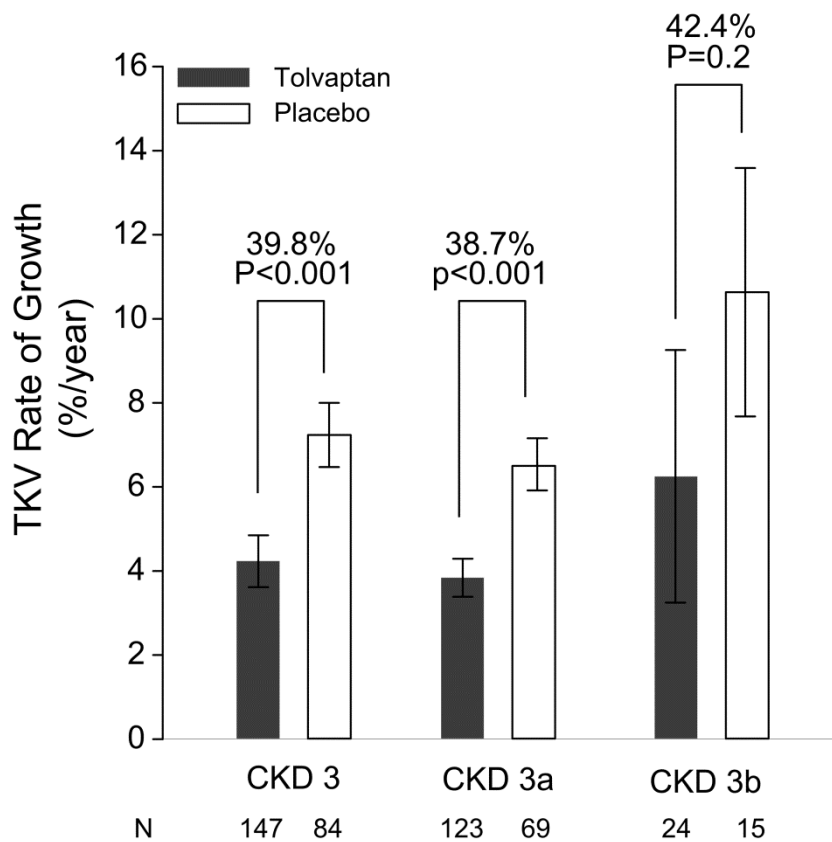


Supplemental Material

EFFECT OF TOLVAPTAN IN ADPKD BY CKD STAGE: RESULTS FROM THE TEMPO 3:4 TRIAL

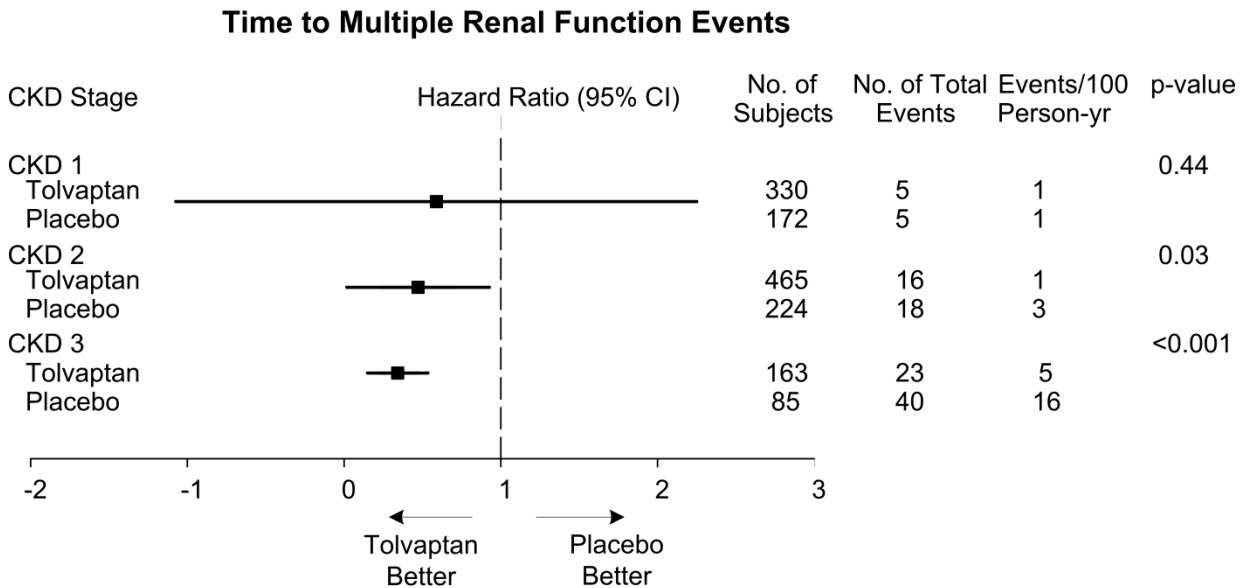
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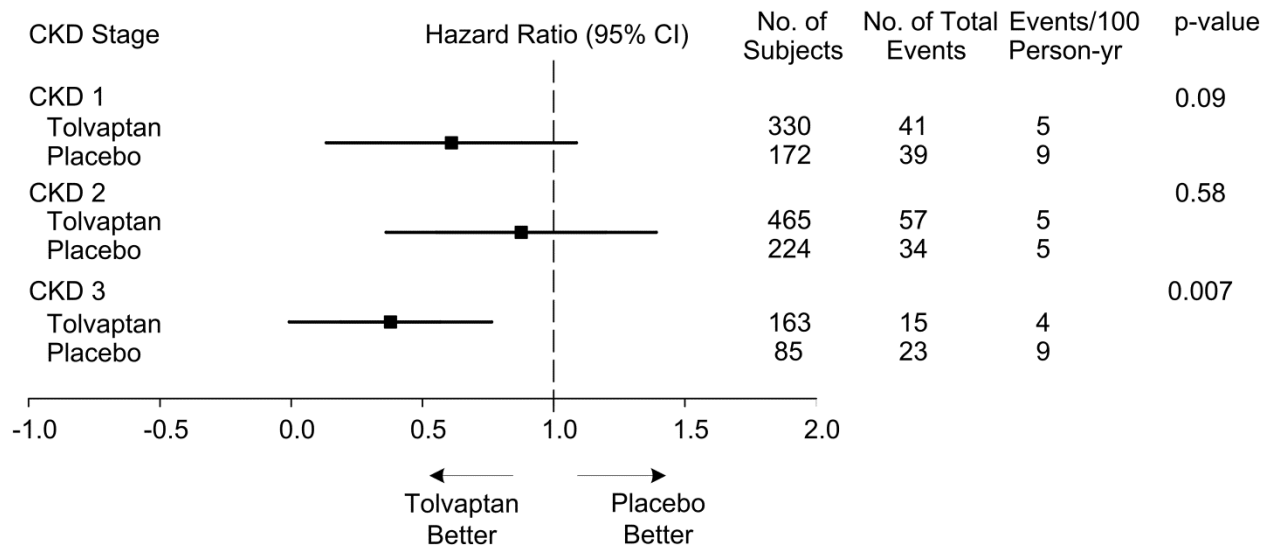
S1: Annualized percent changes in total kidney volume in the intention-to-treat population during the 3-year treatment period by CKD stages 3a and 3b and by treatment arm (black bars = tolvaptan, white bars = placebo; means \pm SEM). The relative treatment effects (39.8, 38.7 and 42.4%) according to CKD stage subgroup, are based on the between-group difference in the slopes, with variance approximated by means of the delta method under the assumption of independence between the slopes is indicated.

S2: Effects of Tolvaptan on the Time to Multiple Investigator-Assessed ADPKD Related Progression Events Hazard ratios for two of the components of the composite end point

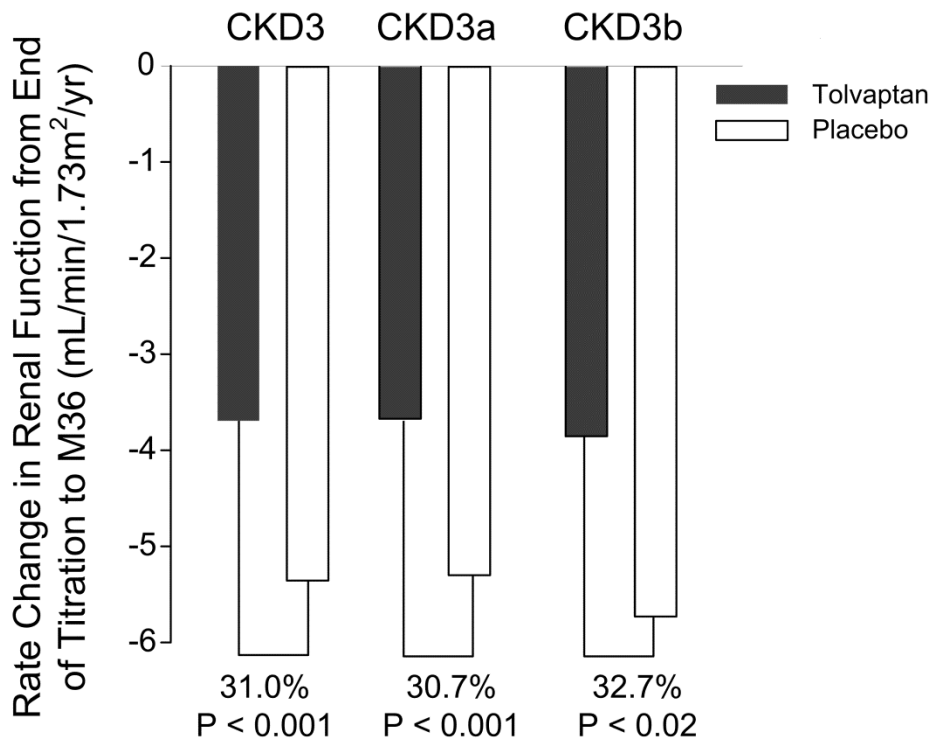


(A) Cumulative hazard of multiple events of worsening renal function defined as worsening kidney function (a 25% reduction in the reciprocal of the serum creatinine level from the value at the end of the dose-adjustment period, reproduced after at least 2 weeks).

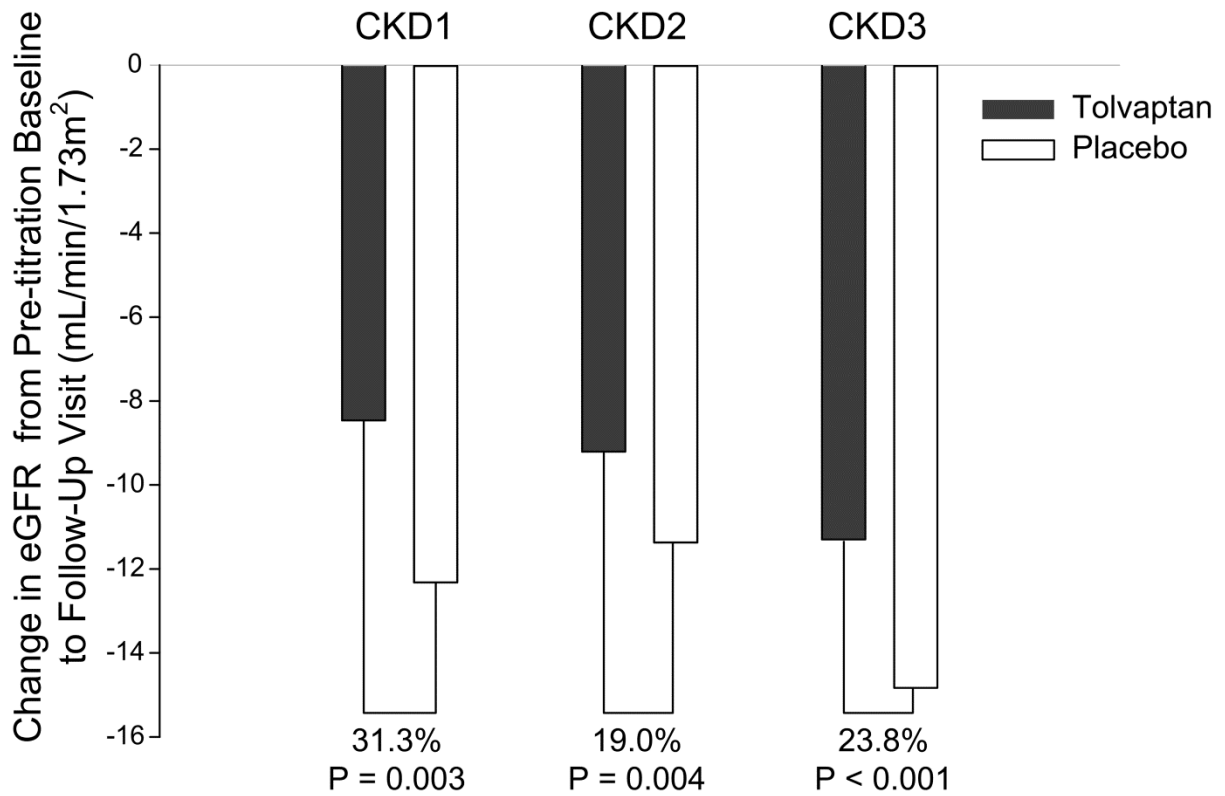
Time to Multiple Renal Pain Events



(B) Cumulative hazard of multiple events of clinically significant kidney pain defined as significant interventions for relief of renal pain. This included surgical or invasive radiological procedures, introduction or increasing the dose of narcotic or tricyclic antidepressant medication, prescribing medical leave or activity restrictions or using a prescription nonnarcotic which carries some risk (eg: NSAIDs).



S3: On-treatment slopes with 95% CI of CKD-EPI eGFR by CKD stages 3a and 3b and by treatment arm in the intention-to-treat population within the treatment period (black bars = tolvaptan and white bars = placebo). The relative treatment effects (31.0, 30.7 and 32.7%) according to CKD stage subgroup, based on the difference in annual change in slope, are shown.



S4: Changes in eGFR from pre-titration baseline to follow-up visit 2 plotted by CKD stage and treatment arm (black bars = tolvaptan and white bars = placebo). Relative percent treatment effects (31.3, 19.0 and 23.8%) are shown for each CKD stage.

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