RESPONSE (NCT04620733) or legacy studies (NCT03602560, NCT02955602, NCT03301506, and NCT04950764). We report interim 2-year efficacy and safety results.

Patients / Materials and Methods: Patients with insufficient response/intolerance to ursodeoxycholic acid could enroll in ASSURE. Key endpoints were composite biochemical response (alkaline phosphatase [ALP] <1.67 × upper limit of normal [ULN], ALP decrease ≥15%, and total bilirubin ≤ULN) and ALP normalization. Pruritus was measured using numerical rating scale (NRS; 0–10). For patients enrolling from RESPONSE, baseline was entry to RESPONSE and analyzed as continuous seladelpar or crossover from placebo; legacy patients were analyzed separately with baseline defined as entry to ASSURE.

Results and Discussion: As of 01/2024, 158 RESPONSE and 179 legacy patients received seladelpar 10 mg daily for up to 155 weeks. In RESPONSE, 61.7% of patients met the endpoint at 12 months (M) vs 20% for placebo. In ASSURE, 61.8% (6M) and 72.4% (12M) met the composite endpoint; 75% (6M) and 93.8% (12M) of placebo crossover patients met the endpoint. In RESPONSE, ALP normalized in 25% of seladelpar and 0 placebo patients at 12M. With continued treatment, 33.3% (6M) and 17.2% (12M) had ALP normalization; 26.9% (6M) and 50% (12M) of crossover patients had ALP normalization. In ASSURE, 6-month change from baseline in pruritus NRS was similar to RESPONSE: −3.8 and −3.7 in continuous and crossover patients, respectively. At 12M and 24M, 73.2% and 69.7% of legacy patients met the endpoint in ASSURE; 42.1% and 42.4% achieved ALP normalization, and reduction in pruritus NRS was −3.8 and −3.1, respectively. There were no treatment-related serious adverse events.

Conclusions: Seladelpar treatment led to improvements in biochemical markers and pruritus, and was well tolerated with long-term use.

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OP-2 WILSON DISEASE (WD) DIAGNOSIS WITH NEXT-GENERATION SEQUENCING (NGS) IN CLINICAL PRACTICE: A PILOT STUDY

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Conflict of interest: Yes, Ultragenyx has provided 25 kits for copper panel genotyping by NGS at Mendelics laboratory

Introduction and Objectives: Wilson disease (WD) is an autosomal recessive disorder caused by a defect in the ATP7B protein, leading to copper overload. ATP7B genotyping has been performed by Sanger method, but NGS techniques have recently become available. Our aim was to analyze the impact of Sanger direct sequencing and NGS in the diagnosis of WD.

Patients / Materials and Methods: A series of 287 WD patients included 160 individuals who provided DNA after informed consent. All patients met ≥4 points of the European WD scoring system. DNA for Sanger sequencing was extracted from peripheral leukocytes and for NGS from oral cells using a buccal swab. ATP7B mutations were identified in 135 patients by Sanger sequencing only, in 17 by NGS and in 8 by both methods. Sanger sequencing was performed as previously published (Deguti et al, 2004). In targeted NGS using a "copper panel" (Laboratório Mendelics), libraries were prepared with Illumina DNA with enrichment, target regions were captured using specific probes (Twist Biosciences v.3) for all exons/intronic regions, and variants and indels were identified using GATL v4 program and CNVs using ExomeDepth.

Results and Discussion: Of the 320 alleles analyzed, the most frequent mutations were p.A1135fs (26.7%), L708P (15.8%), p.H1069Q (5.3%) and p.M645R (3.1%).The remaining 49.1% of alleles had 38 distinct disease-causing mutations, each with a frequency of <3.0%. Sanger sequencing detected a mutation in 264/286 alleles (92.3%), while the NGS method detected a mutation in 50/50 (100%). The table shows the results of the 8 patients genotyped with both methods.

Conclusions: The Sanger direct sequencing methods were laborious and detected mutations in 92.3% of *ATP7B* alleles, while NGS techniques yielded 100%, impacting the WD score by up to 4 points. This can be crucial in difficult and potentially severe cases.

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OP-3 ASSESSING TREATMENT ELIGIBILITY EXPANSION UNDER THE 2024 WHO GUIDELINES FOR CHRONIC HEPATITIS B

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Conflict of interest: No

Introduction and Objectives: The 2024 WHO guidelines for chronic hepatitis B (CHB) aim to expand and simplify treatment eligibility, but these criteria have not been assessed. We aimed to estimate treatment eligibility and uptake according to country-specific