

Native Liver Survival in Odevixibat Serum Bile Acid Responders

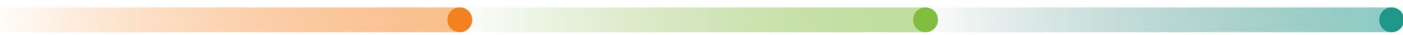
Data From the PEDFIC Studies in Patients With Progressive Familial Intrahepatic Cholestasis

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Disclosures

Richard J. Thompson

I disclose the following financial relationships with a commercial interest:

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- Mirum – Consultant
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- Rectify Therapeutics – Consultant and stockholder

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PEDFIC Centers

Icahn School of Medicine at Mount Sinai

Tübingen University Clinic for Child and Adolescent Medicine

University Medical Center Utrecht

New York Presbyterian Morgan Stanley-Komansky Children's Hospital

ASST Papa Giovanni XXIII Hospital

Saint-Luc University Clinics

University of California – San Francisco

Karolinska University

The Royal Children's Hospital (RCH)

Children's Healthcare of Atlanta – Emory University School of Medicine

University Hospital of Padua

University of Toronto – The Hospital for Sick Children (SickKids)

Riley Hospital for Children at IU Health

Ospedale Regina Margherita

Shaare-Zedek Medical Center

Johns Hopkins Children's Center

Institute of Liver Studies – King's College Hospital

Hospital Universitari Vall d'Hebron

The Children's Hospital of Philadelphia

Birmingham Children's Hospital – Birmingham Women's and Children's NHS Foundation Trust

University and Pediatric Hospital of Lyon

Colorado Children's Hospital

Leeds General Infirmary

Universitaetsklinikum Essen

Cleveland Clinic

Necker Hospital for Sick Children

Schneider Children's Medical Center of Israel

CHLA Children's Hospital Los Angeles

Hôpital Bicêtre - Paris Sud

King Faisal Specialist Hospital and Research Centre

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CHU - Hospital de la Timone

Hospital Universitario La Paz

Children's Memorial Health Institute

Hacettepe University – İhsan Doğramacı Children Hospital

Gazi University Medical Faculty Hospital Emniyet

Baylor College of Medicine – Texas Children's Liver Center

Istanbul University Medical Faculty Hospital

Inonu Universitesi Turgut Ozal Tip Merkezi

Hannover Medical School

Akdeniz University

University Medical Center Groningen

Introduction and Objective

- **PFIC:** A group of rare, inherited liver diseases
 - High serum bile acids, intractable pruritus, progressive liver disease, need for transplantation^{1,2}
- **Odevixibat:** Ileal bile acid transporter (IBAT) inhibitor
 - Efficacy and safety in PFIC evaluated in phase 3 trials^{3,4}

To analyze native liver survival (NLS) in odevixibat-treated patients with PFIC who were serum bile acid responders, partial serum bile acid responders, and non-responders

NLS Assessed in Odevixibat-treated Patients at 6 Months of Treatment According to Serum Bile Acid Responder Status

Key Definitions

NLS	Serum Bile Acid Response	Partial Serum Bile Acid Response	Serum Bile Acid Non-response
Percentage of patients who were liver transplant free	≥70% reduction or ≤70 μmol/L at month 6	≥30% to <70% reduction at month 6	<30% reduction or liver transplant or treatment discontinuation before month 6

Pooled data from the completed PEDFIC 1 and ongoing PEDFIC 2 phase 3 studies in patients with PFIC through a data cutoff of January 31, 2022

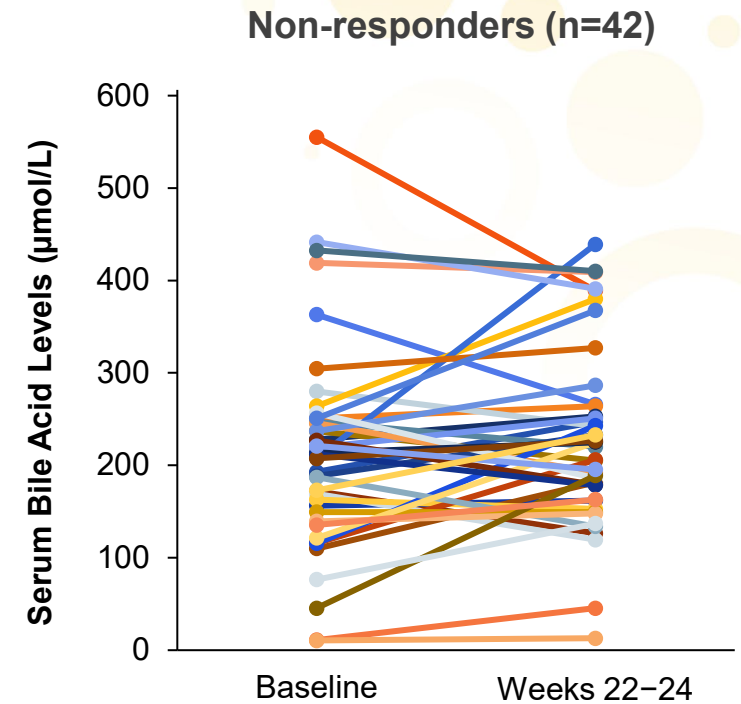
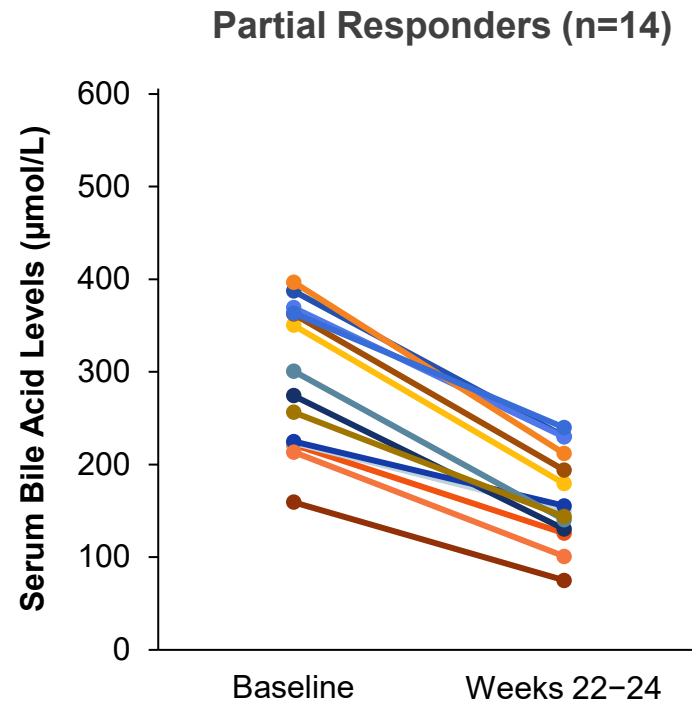
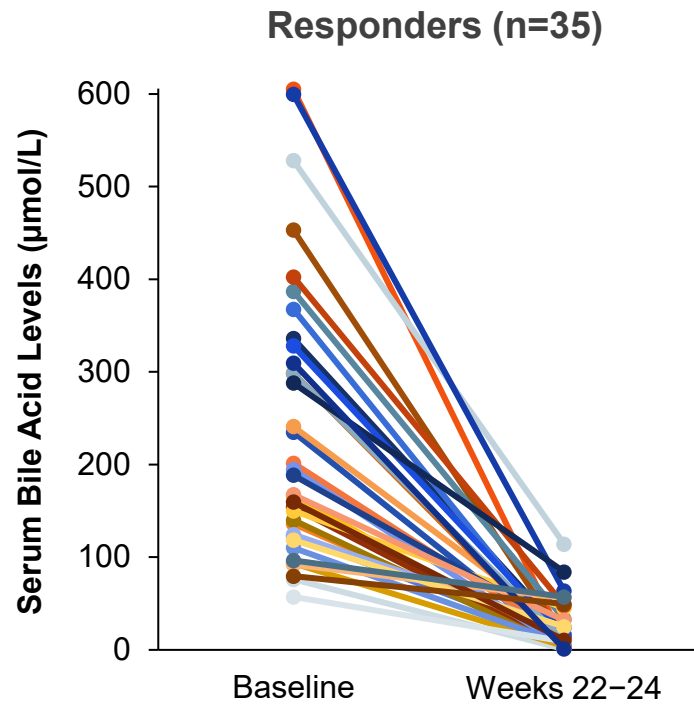
Demographics and Baseline Characteristics

	Overall (n=98)	Serum Bile Acid Responders (n=35)	Partial Serum Bile Acid Responders (n=14)	Non- responders (n=49)
Age, mean (SD), years	6.0 (5.9)	4.8 (4.6)	6.6 (8.1)	6.6 (5.9)
Female, n (%)	46 (47)	18 (51)	6 (43)	22 (45)
Key efficacy measures				
Serum bile acids, mean (SD), $\mu\text{mol/L}$	239 (124)	237 (149)	293 (78)	224 (112)
Pruritus score, mean (SD)	2.9 (0.7)	3.0 (0.6)	3.2 (0.7)	2.7 (0.7)

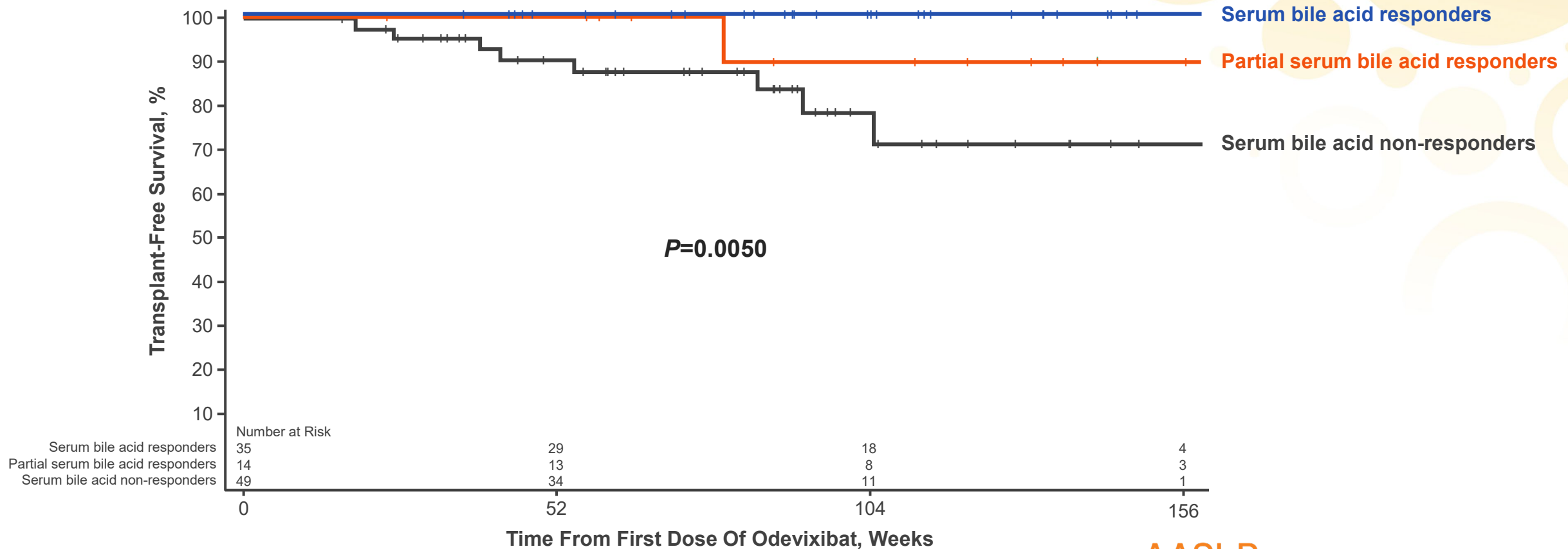
Mean Serum Bile Acids

Reduced 87% in Responders and 44% in Partial Responders at Weeks 22–24

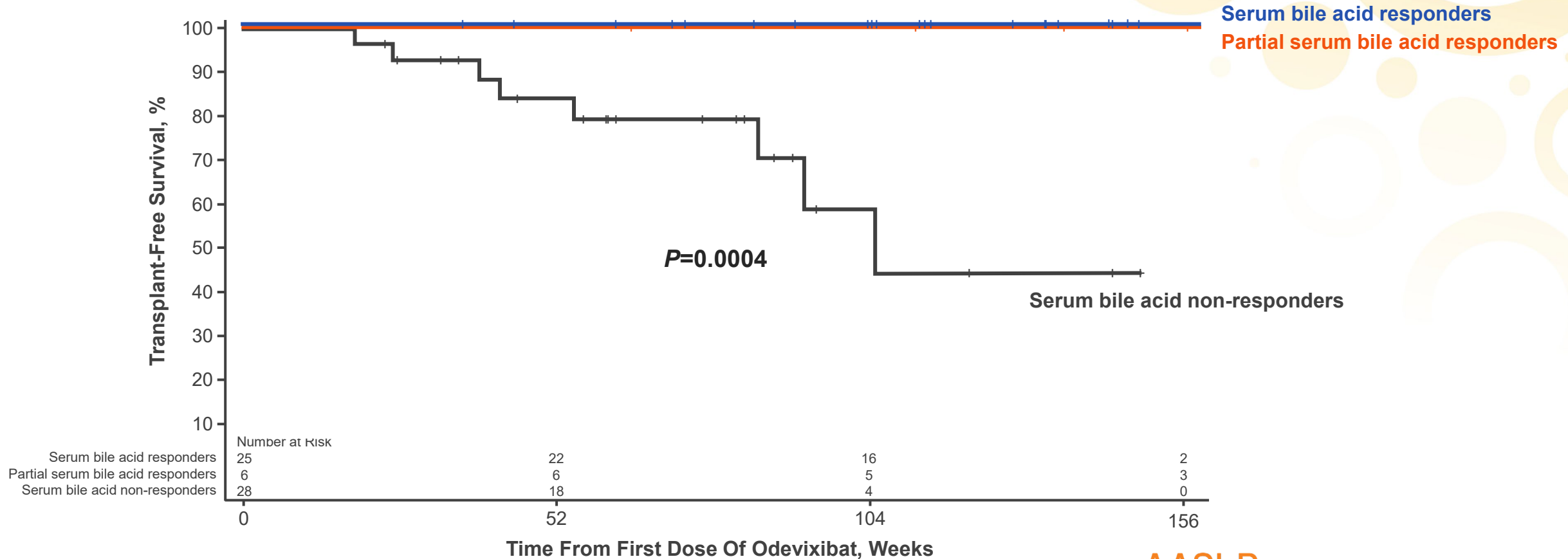
Non-responders had a mean increase of 27%



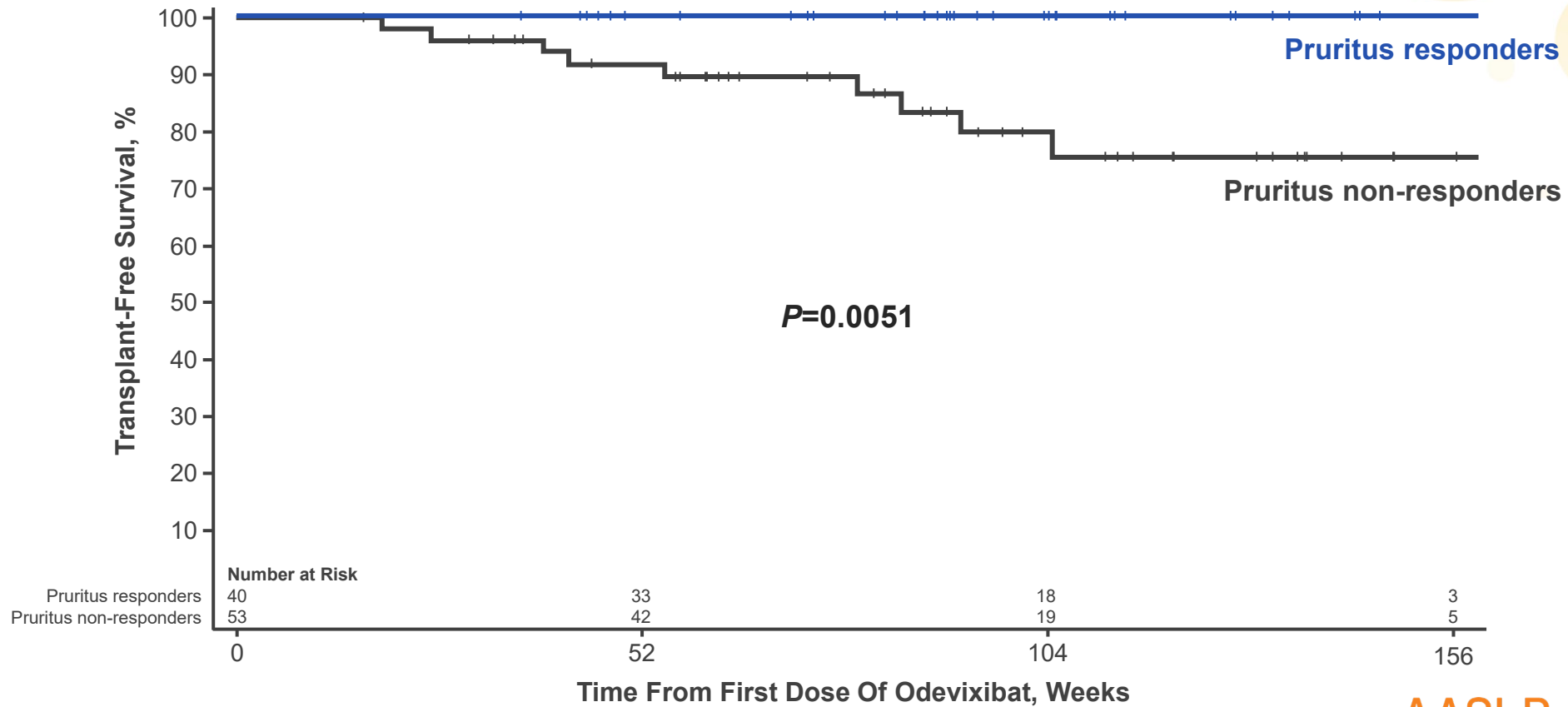
Decrease in Serum Bile Acids at 6 Months of Treatment – Strongly Associated With Native Liver Survival



In Patients With PFIC2 (BSEP Deficiency) – All Bile Acid Responders and Partial Responders Transplant Free



All Patients With a Pruritus Response at Month 6 – Remained Transplant Free

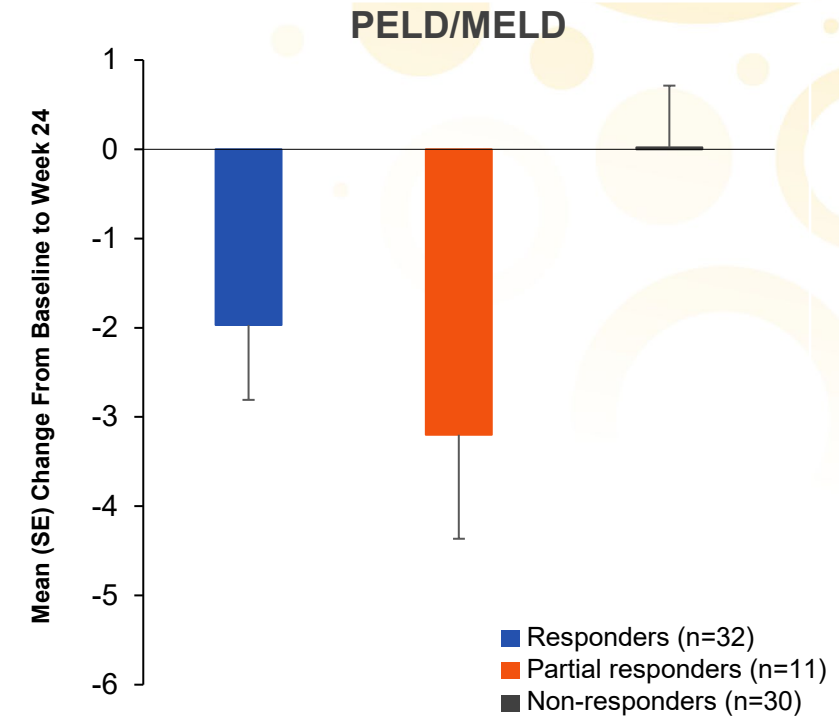
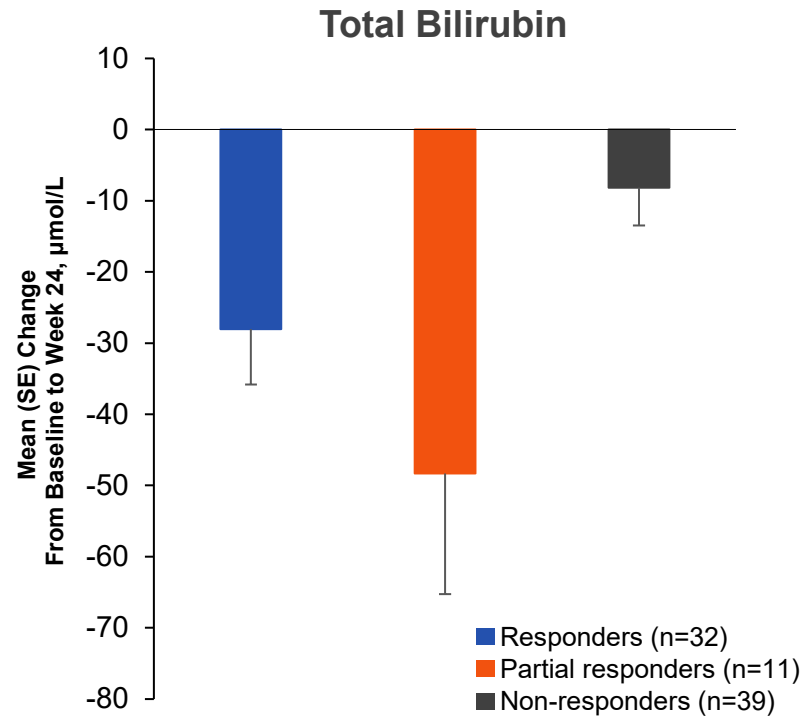
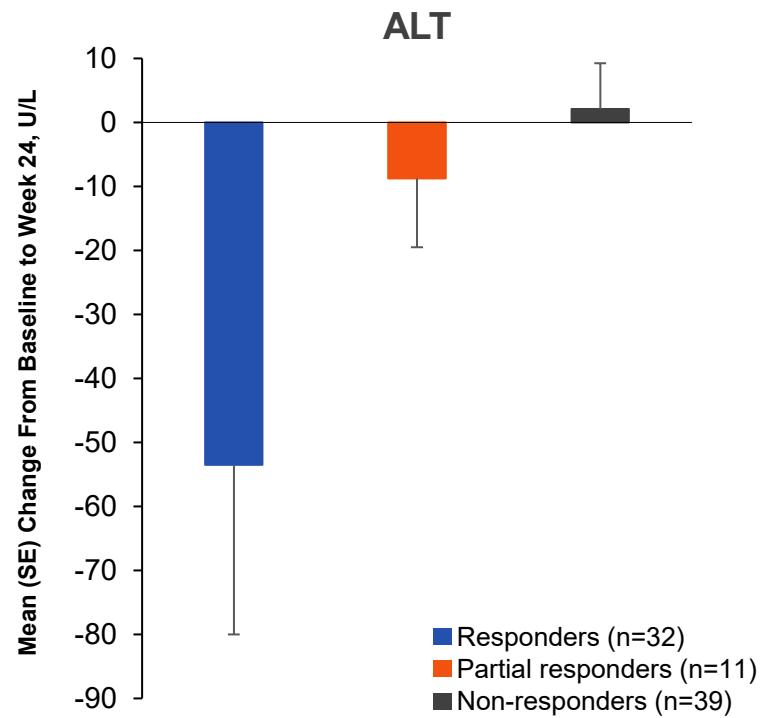


Pruritus Response
 ≥1-point drop in monthly pruritus score from baseline to month 6



P value is based on log-rank test. +, Censored.

Bile Acid Responders Had Mean Improvements in Liver Parameters at Week 24



Summary

- Patients with PFIC treated with odevixibat: decrease in serum bile acids at 6 months strongly associated with native liver survival for up to 3 years
- PFIC2: all bile acid responders and partial responders transplant free
- All patients with a pruritus response remained transplant free
- Bile acid responders had mean improvements in liver function parameters

Key Takeaway

- Patients with PFIC who responded to odevixibat remained liver transplant free for up to 3 years