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

Marta Mitiko Deguti[1], Michele Soares Gomes Gouvêa[2], Debora Raquel Benedita Terrabuio[1], Thiago Ferreira Araújo[2], Gilda Porta[3], Egberto Reis Barbosa[1], Eduardo Luiz Rachid Cançado[1]

[1] *HOSPITAL DAS CLÍNICAS DA FACULDADE DE MEDICINA DA USP, SAO PAULO, Brasil*
[2] *LIM-07 Laboratório de Gastroenterologia e Hepatologia Tropical do IMT da FACULDADE DE MEDICINA DA USP, SAO PAULO, Brasil*
[3] *INSTITUTO DA CRIANÇA DO HOSPITAL DAS CLÍNICAS DA FACULDADE DE MEDICINA DA USP, SAO PAULO, Brasil*

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

Manuel Mendizabal[1], Constanza D Sabate[2], Esteban Gonzalez Ballerga[3], Fernando Gruz[4], Ezequiel Ridruejo[5], Alejandro Soza[6], Jaime Poniachik[7], Grace Vergara[8], Victoria Mainardi[9], Gabriel Mezzano[10], Fernando Bessone[11], Margarita Anders[12], Mario G Pessoa[13], Fernando Cairo[14], Nelia Hernandez[13], Melisa Dirchwolf[15], Hugo Cheinquer[16], Melina Susana[13], Luis Rondeau[13], Grabriel Rifrani[11], Herman Aguirre[10], Daniela Chiodi[13], Carla Enrique[12], Lucia Navarro[14], Eugenia Labaronnie[15], Patricia M Zitelli[13], Alexandre de Araujo[16], Antonella Olivetti[13], Daniela Simian[7], Diego Giunta[8], Marcelo Silva[1], Sebastian Marciano[8]

[1] *Hospital Universitario Austral, Pilar, Argentina*
[2] *HOSPITAL UNIVERSITARIO AUSTRAL, Pilar, Argentina*
[3] *Hospital de Clínicas, Buenos Aires, Argentina*
[4] *Sanatorio Anchorena (San Martín), Buenos Aires, Argentina*
[5] *CEMIC, Buenos Aires, Argentina*
[6] *Universidad Catolica, Santiago, Chile*
[7] *Universidad de Chile, Santiago, Chile*
[8] *Hospital Italiano, Buenos Aires, Argentina*
[9] *Hospital Militar, Montevideo, Uruguay*
[10] *Hospital del Salvador, Santiago, Chile*
[11] *Hospital Centenario, Rosario, Argentina*
[12] *Hospital Aleman, Buenos Aires, Argentina*
[13] *Hospital de Clinicas, San Pablo, Brasil*
[14] *Hospital El Cruce, Florencio Varela, Argentina*
[15] *Hospital Privado de Rosario, Rosario, Argentina*
[16] *Universidad de Rio Grande, Porto Alegre, Brasil*

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

guidelines and evaluate potential treatment expansion based on the WHO guidelines.

Patients / Materials and Methods: This cross-sectional study included consecutive treatment-naïve CHB patients from Argentina, Brazil, Chile, and Uruguay who were referred for the first time to hepatology evaluation between January 2010 and June 2024. Treatment candidacy was evaluated according to both country-specific and WHO guidelines. We then estimated the difference in treatment candidacy between these two approaches.

Results and Discussion: A total of 719 patients with CHB had complete data available to evaluate treatment candidacy according to both guidelines. Of these patients, 67% were male with a median age of 52 years (IQR 38-62), and 8.1% presented with liver decompensation. Among patients, 64% were HBeAg-negative, median HBV DNA level was 43,000 IU/ml (IQR 633-110,000,000 IU/ml), median ALT was 41 U/L (IQR 23-99 U/L), and 47% had an APRI >0.5. According to country-specific guidelines, 57% (95% CI: 53-60) met criteria for treatment. Antiviral treatment was initiated in 84% of eligible patients, primarily with entecavir (63%) and tenofovir (32%). Compared to country-specific guidelines, the proportion of patients meeting treatment criteria under the WHO guidelines increased to 67% (95% CI: 63.8-70.6), resulting in a 10% (95% CI: 8-13) increase in treatment candidacy (table). Treatment expansion was higher in women (15%; 95% CI: 10-20) than in men (8%; 95% CI: 5-11).

Conclusions: According to WHO guidelines, a considerable proportion of CHB patients who do not meet country-specific criteria are eligible for antiviral therapy. Notably, treatment expansion is higher in women. Implementing WHO criteria can enhance treatment rates and advance efforts toward CHB elimination.

		Treatment candidacy by 2024 WHO guidelines		
		NO	YES	total
Treatment candidacy by country-specific guidelines	NO	235 (33%)	75 (10%)	310 (43%)
	YES	0 (0%)	409 (57%)	409 (57%)
	total	235 (33%)	484 (67%)	719 (100)

The absolute number and percentage of individuals for whom the criteria according to the local guidelines were concordant or discordant with the WHO treatment criteria are presented (n=719)

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OP- 4 EPIDEMIOLOGY OF PRIMARY BILIARY CHOLANGITIS IN LATIN AMERICA: PRELIMINARY RESULTS FROM ALLATIN COHORT

Guilherme Grossi Lopes Cançado[1], Rafael Theodoro[1], Ezequiel Ridruejo[2], Lorena Castro Solari[3], Cristiane Alves Villela-Nogueira[4], Pablo Andres Coste Murillo[5], Harlim Rodríguez[6], Carlos Benítez Gajardo[7], Álvaro Urzúa[8], Eira Cerda Reyes[9], Paulo Lisboa Bittencourt[10], Alejandro Sosa[11], Emilia Vera[12], Luciana Costa Faria[1], Maria Lucia Ferraz[13], Mario Guimarães Pessoa[14], Debora Raquel Benedita Terrabuio[14], Eduardo Luiz Rachid Cançado[14], Claudia Alves Couto[1]

[1] *Universidade Federal de Minas Gerais, Belo Horizonte, Brasil*
[2] *Centro de Educación Médica e Investigaciones Clínicas Norberto Quirno, Buenos Aires, Argentina*
[3] *Clinica Universidad de Los Andes, Santiago, Chile*
[4] *Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brasil*
[5] *Hospital R. A. Calderón Guardia, San José, Costa Rica*
[6] *Instituto de Gastroenterología de Cuba, Habana, Cuba*
[7] *UC Christus, Santiago, Chile*
[8] *Universidad de Chile, Santiago, Chile*
[9] *Hospital Militar Central México, Ciudad de México, México*
[10] *Hospital Portugues, Salvador, Brasil*
[11] *Pontificia Universidad Católica de Chile, Santiago, Chile*
[12] *Hospital Regional Guayaquil, Guayaquil, Ecuador*
[13] *Universidade Federal de São Paulo, São Paulo, Brasil*
[14] *Universidade de São Paulo, São Paulo, Brasil*

Conflict of interest: No

Introduction and Objectives: Primary biliary cholangitis (PBC) may present differently depending on various factors such as ethnicity and genetic background. Latin America has a highly admixed population with a unique genetic diversity compared to other regions of the world. However, there is limited information available on the presentation and epidemiology of PBC in this region. This study aims to address the epidemiology of PBC in Latin America.

Patients / Materials and Methods: Ongoing retrospective, international, multicentric cohort study sponsored by ALEH that enrolls PBC patients from different countries in Latin America.

Results and Discussion: Data were accrued on 231 patients [Brazil (52%), Argentina (27.4%), Chile (10.8%), Costa Rica (4.5%), Cuba (3.6%), and Mexico (0.9%)], 92.1% female (mean age at diagnosis 50.5 years), 25.6% with cirrhosis at baseline. Overlap with autoimmune hepatitis was reported in 16.0% of cases. Most patients were symptomatic (67.9%) at diagnosis, with fatigue (41.9%) and pruritus (40.5%) being the main symptoms. Antimitochondrial antibodies (AMA) were positive in 70.8% and antinuclear antibodies (ANA) in 60.6%. Hashimoto thyroiditis (23.7%) and Sjogren syndrome (9.1%) were the most common extrahepatic autoimmune diseases associated with PBC. Mean baseline alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, and bilirubin levels were 445.9 (± 407), 89.8 (± 137.2), 37.6 (± 8.9) U/L, and 1.6 (± 3.1) mg/dL, respectively. Almost all patients (99.1%) were treated with ursodeoxycholic acid (UDCA). 67.4% achieved adequate response to UDCA according to the Toronto criteria and 32% normalized alkaline phosphatase at 12 months. Only 19.9% received second-line therapy, all with fibrates (89.1% bezafibrate, 8.7% ciprofibrate, 4.3% fenofibrate). Of the patients, 9% died, with 33% of deaths being liver-related, while 6% underwent liver transplantation. Hepatocellular carcinoma was diagnosed in 1.7% of patients.

Conclusions: In this unprecedented study, the epidemiology of PBC in Latin America appears similar to that in other parts of the world. However, lower rates of AMA positivity were observed, and most patients were still diagnosed with symptomatic disease. Second-line therapy options were limited to the availability of fibrates only.

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