A. ACID-BASE, NEPHROLITHIASIS AND URIC ACID

FP001 REDUCTION OF THE NUMBER OF DAILY INTAKES AND IMPROVED BLOOD BICARBONATE LEVELS IN DISTAL RENAL TUBULAR ACIDOSIS (dRTA) PATIENTS: INTEREST OF ADV7103, A NEW PROLONGED RELEASE FORMULATION

Aurélie Bertholet-Thomaz², Catherine Guitter¹, Maria A. Manso¹, Luc André Granier¹, the Investigators of the B21OS Study
¹Clinical Affairs, Advicenne S.A., Nîmes, France and ²Service de Néphrologie Pédiatrique, Hôpital Femme Mère Enfant, Centre de Référence des Maladies Rénales et Phosphocalciques Rares, Bron, France

INTRODUCTION AND AIMS: Treatment of distal renal tubular acidosis (dRTA) aims at restoring physiological blood pH (blood bicarbonate levels ≥ 22 mM) and requires individual adjustment of the dose. Current standard of care (SoC) treatments are generally immediate release alkalis with their effect short-lived. Treatment is administered in several daily doses to compensate for short duration of action and induces potential gastro-intestinal (GI) side effects due to a peak of alkali lead in the stomach. These drawbacks may impact compliance. In order to improve the dosing schedule to only two administrations a day, a new prolonged-release granule formulation, ADV7103, consisting of a fixed-dose combination of two alkalizing salts, was developed. The present work aimed at evaluating the number of intakes of current SoC treatments in dRTA patients and the blood bicarbonate levels obtained. Comparison with ADV7103, administered twice a day (morning and evening), was performed.

METHODS: Adults, adolescents, children and infants with dRTA (N=37) were enrolled in a multicentre, open-label, non-inferiority, sequential study. They took their SoC treatment during a first 5 day period (N=35 completed), and then switched to ADV7103. After a titration period to define the appropriate dose, patients took ADV7103 during a 5 day period (N=31 completed). The number of intakes with each treatment was reported individually. Blood bicarbonate levels with SoC and ADV7103 were measured before the first morning alkali dose during 3 consecutive days and the mean values were compared. GI discomfort for both treatments was evaluated using a visual analogue scale.

RESULTS: The number of intakes of SoC was 3-6 intakes/day in 84% of the patients and two intakes/day or less in 16% of the patients. Approximately 1/3 of the patients had to take their medication during the night. There was no particular relationship between the number of intakes of SoC and bicarbonate levels. In many patients bicarbonatemia was not adequately restored with the SoC, even when receiving three intakes or more (Figure 1). Only 29% of the patients treated with SoC, mostly adults and adolescents, reached values of blood bicarbonate ≥ 22 mM. The individual mean blood bicarbonate levels attained with SoC treatments were frequently lower than those observed with ADV7103, particularly in children. The overall average ± SD blood bicarbonate levels were 21.6 ± 3.06 vs 23.0 ± 1.80 mM, respectively, in the per protocol set (N=30). The efficacy of ADV7103, which also afforded reduced GI discomfort when compared to SoC treatments, was clearly demonstrated through its ability to correct metabolic acidosis. A total of 81% of the patients presented blood bicarbonate levels ≥ 22 mM and only 6% (2 patients) presented values < 21 mM.

CONCLUSIONS: Despite high number of daily intakes, blood bicarbonate levels were adequately restored in a limited number of patients with the SoC. In contrast, blood bicarbonate levels were restored in most of the patients with only two daily intakes of ADV7103.