Jim Thornton's prediction of the PITCHES trial results. (#18337)

Author(s)

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1) Have any data been collected for this study already?

It's complicated. We have already collected some data but explain in Question 8 why readers may consider this a valid pre-registration nevertheless.

2) What's the main question being asked or hypothesis being tested in this study?

The PITCHES trial is testing the hypothesis that ursodeoxycholic acid improves baby outcomes in pregnancies complicated by intra-hepatic cholestasis of pregnancy.

3) Describe the key dependent variable(s) specifying how they will be measured.

A composite of perinatal death (as defined by in utero fetal death after randomisation or known neonatal death up to 7 days) or preterm delivery (less than 37 weeks' gestation) or neonatal unit admission for at least 4 hours (between infant delivery and hospital discharge)

4) How many and which conditions will participants be assigned to?

Intervention: UDCA 1g daily (500mg bd), increased in increments of 500mg per day every 3-14 days if there is no biochemical or clinical improvement, based on clinical decision, to a maximum of 2g per day.
Control: Identical placebo tablets administered in the same dose increments.

5) Specify exactly which analyses you will conduct to examine the main question/hypothesis.

The analysis plan has been written and signed off.

6) Describe exactly how outliers will be defined and handled, and your precise rule(s) for excluding observations.

Analysis will be by intention to treat.

7) How many observations will be collected or what will determine sample size? No need to justify decision, but be precise about exactly how the number will be determined.

580 women. 290 per group.

8) Anything else you would like to pre-register? (e.g., secondary analyses, variables collected for exploratory purposes, unusual analyses planned?)

I am a co-investigator. I participated in all aspects of the trial design and recruited a number of participants. Recruitment and follow-up are now complete, the database is locked and analysis is ongoing. However, I have not seen any outcomes by group so these predictions are data independent. These are my personal predictions, not necessarily those of my co-investigators.

I predict the result will be negative. i.e. that the 95% confidence interval for the relative risk of UDCA on the primary outcome will include 1.

I predict that all three pre-specified subgroups will also be negative.

With one exception I predict no statistically significant differences (5% level) in any secondary outcomes, after adjustment for multiple testing.

The exception is "Itch between randomisation and delivery, measured by the worst episode of itch over the past 24 hours (mm on visual analogue scale, assessed at clinic visits)". I predict that the mean worst itch score will be reduced in the UDCA group and that the difference will be statistically significant at the 5% level even after adjusting for multiple testing. However, I also predict that the 95% confidence interval for the mean difference will exclude a 30mm improvement. i.e. that most patients will not regard this as a clinically worthwhile effect.