Item S1. Detailed methods

Data source

Individual patient-level data from the randomized phase 3 TEMPO 3:4 trial of tolvaptan were used in this study.[1] The study design, patient characteristics, and ethical approvals of TEMPO 3:4 have been previously published.[1] In short, 1445 patients aged 18 to 50 years with early autosomal dominant polycystic kidney disease (ADPKD; total kidney volume ≥750 ml and estimated creatinine clearance ≥60 ml per minute) were randomly assigned to receive tolvaptan or placebo for three years.

Outcomes

Liver function abnormalities were measured by elevation in alanine aminotransferase (ALT) to >3 times (3x) and >5 times (5x) the upper limit of normal range (ULN), as well as serious ALT or aspartate aminotransferase (AST) elevation as defined in TEMPO 3:4.[1]

As this is a post-hoc analysis of previously published data, no ethical review was required.

Number needed to harm calculations

Number needed to harm (NNH) values related to liver function abnormalities were assessed over 12 months and 24 months of treatment initiation. NNH was calculated as the reciprocal of the difference in the proportion of patients experiencing an outcome between tolvaptan and placebo over 12 or 24 months. The 95% confidence intervals (CIs) were estimated as the reciprocals of the upper and lower bounds of the 95% CI of the risk difference.[2] If the risk

difference was not statistically significantly different from zero (i.e., the CIs contain infinity), the CIs were denoted as not significant (ns).

REFERENCES

1. Torres VE, Chapman AB, Devuyst O, et al. Tolvaptan in patients with autosomal dominant polycystic kidney disease. *N Engl J Med*. 2012/12/20 2012;367(25):2407-2418. doi:10.1056/NEJMoa1205511
2. Altman DG. Confidence intervals for the number needed to treat. *BMJ*. 1998;317(7168):1309-1312. doi:10.1136/bmj.317.7168.1309