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Authors

Hirschfield, G
Jones, D
Carbone, M
et al.

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LONG-TERM EFFICACY AND SAFETY OF OBETICHOCLIC ACID IN PRIMARY BILIARY CHOLANGITIS: RESPONDER ANALYSIS OF OVER 5 YEARS OF TREATMENT IN THE POISE TRIAL

G. Hirschfield[2], D. Jones[1], M. Carbone[3], C.L. Bowlus[4], F. Nevens[5], A.E. Kremer[6], A. Liberman[7], L. MacConell[7], B. E Hansen[2]

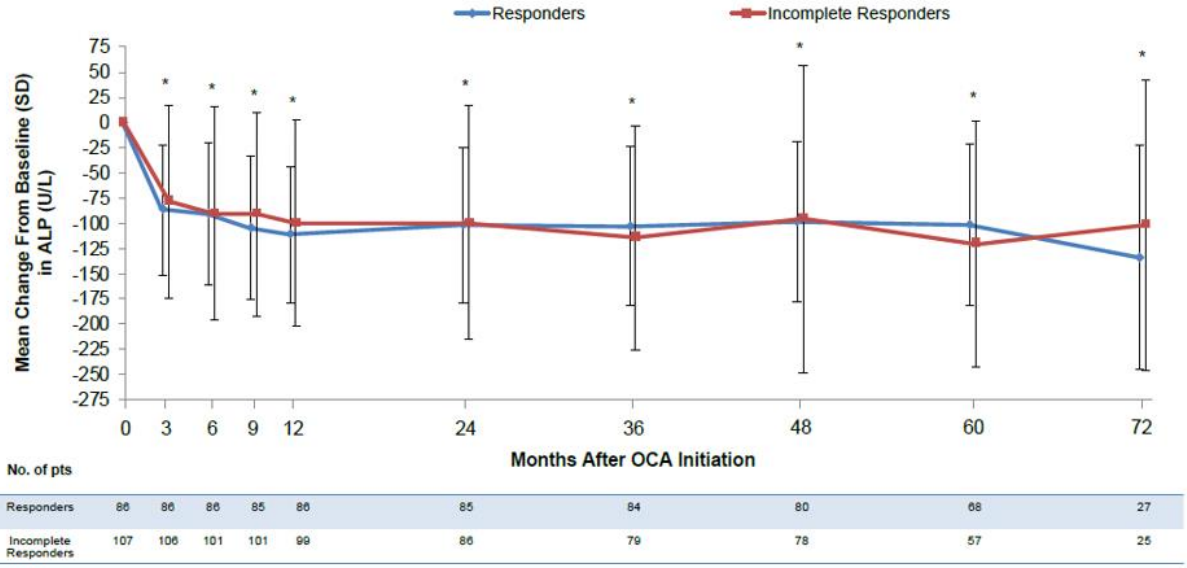
1. Newcastle University, Newcastle upon Tyne, Tyne and Wear, United Kingdom; 2. University of Toronto, Toronto, ON, Canada; 3. Universita degli Studi di Milano-Bicocca, Milano, Lombardia, Italy; 4. University of California Davis School of Medicine, Sacramento, CA; 5. University Hospitals KU, Leuven, Belgium; 6. Friedrich Alexander University of Erlangen–Nürnberg, Erlangen, Germany; 7. Intercept Pharmaceuticals, San Diego, CA

Background: Obeticholic acid (OCA), a potent farnesoid X receptor agonist, is approved as second-line treatment for primary biliary cholangitis (PBC) in patients with an incomplete response or intolerance to ursodeoxycholic acid.
Aims: We evaluated the effect of OCA in PBC patients enrolled in the POISE trial, comparing those who did or did not achieve the POISE response criteria.
Methods: The phase 3, randomized, double-blind, 1-year POISE trial evaluated the efficacy and safety of OCA 5 and 10 mg vs placebo in patients with PBC; a 5-year open-label extension followed in which all patients received OCA. This analysis evaluated longer-term efficacy and safety in patients who achieved the POISE primary endpoint of alkaline phosphatase (ALP) <1.67 × upper limit of normal (ULN), total bilirubin <ULN, and ALP decrease >15% from baseline after 1 year of OCA and in patients who were incomplete responders.
Results: The analysis included 86 patients who achieved the POISE primary endpoint at year 1 of OCA treatment and 107 incomplete responders (mean baseline ALP, 268 vs 356 U/L, respectively; *P*<0.0001). Mean change from baseline in ALP at year 5 was –101 U/L for responders and –121 U/L for incomplete responders (*P*<0.0001; **Figure**). Median (Q1, Q3) baseline GLOBE 10-year risk of event scores were 16 (11, 23) for responders and 25 (15, 43) for incomplete responders. Change from baseline in median (Q1, Q3) GLOBE 10-year risk of event at year 1, which includes age and thus increases with time, was –2 (–4, 2) for responders and –2 (–6, 4) for incomplete responders; at year 5, these changes were 2 (–2, 7) and 4 (–4, 11),

respectively. Median (Q1, Q3) baseline UK-PBC 10-year risk of event scores were 5 (3, 8) for responders and 8 (4, 16) for incomplete responders. Change from baseline in median (Q1, Q3) UK-PBC 10-year risk of event at year 1 was –1 (–3, 0.2) for responders and –1 (–3, 1) for incomplete responders; at year 5, these changes were –0.8 (–2, 0.2) and –0.05 (–2, 2), respectively. The most frequently reported AEs among responders and incomplete responders were pruritus (67%, 86%) and fatigue (35%, 31%).

Conclusions: OCA treatment improved key biochemical markers of PBC, regardless of achieving the POISE primary endpoint after 1 year of OCA treatment. Changes in biochemical parameters over time were often similar between groups.

Figure. Mean (SD) Change From Baseline in Alkaline Phosphatase Levels Through Month 72 by Responder Subgroup



No. of pts										
Responders	86	86	86	85	86	85	84	80	68	27
Incomplete Responders	107	106	101	101	99	86	79	78	57	25

*$P \leq 0.002$ within-treatment comparisons using a paired t-test.

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