

Table S1. Maternal baseline characteristics and outcomes for 527 women included in analysis. Data are n (%), unless otherwise indicated; N is equal to the total number of participants in the group, unless otherwise indicated; <1% of observations are missing, unless indicated.

| | Ursodeoxycholic acid (n = 271) | Placebo (n = 256) |
|---|---|------------------------------|
| Baseline characteristics | | |
| Age, years | 30.6 (5.7) | 30.5 (5.2) |
| Ethnic group | | |
| White | 224 (82%) | 212 (83%) |
| Black | 8 (3%) | 7 (3%) |
| Asian | 28 (10%) | 32 (13%) |
| Other | 9 (3%) | 5 (2%) |
| Not known | 2 (1%) | 0 (0%) |
| Body-mass index at start of pregnancy (kg/m ²), mean (SD) | 27.5 (6.5) | 26.9 (6.2) |
| Previous pregnancy of ≥24 weeks' gestation | 162 (60%) | 169 (66%) |
| History of intrahepatic cholestasis of pregnancy, n/N (%) | 87/159 (55%) | 81/167 (49%) |
| Missing, n | 3 | 2 |
| Gestational age (weeks), median (IQR) | 34.1 (31.9–35.4) | 34.1 (30.7–35.6) |
| <34 weeks | 130 (48%) | 124 (48%) |
| 34 to <37 weeks | 125 (46%) | 115 (57%) |
| ≥37 weeks | 16 (6%) | 17 (7%) |
| Twin pregnancy | 17 (6%) | 14 (5%) |
| Itch score, mean (SD) | 56.4 (24.7) | 59.1 (25.2) |
| Highest baseline serum concentration before randomisation | | |
| Bile acid (µmol/L), geometric mean (95% CI) | 27.7 (25.5–30.1) | 26.2 (24.1–28.3) |
| <40 µmol/L | 209 (77%) | 199 (78%) |
| ≥40 µmol/L | 62 (23%) | 57 (22%) |
| Alanine transaminase, N | 254 | 246 |
| Alanine transaminase (U/L), geometric mean (95% CI) | 68.7 (59.8–78.9) | 56.6 (48.8–65.5) |
| Outcomes | | |
| Maximum dose of trial medication | | |
| One tablet once a day | 4 (1%) | 4 (2%) |
| One tablet twice a day | 171 (63%) | 158 (62%) |
| One tablet three times a day | 61 (23%) | 62 (24%) |
| Two tablets twice a day | 35 (13%) | 32 (13%) |
| Mode of onset of labour | | |
| Spontaneous | 27 (10%) | 40 (16%) |
| Induced or pre-labour rupture of membranes and stimulation | 194 (72%) | 177 (69%) |
| Pre-labour caesarean | 50 (18%) | 39 (15%) |
| Estimated blood loss at delivery, mL | 350 (250–600) | 400 (250–600) |
| <500 | 175 (65%) | 162 (63%) |
| ≥500 and <1000 | 69 (25%) | 65 (25%) |
| ≥1000 | 27 (10%) | 29 (11%) |

Table S2. Perinatal outcomes for 558 infants born to 527 women included in analysis. Data are n (%), median (IQR), or mean (SD), unless otherwise indicated; N is equal to the total number of infants in the group, unless otherwise indicated; <1% of observations are missing, unless otherwise indicated.

| | Ursodeoxycholic acid (n = 288) | Placebo (n = 270) |
|--|---|------------------------------|
| Perinatal death, preterm delivery or neonatal unit admission | 63 (22%) | 68 (25%) |
| In-utero fetal death | 1 (<1%) | 2 (1%) |
| Preterm delivery | 46 (16%) | 49 (18%) |
| Known neonatal death up to 7 days after birth | 0 (0%) | 0 (0%) |
| Neonatal unit admission for >4 h | 38 (13%) | 46 (17%) |
| Gestational age at delivery, weeks | 37.6 (37.1–38.1) | 37.4 (37.1–38.1) |
| Birthweight, g | 3100 (2795–3392) | 3055 (2740–3330) |
| Mode of delivery | | |
| Spontaneous vaginal (cephalic) | 174 (60%) | 152 (56%) |
| Vaginal (breech) | 1 (<1%) | 3 (1%) |
| Assisted vaginal (cephalic) | 18 (6%) | 32 (12%) |
| Pre-labour caesarean | 64 (22%) | 54 (20%) |
| Caesarean | 31 (11%) | 29 (11%) |
| Presence of meconium-stained amniotic fluid | 29 (10%) | 46 (17%) |

Table S3. Demographics of MCID survey respondents.

| | | All women (n = 650) |
|------------|---|---|
| Experience | I am or have been pregnant and have been diagnosed with ICP | 450 (73%) |
| | I am or have been pregnant but have never been diagnosed with ICP | 153 (25%) |
| | Neither of the above | 17 (3%) |
| | | Women with experience of ICP (n = 450) |
| Age | 18–24 | 26 (6%) |
| | 25–34 | 228 (51%) |
| | 35–44 | 176 (39%) |
| | 45–54 | 17 (4%) |
| | 55+ | 3 (1%) |
| | | Clinicians (n = 116) |
| Age | 18–24 | 1 (1%) |
| | 25–34 | 16 (14%) |
| | 35–44 | 48 (41%) |
| | 45–54 | 39 (34%) |
| | 55–64 | 11 (9%) |
| | 65+ | 1 (1%) |
| Gender | Female | 95 (82%) |
| | Male | 20 (17%) |
| | Other | 1 (1%) |

Table S4. Sensitivity analysis excluding women whose adherence to the intervention was less than 90% of trial medication taken, consistently reported.

| | UDCA (n = 205) | Placebo (n = 181) | Adjusted effects estimate (95% CI), p value | Interaction test |
|--|---------------------------|------------------------------|--|-----------------------------|
| Bile acid concentration, all women, N | 195 | 173 | | |
| Bile acid concentration ($\mu\text{mol/L}$), geometric mean (SD) | 22.2 (2.3) | 17.9 (2.7) | GMR 1.20 (1.01 to 1.42) p = 0.036 | |
| Baseline bile acid conc. <40 $\mu\text{mol/L}$, N | 152 | 135 | | |
| Bile acid concentration ($\mu\text{mol/L}$), geometric mean (SD) | 19.3 (2.2) | 15.6 (2.5) | GMR 1.20 (1.00 to 1.45) p = 0.055 | p = 0.718 |
| Baseline bile acid conc. \geq40 $\mu\text{mol/L}$, N | 43 | 38 | | |
| Bile acid concentration ($\mu\text{mol/L}$), geometric mean (SD) | 36.5 (2.0) | 29.6 (2.9) | GMR 1.20 (0.81 to 1.77) p = 0.369 | |
| Baseline bile acid conc. <100 $\mu\text{mol/L}$, N | 183 | 166 | | |
| Bile acid concentration ($\mu\text{mol/L}$), geometric mean (SD) | 21.3 (2.2) | 17.2 (2.6) | GMR 1.22 (1.03 to 1.46) p = 0.025 | p = 0.417 |
| Baseline bile acid conc. \geq100 $\mu\text{mol/L}$, N | 12 | 7 | | |
| Bile acid concentration ($\mu\text{mol/L}$), geometric mean (SD) | 43.5 (2.3) | 51.1 (2.6) | GMR 0.90 (0.40 to 2.01) p = 0.793 | |
| Itch score, all women, N | 191 | 168 | | |
| Itch score (mm), mean (SD) | 49.7 (25.5) | 55.6 (26.7) | MD -4.65 (-9.50 to 0.19) p = 0.060 | |
| Baseline itch score <60 mm, N | 86 | 67 | | |
| Itch score (mm), mean (SD) | 40.7 (24.3) | 44.9 (24.1) | MD -4.81 (-11.95 to 2.34) p = 0.189 | p = 0.975 |
| Baseline itch score \geq60 mm, N | 105 | 101 | | |
| Itch score (mm), mean (SD) | 57.2 (24.1) | 62.6 (26.0) | MD -4.46 (-11.22 to 1.94) p = 0.168 | |
| Baseline bile acid conc. <40 $\mu\text{mol/L}$, N | 151 | 134 | | |
| Itch score (mm), mean (SD) | 50.3 (26.0) | 55.3 (26.5) | MD -4.05 (-9.46 to 1.35) p = 0.143 | p = 0.668 |
| Baseline bile acid conc. \geq40 $\mu\text{mol/L}$, N | 40 | 34 | | |
| Itch score (mm), mean (SD) | 47.6 (23.6) | 56.5 (27.5) | MD -6.92 (-17.93 to 4.09) p = 0.222 | |
| Baseline bile acid conc. <100 $\mu\text{mol/L}$, N | 182 | 162 | | |
| Itch score (mm), mean (SD) | 49.8 (25.6) | 55.9 (26.4) | MD -5.08 (-9.93 to -0.22) p = 0.041 | p = 0.257 |
| Baseline bile acid conc. \geq100 $\mu\text{mol/L}$, N | 9 | 6 | | |
| Itch score (mm), mean (SD) | 49.1 (24.0) | 47.5 (34.5) | MD -8.07 (-40.92 to 24.78) p = 0.639 | |