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## A randomised controlled trial of the efficacy and safety of allopurinol dose escalation to achieve target serum urate in people with gout

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### Abstract

**Objectives** To determine the efficacy and safety of allopurinol dose escalation using a treat-to-target serum urate (SU) approach.

**Methods** A randomised, controlled, parallel-group, comparative clinical trial was undertaken. People with gout receiving at least creatinine clearance (CrCL)-based allopurinol dose for  $\geq 1$  month and SU  $\geq 6$  mg/dL were recruited. Participants were randomised to continue current dose (control) or allopurinol dose escalation for 12 months. In the dose escalation group, allopurinol was increased monthly until SU was  $< 6$  mg/dL. The primary endpoints were reduction in SU and adverse events (AEs).

**Results** 183 participants (93 control, 90 dose escalation) were recruited. At baseline, mean (SD) urate was 7.15 (1.6) mg/dL and allopurinol dose 269 mg/day. 52% had CrCL  $< 60$  mL/min. Mean changes in SU at the final visit were  $-0.34$  mg/dL in the control group and  $-1.5$  mg/dL in the dose escalation group ( $p < 0.001$ ) with a mean difference of 1.2 mg/dL (95% CI 0.67 to 1.5,  $p < 0.001$ ). At month 12, 32% of controls and 69% in the dose escalation had SU  $< 6$  mg/dL. There were 43 serious AEs in 25 controls and 35 events in 22 dose escalation participants. Only one was considered probably related to allopurinol. Five control and five dose escalation participants died; none was considered allopurinol related. Mild elevations in LFTs were common in both groups, a few moderate increases in gamma glutamyl transferase (GGT) were noted. There was no difference in renal function changes between randomised groups.




**Conclusions** Higher than CrCL-based doses of allopurinol can effectively lower SU to treatment target in most people with gout. Allopurinol dose escalation is well tolerated.

**Trial registration number:** ANZCTR12611000845932; Results.

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Footnotes

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**Contributors:** LKS and ND: literature search, study design, data collection, data analysis, data interpretation and manuscript preparation. PTC and JD: study design, data collection, data analysis, data interpretation and manuscript preparation. MLB and CF: study design, data analysis, data interpretation and manuscript preparation. AH and PT: data collection, data analysis, data interpretation and manuscript preparation.

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