

Managing PFIC 7 with odevixibat: Alleviation of pruritus and biochemical response

To the Editor:

We read with great interest the recent publication entitled “Real-world experience with odevixibat in children with progressive familial intrahepatic cholestasis”,¹ which compellingly underscored the clinical utility of odevixibat in managing cholestatic pruritus. In an effort to contribute to the growing body of evidence, we wish to report a case of progressive familial intrahepatic cholestasis type 7 (PFIC 7), associated with a homozygous *USP53* mutation (c.1323_1326del; p.Ile441fs), that was successfully managed with odevixibat therapy.

PFIC 7 is a recently described autosomal recessive disorder resulting from mutations in the *USP53* gene, which encodes a tight junction-associated protein. Although not traditionally classified among the well-established PFIC subtypes, *USP53*-related cholestasis exhibits a comparable clinical phenotype, typically characterized by early-onset jaundice, intractable pruritus, elevated transaminases, and low to normal levels of gamma-glutamyltransferase (GGT). Sensorineural hearing loss may also occur, though inconsistently.² Given its recent characterization, standardized therapeutic protocols for PFIC 7 remain undefined. To our knowledge, this is the first documented report of odevixibat administration in a patient with genetically confirmed PFIC 7.

The patient, a female infant, was initially referred at 2.5 months of age with persistent jaundice since birth. Physical examination revealed hepatomegaly, with the liver palpable 3 cm below the right costal margin. Laboratory investigations demonstrated aspartate aminotransferase (AST) of 152 U/L (normal range: 13–38 U/L), alanine aminotransferase (ALT) of 123 U/L (normal range: 8–32 U/L), total bilirubin of 5.9 mg/dl (normal range: 0.4–1.0 mg/dl), direct bilirubin of 3.1 mg/dl (normal range: 0.1–0.5 mg/dl), and GGT of 122 U/L (normal range: 6–26 U/L). Extensive metabolic and infectious work-up yielded unremarkable results.

The family history was significant for a sibling who had undergone liver transplantation at 3 months of age for neonatal cholestasis and had succumbed to postoperative complications. No definitive diagnosis had been established at that time. Following the identification of a homozygous *USP53* mutation in the index case, retrospective analysis of the deceased sibling's stored newborn screening sample confirmed the same mutation, thereby establishing a posthumous diagnosis of PFIC 7.

Initial management consisted of ursodeoxycholic acid and fat-soluble vitamin supplementation. However, the patient subsequently developed severe pruritus with associated sleep disruption and skin excoriations. Adjunctive therapies, including cholestyramine and rifampin, were introduced without meaningful clinical benefit.

At 21 months of age, odevixibat therapy was commenced. The therapeutic response was both rapid and striking: pruritus resolved completely within 2 weeks, accompanied by marked improvements in sleep quality, behavior, and skin integrity. While transaminase levels exhibited a moderate reduction, serum bile acid concentrations demonstrated a robust biochemical response, decreasing from 93.4 $\mu\text{mol/L}$ (normal range: 0–10) pre-treatment to 14.7 $\mu\text{mol/L}$ after 1 month. During continued therapy, bile acid levels remained consistently within the range of 10–20 $\mu\text{mol/L}$, corresponding with sustained symptom control.

Four months after initiation, therapy was temporarily discontinued due to logistical constraints. Within a few days, the patient experienced a recurrence of pruritus, followed by the onset of jaundice. Notably, both symptoms abated swiftly upon re-initiation of odevixibat approximately 1 month later. This reproducible, temporally associated response highlights not only the clinical efficacy of odevixibat but also the critical importance of uninterrupted access in managing chronic cholestatic conditions.

At the time of submission of this letter, the patient is 37 months old and has been maintained on uninterrupted odevixibat therapy for the past 13 months. She demonstrates growth within normal percentiles for age and developmental milestones, preserved hearing, stable liver function, and no evidence of progressive hepatic dysfunction. Biochemical parameters, including bile acid levels, remain well-controlled (Table 1).

This case exemplifies several clinically relevant observations that align closely with the findings of Di Giorgio *et al.*: (i) Odevixibat elicits rapid and sustained resolution of pruritus in patients with PFIC, including those with genetically distinct subtypes such as PFIC 7. (ii) The decline in serum bile acids strongly correlates with clinical improvement, occurring in parallel with a moderate decrease in transaminase levels. (iii) Treatment interruption results in prompt symptom relapse, while re-initiation yields rapid resolution, underscoring both the efficacy of the agent and the necessity of uninterrupted administration. (iv) The medication was well tolerated, with no adverse events reported throughout the treatment course.

While liver transplantation remains the definitive therapeutic option for many patients with PFIC and progressive hepatic failure,³ and the efficacy of surgical biliary diversion in PFIC 7 has yet to be established,^{4,5} odevixibat offers a non-invasive alternative that may significantly enhance quality of life and potentially delay or obviate the need for surgical intervention in selected cases. Our experience supports the expansion of ileal bile acid transporter inhibitor use beyond PFIC types 1–3 to encompass *USP53*-related cholestasis.

In conclusion, we present the first reported case of odevixibat use in PFIC 7, demonstrating compelling clinical and

Table 1. Serial laboratory parameters before and after odeixibat treatment.

Timepoint	ALT/AST (U/L)	Total/direct bilirubin (mg/dl)	GGT (U/L)	Total serum bile acids (μmol/L)
At initial presentation	123/152	5.9/3.10	122	–
Before initiation of odeixibat	153/135	0.29/0.13	20	93.4
Odeixibat initiation				
1 month after initiation	210/246	0.2/0.12	–	14.7
2 months after initiation	33/216	0.4/0.11	21	–
4 months after initiation	112/189	0.3/0.18	22	–
Odeixibat interruption				
2 weeks after interruption	344/170	0.8/0.50	20	41.3
1 month after interruption	119/115	4/3.90	33	60.2
Odeixibat re-initiation				
2 months after re-initiation	252/138	0.4/0.21	19	–
5 months after re-initiation	90/58.5	0.4/0.12	21	20
13 months after re-initiation	69.5/59.3	0.4/0.15	17	10

biochemical improvement, particularly in bile acid reduction and resolution of refractory pruritus. We advocate for heightened awareness of PFIC 7 in the differential diagnosis of neonatal cholestasis and propose odeixibat as a promising therapeutic option. Further longitudinal studies are warranted to elucidate its role in modulating disease progression and enhancing transplant-free survival.

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Received 2 August 2025; Received in revised form 27 August 2025;

Accepted 3 September 2025; Available online 10 September 2025

<https://doi.org/10.1016/j.jhepr.2025.101593>

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Financial support

No support was received.

Conflict of interest

The authors declared that no conflict of interest exists.

Please refer to the accompanying ICMJE disclosure forms for further details.

Authors' contributions

A. S. Ala and A Islek substantially contributed to the conception and design of the manuscript. All authors drafted the article and made critical revisions related to the intellectual content of the manuscript and approved the final version of the article to be published.

Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jhepr.2025.101593>.

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