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# PRURITUS EXPERIENCE IN PATIENTS WITH PRIMARY BILIARY CHOLANGITIS (PBC) TREATED WITH OBETICHOLIC ACID (OCA) FOR UP TO 6 YEARS IN THE POISE TRIAL: PATIENT-REPORTED IMPACT ON QUALITY OF LIFE

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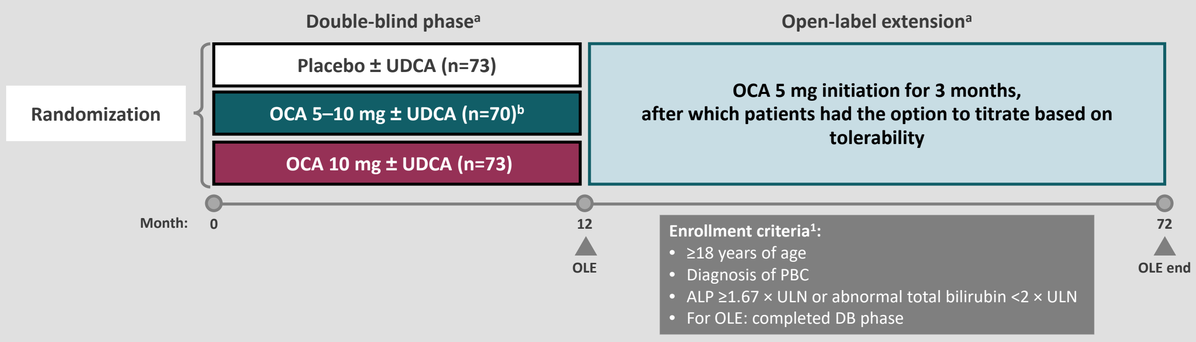
## INTRODUÇÃO

- Primary biliary cholangitis (PBC) is a rare chronic liver disease that may lead to fibrosis and cirrhosis[1-3]
- Obeticholic acid (OCA) is a potent farnesoid X receptor agonist approved as second-line treatment for PBC in patients with incomplete response or intolerance to ursodeoxycholic acid (UDCA)[4]
- The phase 3, double-blind (DB) PBC OCA International Study of Efficacy (POISE) evaluated the efficacy and safety of OCA in the treatment of patients with PBC for up to 6 years[5]
  - In POISE, pruritus was the most common treatment-emergent adverse event (TEAE) observed across all subgroups and was generally mild to moderate in severity
  - In the DB phase, 8 patients discontinued due to pruritus, including 1 patient (1%) in the OCA 5–10 mg group and 7 patients (10%) in the OCA 10 mg group[1]; 8 patients (4%) discontinued due to pruritus in the open-label extension (OLE) phase
- We evaluated the impact of OCA treatment on patient-reported outcome measures (PROs) of pruritus through 6 years

## MATERIAL/MÉTODOS

- The phase 3, randomized, DB, 1-year POISE trial evaluated the efficacy and safety of OCA 5 mg and 10 mg versus placebo in patients with PBC
- The DB phase was followed by a 5-year OLE in which all patients received OCA (**Figure 1**)[1]

**Figure 1.** POISE DB and OLE Study Design[5]




[a]Study treatment was administered with standard of care UDCA (13–15 mg/kg) or alone in patients unable to tolerate UDCA.[1]
[b]5 mg OCA for 6 months then titrated to 10 mg OCA if tolerated and ALP ≥1.67 x ULN or bilirubin >ULN, or <15% reduction in ALP.[5]

- Three PRO scales of pruritus were assessed at baseline and every 3 months (**Table 1**)

**Table 1.** Patient-Reported Outcomes Used to Assess Pruritus Severity in POISE

| Patient-Reported Outcome Scale | Score Range and Interpretation |
|---|---|
| **Pruritus Severity Visual Analogue Scale (VAS)[6]** | 0 (none)–100 (severe) |
| **5-D Pruritus Questionnaire (5-D)[7]** | 5 (none)–25 (severe) |
| **PBC-40[8]** | |
| Itch Domain | 0 (none)–15 (severe) |
| General Symptoms Domain | 6 (none)–35 (severe) |
| Fatigue Domain | 11 (none)–55 (severe) |
| Cognitive Function Domain | 6 (none)–30 (severe) |
| Social Domain | 8 (none)–50 (severe) |
| Emotional Domain | 3 (none)–15 (severe) |

- Pruritus was managed with concomitant medications, temporary OCA dose interruption, or OCA dose reduction

## RESULTADOS

### PATIENT CHARACTERISTICS

- Demographics and characteristics of study patients included in this analysis are summarized in **Table 2**

**Table 2.** Patient Characteristics

| Characteristic | Total OCA (N=193) |
|---|---|
| Age, years (range) | 55.4 (10.0) |
| Female, n (%) | 177 (92) |
| White, n (%) | 181 (94) |
| PBC Duration, years | 8.5 (6.0) |
| History of Pruritus, n (%) | 121 (63) |
| UDCA at Baseline, n (%) | 180 (93) |
| UDCA Dose, mg/kg | 15.8 (5.0) |
| ALP, U/L[a] | 317.1 (120.2) |
| >3x ULN | 51 (26) |
| Total Bilirubin, µmol/L[a] | 11.5 (7.0) |
| >ULN | 21 (11) |
| Direct Bilirubin, µmol/L[a] | 5.3 (5.6) |
| >ULN | 95 (49) |
| Albumin, g/L[a] | 42.9 (3.2) |
| <LLN | 33 (17) |
| Platelets, $10^9$/L[a] | 225.4 (84.2) |
| <LLN | 35 (18) |

Values are mean (SD) unless otherwise noted. [a]Values are based on OCA baseline.

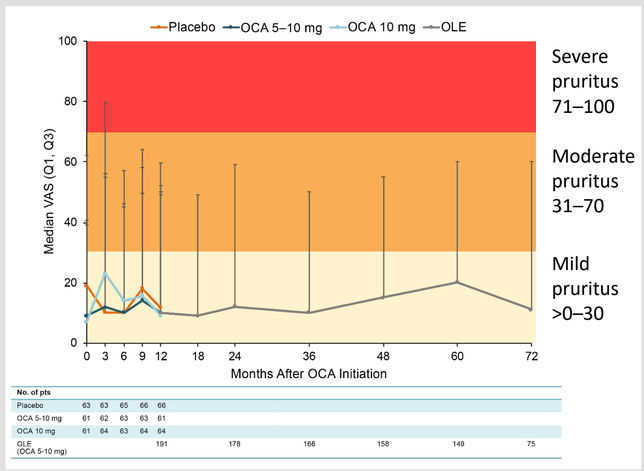
### PATIENT DISPOSITION IN THE POISE TRIAL

- Once the primary objective was met and durability of response was demonstrated
  - 76% of patients completed the study protocol as specified
  - 83 patients who completed the study protocol as specified did not reach OLE month 60 due to study closure
- 82% of patients completed 4 years of OCA treatment in the OLE
- 60% of patients completed 5 years of OCA treatment in the OLE
- 52 patients (36%) who received OCA in the DB phase completed 6 years in total on OCA treatment

### PATIENT-REPORTED OUTCOMES

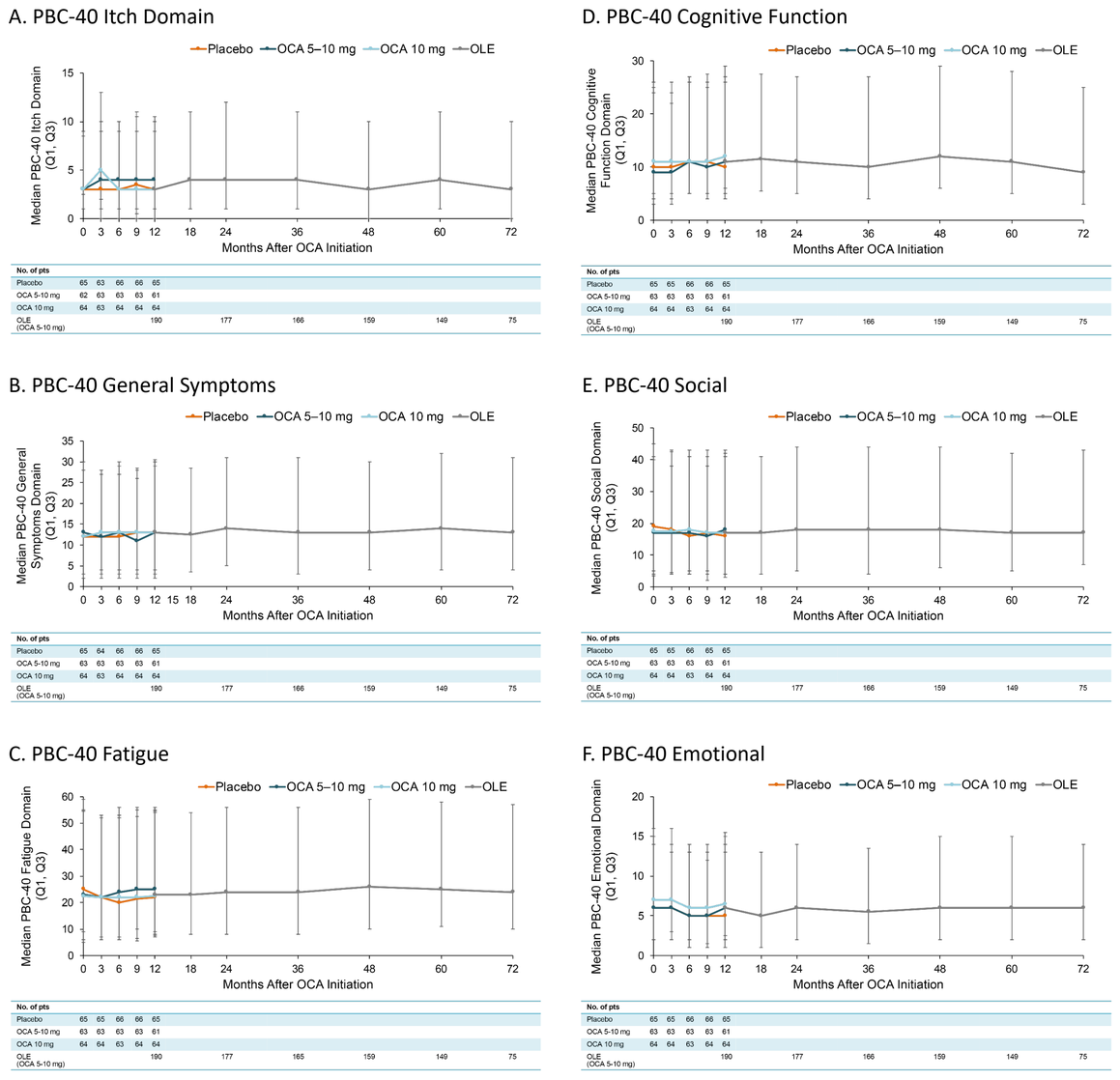
- Median pruritus VAS scores in the OCA 10 mg group were higher than placebo scores at DB month 3 but similar across groups by DB month 12; all VAS scores remained mild and stable through the OLE (**Figure 2**)

**Figure 2**. Median Pruritus VAS Scores Based on DB Baseline Through Month 72 by Treatment Arm, Safety Population




- Median 5-D scores in the OCA treatment groups were similar to placebo in the DB phase and remained stable through the 5-year OLE (data not shown)
- Median PBC-40 scores are summarized in **Figure 3**
  - PBC-40 Itch Domain scores were higher in the OCA 10 mg treatment group than placebo at DB month 3 but similar by DB month 12; as with the other PROs, the PBC-40 Itch Domain scores remained stable through the 5-year OLE
  - Similar findings were observed for scores on the other PBC-40 domains

**Figure 3**. Median PBC-40 Scores by Domain Based on DB Baseline Through Month 72 by Treatment Arm, Safety Population




## CONCLUSÕES

- In the phase 3 POISE trial, pruritus was the most common TEAE observed across all subgroups
  - Pruritus was generally mild to moderate in severity
  - Only 8 patients each in the DB and OLE phase (16 total patients) discontinued the trial due to pruritus
- The findings of this analysis demonstrate that a subset of patients in the POISE trial experienced mild pruritus
  - These observations were sustained from DB month 12 through the 5-year OLE phase
  - The patients' quality of life, reflected by the PBC-40, was not impacted by the occurrence of pruritus

## REFERÊNCIAS

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