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P045 -Efficacy and side-effects of tolvaptan in autosomal dominant polycystic kidney disease (ADPKD) - a single centre experience

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Introduction
The most common inherited kidney disease, ADPKD, comprises progressive growth of renal cysts and declining renal function [1] [2]. Tolvaptan is the first disease modifying agent for ADPKD and is recommended for those with CKD 2-3 or rapidly progressive disease [4] [3] but adverse effects may limit its use [3]. Here baseline characteristics and outcomes of patients considered for tolvaptan in our ADPKD clinic are compared with those in published literature.

Method
Clinic attendance records, letters, laboratory results and imaging of patients referred to a tertiary ADPKD clinic were reviewed at 0, 3, 6, 9, 12 and 18 months. Baseline total kidney volume (TKV; a surrogate marker for renal function) was taken from any pre-tolvaptan CT/MR imaging. Those ineligible for tolvaptan as per NICE guidelines were excluded from analysis.

Results
Twenty-three patients were eligible for tolvaptan; eleven males, aged 32-69 years (mean; 49, median; 51). Baseline eGFR; 30-84 ml/min/1.73m2 (mean; 50, median; 42), TKV; 703-4720 cm3 (mean; 1939cm3, median; 1652cm3). Seven discontinued treatment; cited reasons included thirst (2/23), urinary frequency (2/23), falling eGFR (2/23), deranged LFTs (1/23), deep vein thrombosis (DVT) (1/23) and follow up non-attendance (1/23). In total, 17/23 patients suffered side effects, often in combination. The most commonly occurring side effects were raised uric acid (10/23) and deranged LFTs (7/23) (Table 1).

Discussion
Within the limits of the small sample, our data appears to reflect that of the TEMPO trial. Our patients discontinued tolvaptan for similar reasons as in the TEMPO trial; thirst, urinary frequency and falling eGFR. Our discontinuation rate was, however, higher (30% vs 23%). Reported side effects were similar to those described in the literature, but our most commonly reported side effect (raised uric acid) was never cited as indication to discontinue. Dose dependent deranged liver enzymes were reported in our data but no cases of acute severe liver injury as was observed in the TEMPO trial. After through investigation one case of DVT was thought to be associated with tolvaptan amongst our cohort.
Our data demonstrated positive trends between the proportional change in eGFR and (i) the maximum tolerated tolvaptan dose (Figure 1) and (ii) the baseline eGFR. This suggests a dose related benefit of tolvaptan, in keeping with TEMPO trial findings, but also an additional benefit when tolvaptan is started earlier; at a higher baseline eGFR. Our data demonstrated a negative trend between the proportional change in eGFR and duration of treatment, indicating persistent renal function decline despite treatment; in keeping with TEMPO trial findings.

Conclusion
Trends in our data reflect those of the TEMPO trial: Higher tolerated doses of tolvaptan were associated with slower decline in renal function. Tolerance of treatment was, however limited by side effects. Given the frequency of side effects, our findings support the current eligibility specifications [4]. Interpretation of

our data is limited by small sample size and short follow up. Further study is required to assess whether these observed trends will persist: On-going follow up of these patients will provide further data annually.