Abstract: P4555

**Efficacy and safety of valsartan in children aged 1-5 years with hypertension, with or without chronic kidney disease: A 6-week randomised, multicentre, double-blind study followed by open-label phase**

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Background: Hypertension is a leading cause of disability and mortality worldwide. In the paediatric population, hypertension and chronic kidney disease (CKD) have raised significant health concern due to the risk of target organ damage similar to that seen in adults. Management of hypertension may therefore prevent decline in renal function and progression of CKD to end organ damage. Currently, there are no angiotensin receptor blockers approved in EU for hypertensive children younger than 6 years.

**Purpose:** To evaluate a dose-dependent reduction in mean systolic blood pressure (MSBP), safety and tolerability of two doses of valsartan (VAL) solution (0.25 mg/kg/day and 4 mg/kg/day) in children aged 1-5 years with hypertension with or without CKD.

**Methods:** This study comprised of a randomised multicentre double-blind (DB) double-dummy phase I (6-weeks) followed by an open-label (OL) titration phase II (20-weeks). In phase I, patients with history of hypertension were randomised 1:1 to receive VAL (0.25 or 4 mg/kg/day). Patients received VAL 1 mg/kg/day, optionally titrated to 2 mg/kg/day to 4 mg/kg/day based on BP response in phase II.

**Results:** Of the 127 randomised patients, 120 completed phase I, and 114 (55 CKD; 59 non-CKD) phase II. Baseline characteristics and demographics were comparable between treatment groups, and within the CKD and non-CKD subgroups.

In the DB phase, a clinically and statistically significant reduction was observed in MSBP at week 6 in the VAL 4 mg/kg group (8.5 mmHg) compared with the VAL 0.25 mg/kg group (4.1 mmHg, respectively; P=0.0157; baseline 113.3 mmHg vs. 116.0 mmHg, respectively). A positive dose-response relationship (i.e. slope for dose per body weight, mg/kg) was observed in MSBP reduction between the VAL 0.25 mg/kg and VAL 4.0 mg/kg group (P=0.0012).

In CKD patients, there was a significant reduction in MSBP from baseline to week 6 in the VAL 4 mg/kg group (9.2 mmHg) compared with the VAL 0.25 mg/kg group (1.2 mmHg; P=0.0096). MSBP reduction in non-CKD group was numerically larger with higher dose (7.8 mmHg vs 6.9 mmHg) but difference was not statistically significant (P=0.6531).

Incidence of adverse events (AEs) was lower with VAL 4 mg/kg (41.9%) vs VAL 0.25 mg/kg (51.6%); similar in the CKD (48.4%) and non-CKD (45.3%) subgroups and not dose dependent. The most common AE was respiratory tract infection (5.6%). Serious AEs occurred in 3.2% patients with similar incidence in each dose group. Discontinuation due to AEs was 1.6%, all in VAL 0.25 mg/kg group. One patient in low dose and 2 in
high dose group had potassium values >5.5 mEq/L. Incidence of AEs in OL phase was 76.7% with pyrexia being most frequent (16.7%).

Conclusion: Valsartan produced clinically relevant reductions in BP with a statistically significant dose response in children aged 1-5 years with hypertension, with or without CKD. Long-term efficacy was maintained and was generally well tolerated.