32

Long-term management of metabolic parameters in distal renal tubular acidosis (dRTA) with a novel prolonged-release treatment

Professor Detlef Bockenhauer[2], Doctor Aurélia Bertholet-Thomas[3], Doctor Maria Asunción Manso Silván[1], Ms Catherine Guittet[1], Doctor Victor Vavas Serrano[4], Doctor Luc André Granier[1], Professor Pierre Cochat[3]
[1]Advicenne, Nîmes, France, [2]Great Ormond Street Hospital for Children, NHS Foundation Trust, London, UK, [3]Centre de référence des maladies rénales rares. Hôpital Mère Enfant, Bron, France, [4]Advicenne, Madrid, Spain

Introduction
An innovative prolonged-release granule combination of potassium citrate and potassium bicarbonate, ADV7103, with a simplified age-adapted dosing regimen, has been shown to improve management of plasma bicarbonate levels in patients with distal renal tubular acidosis (dRTA) when compared to standard of care (SoC) treatments. ADV7103 has also been shown to maintain normal plasma potassium levels in most patients. This study aimed to investigate long-term treatment efficacy and patient satisfaction.
Materials/Methods
A cohort of adult and paediatric patients with dRTA (N=30, 6 adults, 8 adolescents, 13 children and 3 infants/toddlers), having completed a previous short-term phase II/III study with ADV7103, were included in a multicentre (N=12), open-label, 24-month extension study. Participants received ADV7103 twice daily at appropriate doses, as defined in the previous study and further adapted if required. Plasma bicarbonate and potassium levels were measured in blood samples drawn before first morning dose, at baseline (last visit of short-term study) and after 3, 6, 12, 18 and 24 months of treatment. Only non-haemolysed blood samples were considered for plasma potassium determinations. Urinary excretion parameters were measured at the same time points. Quality of life improvement was evaluated by patients and/or their parents using a 100-mm visual analogue scale. Descriptive statistical analyses of the data were performed.
Results
Most patients demonstrated normalised plasma bicarbonate and potassium levels for the duration of the 24-month ADV7103 treatment. After 12 months of treatment, 4 patients presented plasma bicarbonate levels below normal range and only 2 patients showed plasma potassium levels below normal range. At 24 months, the overall mean ± SD plasma bicarbonate level was 22.8 ± 2.9 mmol/L, plasma potassium level was 3.8 ± 0.3 mmol/L, and urine calcium/creatinine excretion ratio was 0.3 ± 0.2 mmol/mmol, with average alkali doses of 2.3±1.3, 2.6±1.7, 3.4±1.3 and 4.8±2.0 mEq/kg/day in adults, adolescents, children and infants/toddlers, respectively. Improvements of urinary excretion parameters observed in the previous study were maintained and positive effects on some parameters (in particular citrate and calcium) were noted. The evolution of mean plasma bicarbonate and potassium values, as well as of calcium excretion is shown in Figure 1. Patients and/or their parents reported an average improvement of quality of life of 80.7% and 88.9% at 6 and 24 months of this study, respectively, compared to previous SoC treatments.
Discussion
The results of this 24-month extension study show ADV7103 allows a sustained control of metabolic acidosis and hypokalaemia in patients with dRTA, and thus confirm observations from the short-term phase II/III study. Both patients and/or their parents were extremely satisfied in terms of improvement of quality of life showed with ADV7103. Taken together these data ADV7103 could represent an effective first-line treatment for dRTA.