# Serum Bile Acid Levels, Pruritus Scores, and Growth Over Time in Odevixibat Responders: Pooled Data From the PEDFIC Studies in Patients With Progressive Familial Intrahepatic Cholestasis

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## INTRODUCTION

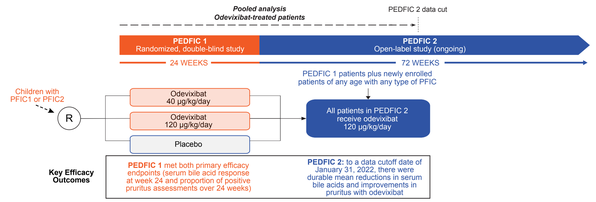
- Progressive familial intrahepatic cholestasis (PFIC) is a group of rare, inherited liver diseases whose clinical signs and symptoms may include elevated serum bile acids, pruritus, poor growth, and progressive hepatic damage[1]
- Odevixibat, an ileal bile acid transporter inhibitor, is approved in the United States for treatment of pruritus in patients 3 months of age and older with PFIC[2]
- The efficacy and safety of odevixibat were assessed in patients with PFIC in the phase 3 PEDFIC 1 and PEDFIC 2 studies[3,4]
  - Key efficacy endpoints in both studies were related to the effects of odevixibat on serum bile acids and pruritus; growth was assessed as a secondary endpoint
- Using pooled data from these studies, we analyzed serum bile acids, pruritus, and growth over time in odevixibat-treated patients who received treatment for ≥6 months and met treatment response criteria

## METHODS

### Study Designs and Patient Population

- PEDFIC 1 (NCT03566238) was a 24-week, randomized, placebo-controlled study in children with PFIC1 and PFIC2[3] (**Figure 1**)
- PEDFIC 2 (NCT03659916) is an ongoing 72-week extension study in patients of any age with any PFIC type[4] (**Figure 1**)
- Patients eligible for the PEDFIC studies had elevated serum bile acids (≥100 µmol/L) and a scratching score ≥2 (on a scale of 0 to 4) prior to randomization/screening

**Figure 1. PEDFIC 1 and PEDFIC 2 Study Designs and Key Efficacy Outcomes**




PFIC, progressive familial intrahepatic cholestasis; R, randomization.

### Assessments

- In both PEDFIC 1 and PEDFIC 2, serum bile acid measurements were taken at all study visits and pruritus was scored twice daily by caregivers using a validated scale[5]
  - On this scale, higher scores indicate worse symptoms, and a decrease of ≥1 point from baseline is clinically meaningful
  - Patient-level pruritus assessments are presented as the average over a 1-month (up to the first 24 weeks in PEDFIC 2) or 12-week interval
- Safety monitoring included assessment of treatment-emergent adverse events (TEAEs)

### Analyses

- Data from PEDFIC 1 and PEDFIC 2 were pooled in an analysis that spans from patients' first dose of odevixibat to a cutoff date of January 31, 2022
- Changes in serum bile acids, pruritus, and growth over time were assessed in patients treated with odevixibat for ≥6 months who met criteria for treatment response, which was defined as either: a) serum bile acids reduced by ≥70% or levels ≤70 µmol/L, b) a ≥1-point drop in monthly or 12-week interval pruritus score, or both a and b, based on last assessment up to week 72
  - Data from patients who received placebo for up to 24 weeks in PEDFIC 1 (n=20),[3] regardless of responder status, are included below for context

## RESULTS

### Patients

- At the data cutoff, a total of 89 patients had received odevixibat for ≥6 months; of these, 49 patients (mean [range] duration of exposure, 110 [39–115] weeks) were serum bile acid and/or pruritus responders
  - Demographic and baseline characteristics for odevixibat responders are shown in **Table 1**

**Table 1. Demographics and Baseline Characteristics**

| | Odevixibat Responders n=49 | Placebo-Treated Patients From PEDFIC 1 n=20 |
|---|---|---|
| **Age, mean (SD), years** | 5.0 (4.4) | 3.8 (3.9) |
| **Male, n (%)** | 26 (53) | 12 (60) |
| **PFIC type, n (%)** | | |
| PFIC1 (FIC1 deficiency) | 15 (31) | 5 (25) |
| PFIC2 (BSEP deficiency) | 29 (59) | 15 (75) |
| PFIC3 (MDR3 deficiency) | 3 (6) | – |
| Other (MYO5B deficiency) | 2 (4) | – |
| **Pruritus score, mean (SE)** | 3.0 (0.1) | 3.0 (0.1) |
| **Serum bile acids, mean (SE), µmol/L** | 237 (19) | 248 (22) |
| **UDCA use, n (%)** | 38 (78) | 18 (90) |
| **Rifampicin use, n (%)** | 27 (55) | 17 (85) |
| **ALT, mean (SD), U/L** | 104 (126) | 77 (56) |
| **AST, mean (SD), U/L** | 92 (60) | 90 (52) |
| **Total bilirubin, mean (SD), mg/dL** | 2.9 (3.0) | 3.1 (3.4) |
| **Height Z score, mean (SD)** | –1.3 (1.4) | –2.3 (1.5) |
| **Weight Z score, mean (SD)** | –0.6 (1.2) | –1.5 (1.4) |

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BSEP, bile salt export pump; FIC, familial intrahepatic cholestasis; MDR3, multidrug resistance protein 3; PFIC, progressive familial intrahepatic cholestasis; UDCA, ursodeoxycholic acid.

**Figure 2. Serum Bile Acid Levels in Odevixibat Responders and Placebo-Treated Patients With PFIC1 (A), PFIC2 (B), and PFIC3 or MYO5B Deficiency (C)**

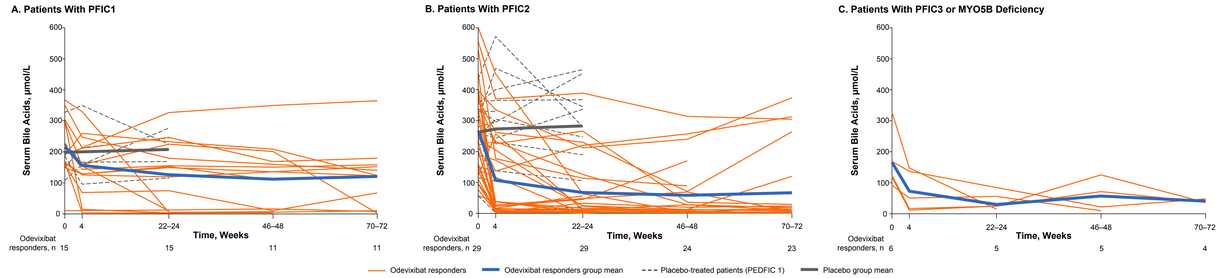
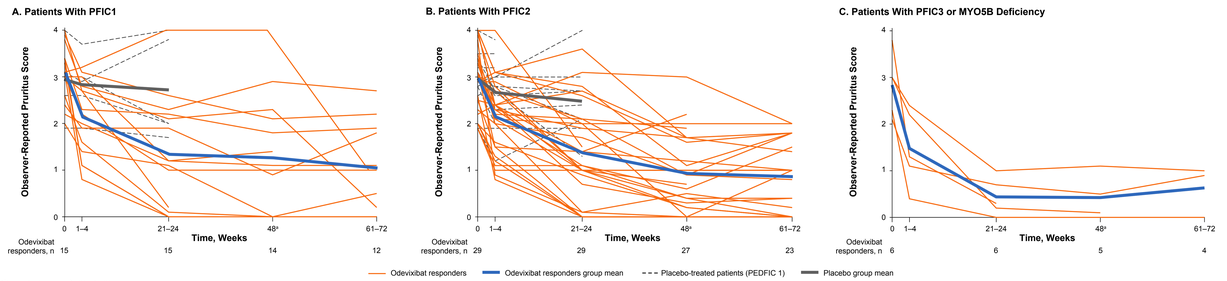



**Figure 3. Pruritus Scores in Odevixibat Responders and Placebo-Treated Patients With PFIC1 (A), PFIC2 (B), and PFIC3 or MYO5B Deficiency (C)**




[a]Represents either weeks 37–48 or 45–48.

**Figure 4. Height Z Scores in Odevixibat Responders and Placebo-Treated Patients With PFIC1 (A), PFIC2 (B), and PFIC3 or MYO5B Deficiency (C)**

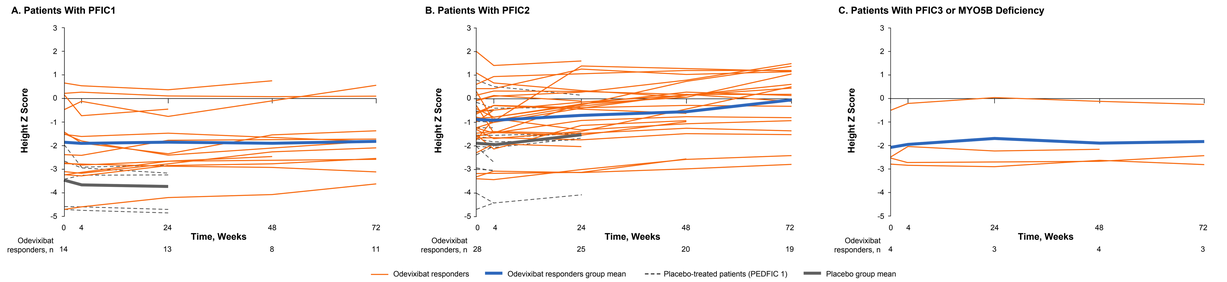
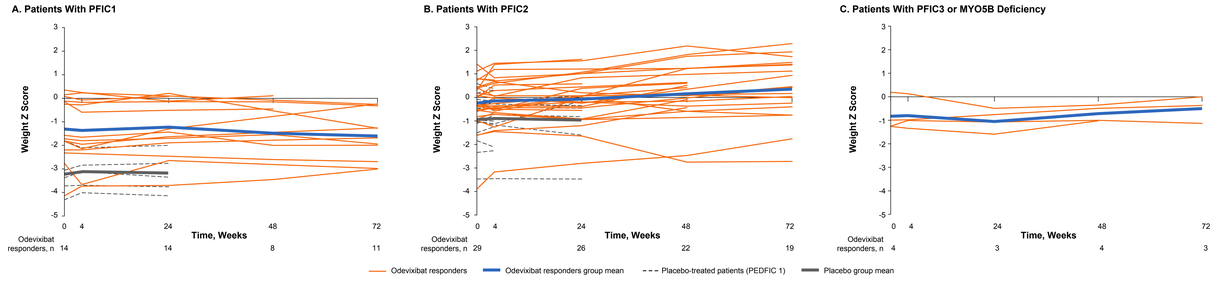



**Figure 5. Weight Z Scores in Odevixibat Responders and Placebo-Treated Patients With PFIC1 (A), PFIC2 (B), and PFIC3 or MYO5B Deficiency (C)**




### Serum Bile Acids and Pruritus

- Serum bile acid levels over time are shown for individual patients with PFIC1, PFIC2, PFIC3, or MYO5B deficiency in **Figure 2**
  - In the overall group of odevixibat responders, mean serum bile acid levels were 83 µmol/L at weeks 22–24 and 81 µmol/L at weeks 70–72
    - Patients who received placebo in PEDFIC 1 had slightly higher mean serum bile acids at weeks 22–24 vs baseline
- Pruritus scores over time are shown for individual patients with PFIC1, PFIC2, PFIC3, or MYO5B deficiency in **Figure 3**
  - Some odevixibat responders had continued reductions in pruritus scores over time; mean pruritus scores in odevixibat responders across PFIC types were 1.3 at weeks 21–24 and 0.9 at weeks 61–72
    - In patients who received placebo in PEDFIC 1, mean pruritus score at weeks 21–24 was 2.5

### Growth

- Growth in individual patients with PFIC1, PFIC2, PFIC3, or MYO5B deficiency is shown in **Figures 4** and **5**, respectively
  - Mean height Z scores in odevixibat responders across PFIC types were –1.1 at week 24 and –0.8 at week 72; mean values at these time points for weight Z score were –0.5 and –0.4, respectively
    - In patients who received placebo in PEDFIC 1, mean height and weight Z scores worsened over 24 weeks

### Safety

- TEAEs were reported in 96% of patients with ≥6 months' odevixibat exposure and treatment response; most were mild to moderate in severity (**Table 2**)
  - There were no drug-related serious TEAEs or deaths in these patients

**Table 2. Summary of Treatment-Emergent Adverse Events in Patients With ≥6 Months of Odevixibat Exposure**

| | Odevixibat Responders, n=49 |
|---|---|
| **Any TEAE** | 47 (96) |
| **Severe TEAEs** | 7 (14) |
| **Drug-related TEAEs** | 29 (59) |
| **Serious TEAEs** | 9 (18) |
| **Drug-related serious TEAEs** | 0 |
| **TEAEs leading to discontinuation** | 1 (2) |
| **TEAEs occurring in ≥10% of patients, by preferred term** | |
| Upper respiratory tract infection | 21 (43) |
| Diarrhea | 19 (39) |
| Pyrexia | 14 (29) |
| Blood bilirubin increased | 11 (22) |
| Nasopharyngitis | 11 (22) |
| Cough | 10 (20) |
| ALT increased | 9 (18) |
| Vomiting | 9 (18) |
| Influenza | 7 (14) |
| Abdominal pain | 6 (12) |
| Otitis media | 6 (12) |
| AST increased | 5 (10) |
| Ear infection | 5 (10) |

ALT, alanine aminotransferase; AST, aspartate aminotransferase; TEAE, treatment-emergent adverse event.

## CONCLUSIONS

- These data, which include patients with a mean of 110 weeks (range, 39–115 weeks) of exposure to odevixibat, represent the longest period of odevixibat treatment assessed to date in patients with PFIC
- Among patients with ≥6 months' exposure to odevixibat who met treatment response criteria, mean reductions in serum bile acids and pruritus were sustained over time
  - In general, reductions in these parameters occurred across PFIC types
- Mean improvements in growth were observed in the overall odevixibat-treated population
- Odevixibat was generally well tolerated

## REFERENCES

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## AUTHOR DISCLOSURES

**L. D'Antiga:** Albireo, Alexion, Mirum, Selecta, Vivet, Spark, Tome, and Genespire – Consultant
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