

Baseline Characteristics and Risk Profiles of 1111 Patients With Primary Biliary Cholangitis (PBC) in Need of Second-Line Therapy

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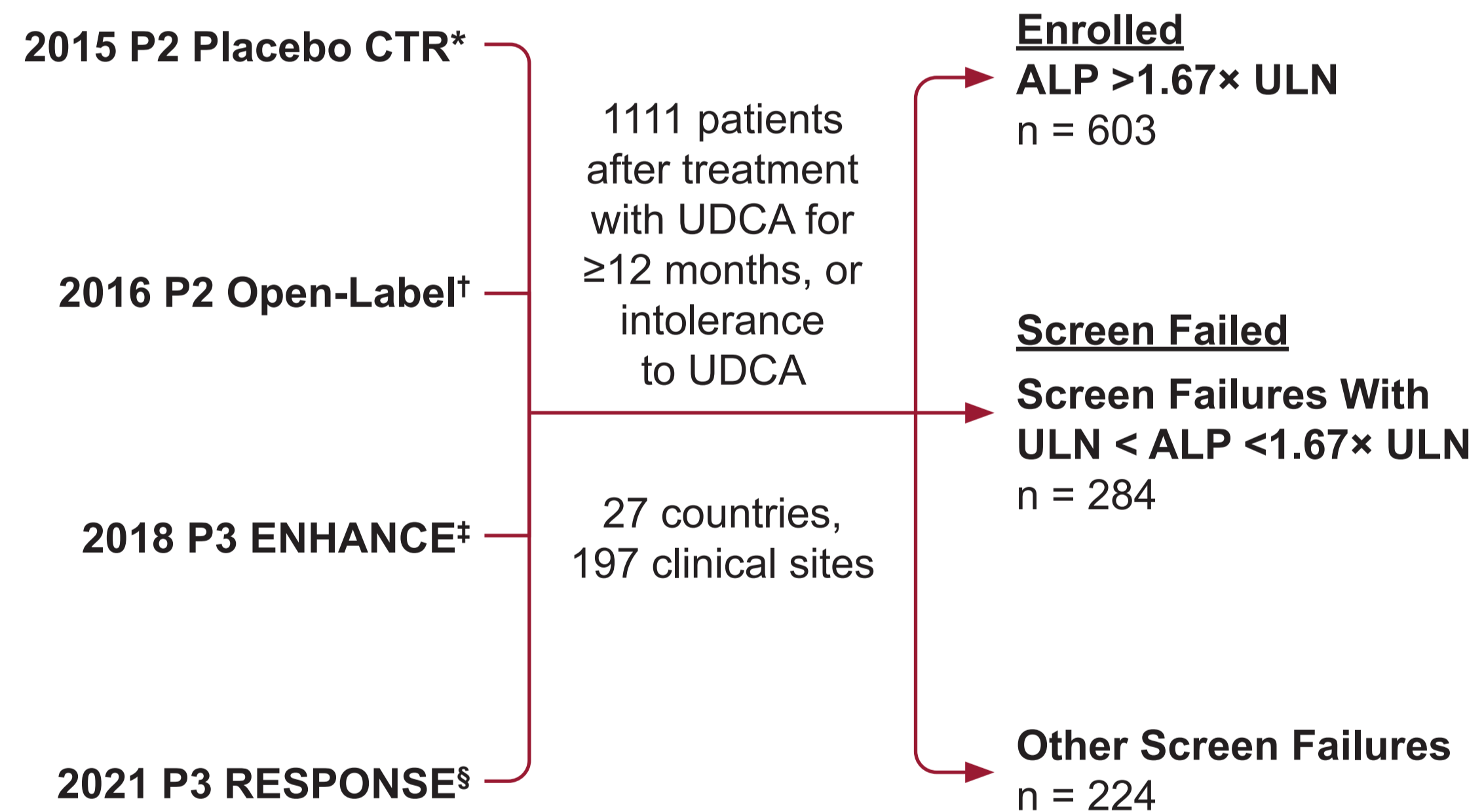
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BACKGROUND AND AIMS

- Ursodeoxycholic acid is the first-line treatment for primary biliary cholangitis
- Up to 40% of patients receiving UDCA have an ALP $\geq 1.67 \times$ ULN and are usually considered for second-line therapy to prevent progression¹
- Cohort studies show that any elevation of ALP or bilirubin indicates an increased risk of adverse outcomes²
- We examined patients who screen failed due to elevated ALP $< 1.67 \times$ ULN to further characterize this population, including the presence of additional risk factors for progression

METHODS

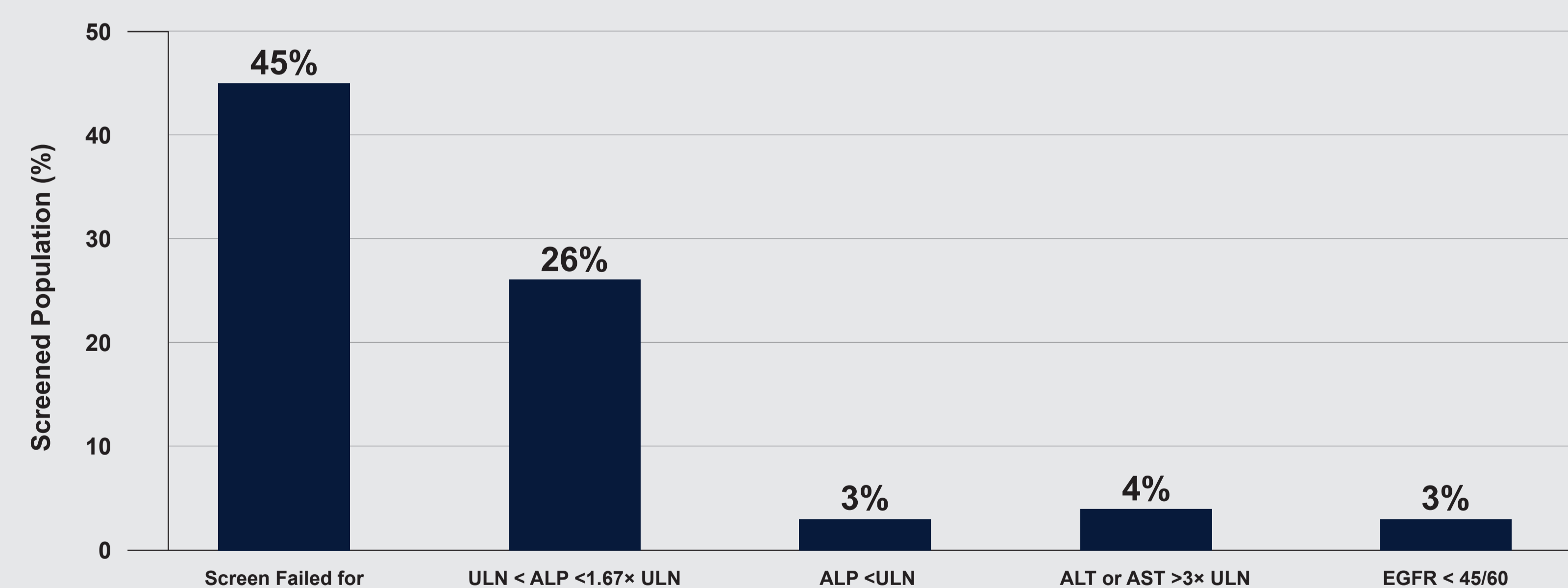


- ALP levels of $\geq 1.67 \times$ ULN were required for enrollment
- We compared the baseline characteristics and risk profiles of patients enrolled (ALP $\geq 1.67 \times$ ULN) to those who screen failed due to ALP, with $< 1.67 \times$ ULN but $> ULN$
- We assessed key characteristics reflecting risk of progression in the Enrolled and Screen Failed cohorts and summarized percentages of patients with elevated risk based on total bilirubin, ELF, and other parameters

Demographic and Baseline Characteristics

Mean \pm SD	Enrolled (n = 603)	Screen Failed With ULN $< 1.67 \times$ ULN (n = 284) [¶]	All (N = 1111)
Female, n (%)	570 (94.5)	264 (93.0)	1044 (94.0)
Age, years	56 \pm 9.3	58 \pm 9.6	57 \pm 9.5
Duration of PBC, years	8 \pm 6.5	NA	NA
UDCA dose, mg/kg/day	14.8 \pm 3.89	NA	NA
% on UDCA	92%	NA	NA
ALP, U/L	303.6 \pm 123.58	160.9 \pm 19.02	275.8 \pm 162.24
TB, mg/dL	0.7 \pm 0.32	0.7 \pm 0.36	0.8 \pm 0.56
ALT, U/L	46.7 \pm 22.33	30.8 \pm 15.79	47.2 \pm 35.45
GGT, U/L	246.0 \pm 213.83	117.2 \pm 85.46	226.5 \pm 255.24
AST, U/L	40.4 \pm 16.51	28.4 \pm 12.83	41.1 \pm 27.63
Platelet count, 10 ³ cells/ μ L	243.9 \pm 79.02	234.7 \pm 73.79	237.0 \pm 80.62
Albumin, g/dL	4.1 \pm 0.27	4.2 \pm 0.29	4.1 \pm 0.31
ELF score	9.9 \pm 1.03	9.5 \pm 0.90	9.9 \pm 1.06
Liver stiffness, kPa	9.7 \pm 6.38	NA	NA

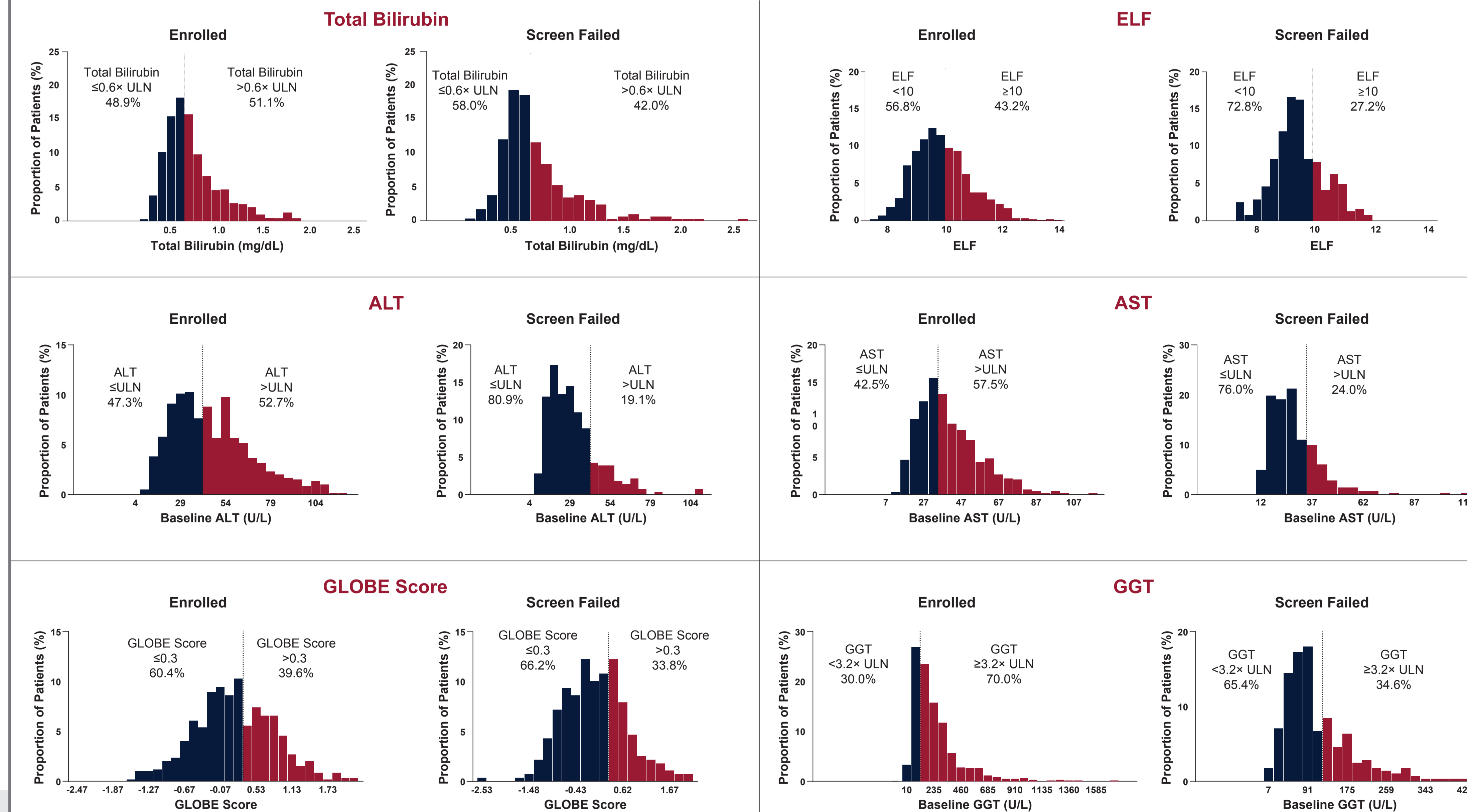
The Most Common Reasons for Screen Failure#



- Studies enrolled 54% of screened patients (n = 603) with a duration of PBC of 8 \pm 6.5 years and on a UDCA dose of 14.8 \pm 3.89 mg/kg/day (92% were on UDCA)
- Overall, 26% of patients (n = 284) screen failed due to ALP $> ULN$ but $< 1.67 \times$ ULN
- Meaningful differences in baseline values in the Enrolled and Screen Failed cohorts were in ALP, ALT, and GGT

RESULTS

Distribution of Key Patient Characteristics in Enrolled and Screen Failed Cohorts



CONCLUSIONS

- We found that in this large international cohort of UDCA-treated patients with PBC who have ALP levels above normal but $< 1.67 \times$ ULN, clinical risk factors for disease were common
- Consideration should be given to including this population in clinical research of second-line therapies with a goal of normalization of ALP

REFERENCES

1. Lindor KD, et al. *Hepatology*. 2019;69(1):394-419. 2. Murillo Perez CF, et al. *Am J Gastroenterol*. 2020;115(7):1066-1074.

DISCLOSURES

GH: Consulting, CymaBay Therapeutics, Escent, Gilead, GlaxoSmithKline, Intercept, Ipsen, Mirum, and Pliant; Lectures, presentations, speaker bureaus, manuscript writing, or educational events, GlaxoSmithKline, Intercept, and Ipsen. KK: Consulting, 89 Bio, Calliditas, CymaBay Therapeutics, Department of Justice, Genfit, Gilead, Inpharm, Intercept, Ipsen, Madrigal, Mirum, NGM, Pliant, and Zydus; Speaker bureau, 89 Bio, AbbVie, CymaBay Therapeutics, Genfit, Gilead, and Intercept; Grants, 89 Bio, CymaBay Therapeutics, Genfit, Gilead, GlaxoSmithKline, Hanmi, HighTide, Intercept, Janssen, Madrigal, Mirum, NGM, Pfizer, Pliant, Viking, and Zydus; Stock, Inpharm; Royalties, UpToDate; Data safety/advisory boards, CTI, Durect, and Labcorp; Materials or other services, Sonic Insight. AEK: Consulting, AbbVie, Bayer, Beiersdorf, CymaBay Therapeutics, Escent, FMC, Gilead, GlaxoSmithKline, Guidepoint, Intercept, Medscape, Mirum, MSD, Myr, Roche, and Viofor; Lectures, presentations, speaker bureaus, manuscript writing, or educational events, AbbVie, AOP Orphan, Bayer, Bristol Myers Squibb, CMS, CymaBay Therapeutics, Dr. Falk, Eisai, Eli Lilly, Gilead, GlaxoSmithKline, Intercept, Janssen, MSD, Newbridge, Novartis, and Zambon; Grants, AbbVie, AOP Orphan, Bayer, Bristol Myers Squibb, CMS, CymaBay Therapeutics, Dr. Falk, Eisai, Eli Lilly, Gilead, GlaxoSmithKline, Intercept, Janssen, MSD, Newbridge, Novartis, and Zambon; Advisory boards, AbbVie, Bayer, Beiersdorf, CymaBay Therapeutics, Escent, FMC, Gilead, GlaxoSmithKline, Guidepoint, Intercept, Medscape, Mirum, MSD, Myr, Roche, and Viofor. JMW: Grants, CymaBay Therapeutics, Genfit, Eli Lilly, Intercept, Novartis, and Sagiment; Advisory boards, Arena, Blade, CymaBay Therapeutics, Eli Lilly, Fractyl, Intercept, Ipsen, Kezar, Labcorp, Moderna, Novartis, Sagiment, and Taiwan J; Board Member and stock owner, Athenex. CB: Consulting, BiomX, CymaBay Therapeutics, Eli Lilly, GlaxoSmithKline, Mirum, Shire, and Trevi Therapeutics; Grants, Arena, Bristol Myers Squibb, Calliditas, Chemoab, COUR Pharmaceuticals, CymaBay Therapeutics, Eli Lilly, Genfit, Gilead, GlaxoSmithKline, Hanmi, Intercept, Novartis, Novo Nordisk, Pliant, Takeda, and TARGET. CL: Consulting, Calliditas, Cara Therapeutics, CymaBay Therapeutics, Escent, Genfit, Gilead, GlaxoSmithKline, Intercept, Ipsen, Mirum, and Target RWE; Grants, Calliditas, Cara Therapeutics, CymaBay Therapeutics, Escent, Genfit, Gilead, GlaxoSmithKline, HighTide, Intercept, Ipsen, Mirum, Novartis, Target RWE, and Zydus; Advisory boards, Cara Therapeutics, CymaBay Therapeutics, and GlaxoSmithKline. MJM: Consulting, CymaBay Therapeutics, GlaxoSmithKline, Ipsen, and Mallinckrodt; Speaker bureau, Intra-Sana; Grants, CymaBay Therapeutics, Genfit, GlaxoSmithKline, Intercept, Mallinckrodt, Mirum, and TARGET. All other authors are employees of CymaBay Therapeutics, Inc.

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ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CTR, control; EGFR, estimated glomerular filtration rate; ELF, enhanced liver fibrosis; GGT, gamma-glutamyl transferase; NA, not available; TB, total bilirubin; UDCA, ursodeoxycholic acid; ULN, upper limit of normal.