-week ASSERT study, treatment with odevixibat resulted in significant improvements in pruritus and reductions in bile acids versus placebo in patients with ALGS. Here, we summarize effects related to FSVs in ASSERT. **Methods:** Patients eligible for ASSERT were those of any age with ALGS, history of significant pruritus, and elevated serum bile acids; patients were randomized 2:1 to odevixibat 120 μg/kg/day or placebo. Vitamins A, D, E, and international normalized ratio (INR; surrogate for vitamin K) were measured at screening, randomization, and 2−6 times through week 24. Treatment-emergent adverse events (TEAEs) resulting from new or worsening FSV deficiency refractory to clinically recommended vitamin supplementation and possible sequelae of FSV deficiency were evaluated. **Results:** Overall, 52 patients (mean age, 6.3 y) received odevixibat (n = 35) or placebo (n = 17); all 52 patients completed the study. At baseline, mean levels of vitamins A, D, E, and INR were generally within normal range, reflective of vitamin supplementation received by most patients. Overall, no clinically relevant changes were observed in mean FSV levels or INR in patients receiving odevixibat or placebo during the study. In total, 6 patients reported TEAEs related to FSV levels (odevixibat, n = 3 [9%]; placebo, n = 3 [18%]). Two of these (odevixibat, n = 1 [3%]; placebo, n = 1 [6%]) had TEAEs of vitamin D deficiency that were refractory to clinically recommended vitamin supplementation; both were nonserious, did not lead to treatment interruption, and were assessed as unrelated to study drug. The 4 additional patients with TEAEs related to FSV levels had increased INR (odevixibat, n = 1; placebo, n = 2) or decreased vitamin A and vitamin E serum levels (odevixibat, n = 1 each [both in the same patient]) that were not considered refractory to clinically recommended vitamin supplementation. TEAEs of possible sequelae of FSV deficiency had a similar incidence with odevixibat (n = 5 [14%]) and placebo (n = 3 [18%]; Table); the most common in the odevixibat group was hematoma, reported in 3 (9%) patients and all attributed to trauma. Most TEAEs possibly secondary to FSV deficiency were reported as Grade 1 or 2 in intensity, were nonserious, and did not lead to treatment interruption or discontinuation. Review of the Kaplan-Meier curve for time to onset of these sequelae indicated no difference between treatment groups. **Conclusion:** In the ASSERT study, treatment of patients with ALGS with odevixibat for up to 24 weeks was not associated with clinically meaningful changes in mean FSV levels or INR. Possible sequelae of FSV deficiency were reported at similar incidence with both odevixibat and placebo.

Symbols: ♦, Poster of Distinction; ★, Foundation Award Recipient

Table: TEAEs of Potential Sequelae of FSV Deficiency in Patients With Alagille Syndrome in ASSERT

Patients, n (%)	Placebo (n=17)	Odevixibat (n=35)
Any potential sequelae events	3 (18)	5 (14)
Hematoma	0	3 (9)
INR increased	2 (12)	1 (3)
Coagulopathy	0	1 (3)
Hematemesis	0	1 (3)
Contusion	0	1 (3)
Epistaxis	2 (12)	0

FSV, fat-soluble vitamin; INR, international normalized ratio; TEAE, treatment-emergent adverse event.

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4616-C | ODEVIXIBAT EFFICACY AND SAFETY ACROSS PATIENT SUBGROUPS: AN EVALUATION OF POOLED DATA FROM THE PEDFIC 1 AND PEDFIC 2 TRIALS

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Symbols: ♦, Poster of Distinction; ★, Foundation Award Recipient