

## Management of blood and urine parameters in distal renal tubular acidosis (dRTA) with a novel prolonged-release treatment

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### Introduction

Distal renal tubular acidosis (dRTA) is a rare and potentially severe condition characterised by hyperchloremic metabolic acidosis and hypokalemia, requiring appropriate metabolic control. Currently there are no drugs registered for dRTA treatment, however different standard of care (SoC) treatments exist, which exhibit important limitations, such as short duration of action, poor gastric tolerability and low acceptability. This study evaluates the clinical benefit of a new prolonged-release granule combination of potassium citrate and potassium bicarbonate (ADV7103) compared to SoC in patients with dRTA.

### Methods

In a multicentre, open-label, non-inferiority, sequential study, 5-day steady state treatment periods were compared in adult and paediatric patients (N=37 enrolled): first with SoC (multiple daily intakes required) and subsequently with ADV7103 (morning and evening). Plasma bicarbonate and potassium levels were measured over 3 consecutive days and calcium/creatinine (UCa:UCr), citrate/creatinine (UCi:UCr) and calcium/citrate (UCa:UCi) urinary excretion ratios were measured over 2 consecutive days. All measurements were performed before first morning doses. For each parameter, proportions of responders (patients with normal values) and non-responders were compared, and the difference between treatments evaluated using McNemar's test in the intent to treat set.

### Results

The responder rates obtained for each parameter with both treatments are shown in Table 1. Considering plasma bicarbonate levels, in patients with comparable data from both treatment periods (N=30), 17 (56.7%) of patients were non-responders (abnormally low levels) with SoC and 3 (10%) with ADV7103. When switching to ADV7103, 82.4% (14/17) of non-responders with SoC became responders, while none of the responders with SoC became non-responders. This difference between treatments was statistically significant ( $p < 0.001$ ). No statistically significant difference was observed for plasma potassium levels and the response rate was high for both treatments (82.8%, 24/29 in both cases), although there was a trend towards increasing values with ADV7103 (4.08 vs. 3.83 mmol/L with SoC).

No significant difference between treatments was shown for UCa:UCr (N=30). However, only three patients presented hypercalciuria: 1 under SoC treatment, 1 with ADV7103 and 1 during both periods. For UCi:UCr (N=17), hypocitraturia was noted in 16 (94.1%) of patients with SoC and in 10 (58.8%) of patients treated with ADV7103. When switching to ADV7103, 43.8% (7/16) of non-responders with SoC became responders and only one responder with SoC became non-responder, but the difference was not significant due to the limited number of patients in this analysis ( $p = 0.070$ ). For UCa:UCi (N=20), 16/20 (80%) of the patients presented abnormally high values with SoC and 40% with ADV7103. When switching to ADV7103, 56.3% (9/16) of non-responders became responders, while only one responder became non-responder and this difference between treatments was statistically significant ( $p = 0.021$ ).

### Discussion

The clinical benefit of ADV7103 over current SoC treatments is indicated by the increased response rates for normalisation of plasma bicarbonate levels after switching to this new prolonged-release formulation. The increased rate of normalisation of UCa:UCi excretion ratio also suggests a reduced risk of stone formation with ADV7103 treatment.