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

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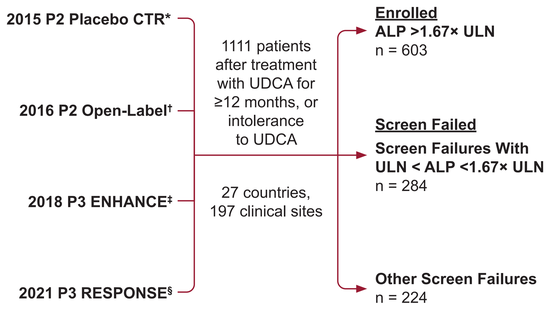
## BACKGROUND AND AIMS

- Ursodeoxycholic acid is the first-line treatment for primary biliary cholangitis
- Up to 40% of patients receiving UDCA have an ALP ≥1.67× ULN and are usually considered for second-line therapy to prevent progression[1]
- Cohort studies show that any elevation of ALP or bilirubin indicates an increased risk of adverse outcomes[2]
- We examined patients who screen failed due to elevated ALP <1.67× ULN to further characterize this population, including the presence of additional risk factors for progression

## METHODS



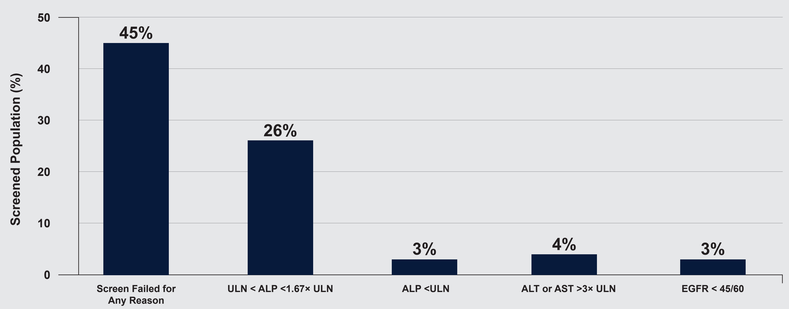

- ALP levels of ≥1.67× ULN were required for enrollment
- We compared the baseline characteristics and risk profiles of patients enrolled (ALP ≥1.67× ULN) to those who screen failed due to ALP, with <1.67× ULN but >ULN
- We assessed key characteristics reflecting risk of progression in the Enrolled and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

## RESULTS

### Demographic and Baseline Characteristics

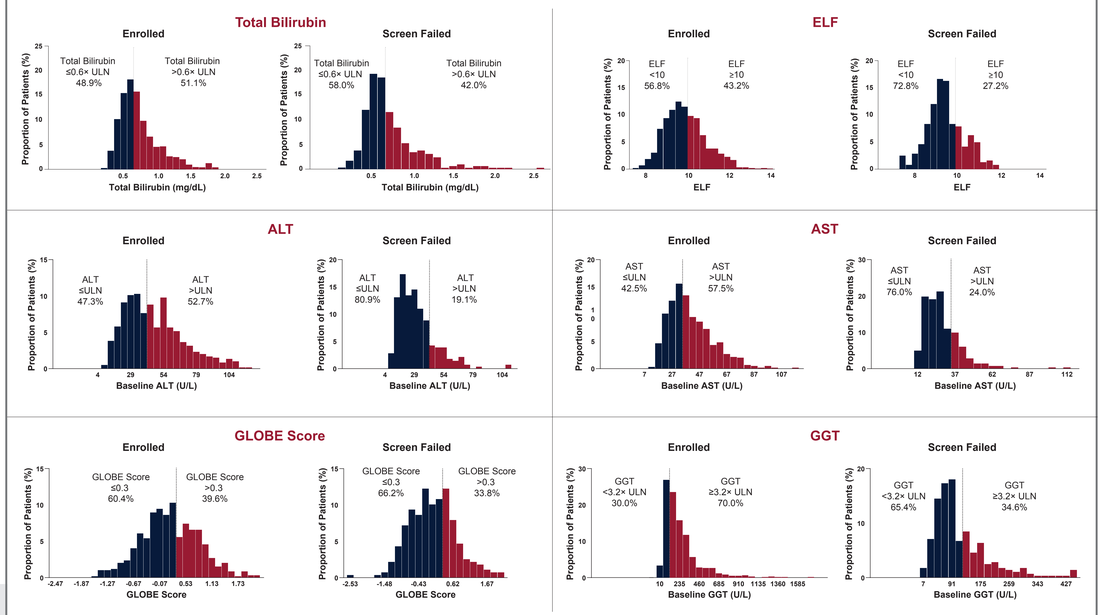
| Mean ± SD | Enrolled (n = 603) | Screen Failed With ULN < ALP <1.67× ULN (n = 284)¶ | All (N = 1111) |
|---|---|---|---|
| Female, n (%) | 570 (94.5) | 264 (93.0) | 1044 (94.0) |
| Age, years | 56 ± 9.3 | 58 ± 9.6 | 57 ± 9.5 |
| Duration of PBC, years | 8 ± 6.5 | NA | NA |
| UDCA dose, mg/kg/day‖ | 14.8 ± 3.89 | NA | NA |
| % on UDCA | 92% | NA | NA |
| ALP, U/L | 303.6 ± 123.58 | 160.9 ± 19.02 | 275.8 ± 162.24 |
| TB, mg/dL | 0.7 ± 0.32 | 0.7 ± 0.36 | 0.8 ± 0.56 |
| ALT, U/L | 46.7 ± 22.33 | 30.8 ± 15.79 | 47.2 ± 35.45 |
| GGT, U/L | 246.0 ± 213.83 | 117.2 ± 85.46 | 226.5 ± 255.24 |
| AST, U/L | 40.4 ± 16.51 | 28.4 ± 12.83 | 41.1 ± 27.63 |
| Platelet count, $10^3$ cells/µL | 243.9 ± 79.02 | 234.7 ± 73.79 | 237.0 ± 80.62 |
| Albumin, g/dL | 4.1 ± 0.27 | 4.2 ± 0.29 | 4.1 ± 0.31 |
| ELF score | 9.9 ± 1.03 | 9.5 ± 0.90 | 9.9 ± 1.06 |
| ELF ≥10.0, n | 223 | 65 | 377 |
| Liver stiffness, kPa‖ | 9.7 ± 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 ± 6.5 years and on a UDCA dose of 14.8 ± 3.89 mg/kg/day (92% were on UDCA)
- Overall, 26% of patients (n = 284) screen failed due to ALP >ULN, but <1.67× ULN
- Meaningful differences in baseline values in the Enrolled and Screen Failed cohorts were in ALP, ALT, and GGT

### 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× 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, Escient, 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, Inipharm, 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,* Inipharm; *Royalties,* UpToDate; *Data safety/advisory boards,* CTI, Durect, and Labcorp; *Materials or other services,* Sonic Insight. **AEK:** *Consulting,* AbbVie, Bayer, Beiersdorf, CymaBay Therapeutics, Escient, 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, Escient, FMC, Gilead, GlaxoSmithKline, Guidepoint, Intercept, Medscape, Mirum, MSD, Myr, Roche, and Viofor. **JMV:** *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, Chemomab, 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, Escient, Genfit, Gilead, GlaxoSmithKline, Intercept, Ipsen, Mirum, and Target RWE; *Grants,* Calliditas, Cara Therapeutics, CymaBay Therapeutics, Escient, 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.