that after 1 month of treatment in case of target BP levels were not achieved torasemid was added.

The level of central SBP was significantly decreased in both groups, about 20,13 ± 5,89 mmHg in the olmesartan group and 16,15 ± 4,59 mmHg in perindopril group. The difference in the central SBP levels in two groups was 4 mmHg. In olmesartan group Aix decreased by 8.13 % and by 2.6% in perindopril arm ($p < 0,05$). For both groups it was shown an improvement of elastic properties of arteries by reducing of PWVe. In olmesartan group PWVe decreased by 2.43 m/s and for perindopril it decreased by 1 m/s ($p < 0.05$ between groups, probably due to the small number of observations). In the subgroup of torasemid combinations rate of decline of cSBP did not significantly differ and it was decreased to 12.43 mmHg in olmesartan/torasemid and 13.67 mmHg perindopril/torasemid subgroups. In olmesartan/torasemid subgroup Aix decreased by 14.4 % and in the perindopril/torasemid subgroup it did not change ($p < 0.05$ between groups). PWVe in olmesartan monotherapy subgroup decreased by 2.72 m/s compared to 0.88 m/s in perindopril monotherapy subgroup ($p < 0.05$ between subgroups).

Conclusion: The decrease of central aortic pressure in both groups was significant and similar. With the same reduction of office blood pressure and ABPM in olmesartan group Aix decreased significantly in both monotherapy and in torasemid combination subgroups compared with perindopril. PWV decreased in both groups, but in monotherapy olmesartan this decrease was significantly greater compared to perindopril.

Keywords: central blood pressure; arterial hypertension; olmesartan; perindopril

P-14

Long-term safety of fixed-dose combinations: azilsartan medoxomil/chlorthalidone (AZL-M/CLD) vs olmesartan medoxomil/hydrochlorothiazide (OLM/HCTZ) in hypertensive subjects with stage 3 chronic kidney disease

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Patients with chronic kidney disease (CKD) risk deteriorating renal function in the setting of effective blood pressure (BP) control, especially when RAAS-blockers are administered in combination with diuretics. A 52-wk, randomized, open-label, titrate-to-target BP study evaluated the safety and tolerability of the fixed-dose combinations AZL-M/CLD vs OLM/HCTZ in hypertensive subjects (clinic systolic BP [SBP] 135-160 mmHg on stable doses of 2-3 antihypertensive medications) with stage 3 CKD (eGFR 30-<60 mL/min/1.73 m^2).

Subjects discontinued antihypertensive medications 2 days before randomization and first received AZL-M/CLD 20/12.5 mg qd (n=77) or OLM/HCTZ 20/12.5 mg qd (n=76). If BP <130/80 mmHg was not achieved, doses could be up-titrated (AZL-M/CLD to 40/25 mg; OLM/HCTZ to 40/25 mg [US] or 20/25 mg [Europe]) and additional antihypertensive agents (except ACEI/ARB and diuretic) added during wks 4-52. Primary endpoint was percentage of subjects with ≥1 AE through Week 52.

Baseline demographics were generally similar between groups (mean age 68 yr, BP 150/85 mmHg, eGFR 48 mL/min/1.73 m^2, 42% diabetes). Seventeen (22.1%) AZL-M/CLD and 15 (19.7%) OLM/HCTZ subjects discontinued, for AEs. AZL-M/CLD showed greater SBP reductions by wks 2 and 4 (i.e., prior to titration), and similar or numerically slightly greater reductions from wk 4-42, with similar mean [SD] change from baseline at final visit (-24.3 [16.10], and -23.7 [11.30] mmHg for AZL-M/CLD and OLM/HCTZ, respectively). DBP reductions were generally similar between groups. At study end, more OLM/HCTZ than AZL-M/CLD patients were on the highest study drug dose (48.7% vs 29.9%) and were taking additional antihypertensive medications (26.3% vs 16.9%).

AEs occurred in 88.3% of patients on AZL-M/CLD vs 76.3% on OLM/HCTZ. Serious AEs were reported in 10.4% on AZL-M/CLD vs 11.8% on OLM/HCTZ. One death (pulmonary artery thrombosis) occurred in the OLM/HCTZ arm. Common AEs (AZL-M/CLD vs OLM/HCTZ) were blood creatinine increased (44.2% vs. 38.2%), dizziness (7.8% vs. 6.6%) and headache (10.4% vs. 2.6%). Subjects with consecutive SCr elevations ≥50% from baseline and >ULN or eGFR ≤20 mL/min/1.73 m^2 were similar between groups (5.3% in AZL-M/CLD vs 5.4% in OLM/HCTZ).

The safety and tolerability of long-term treatment with AZL-M/CLD and OLM/HCTZ in a titrate-to-target BP study were comparable in hypertensive subjects with stage 3 CKD.

Keywords: azilsartan medoxomil; chlorthalidone; chronic kidney disease; creatinine elevation

P-15

Long-term safety of nebivolol and valsartan combination therapy in patients with hypertension: an open-label, single-arm, multicenter study

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The long-term safety of a free-tablet combination consisting of the β1-selective blocker nebivolol (Neb) and the angiotensin-receptor blocker valsartan (Val) was assessed in a Phase III, open-label, single-arm, multicenter trial (NCT01415505). Adults with stage 1 or 2 hypertension entered a 4-week single-blind placebo run-in phase, followed by 52-week treatment with Neb 5 mg/d and Val 160 mg/d and a 1-week down titration phase. Treatment was titrated to achieve BP goal (SBP/DBP ≤140/90 mmHg without diabetes or ≤130/80 mmHg with diabetes) to Neb/Val 10/320 mg/d at Week 2 and up to 20/320 mg/d, with the addition of HCTZ (12.5 mg/d titrated to 25 mg/d) if needed. Safety and tolerability were assessed by means of adverse events (AEs), vital signs, clinical laboratory parameters, ECGs and physical examinations. Efficacy assessments included change from baseline in trough seated DBP and SBP and the percentage of patients who achieved BP goal. All analyses were performed using descriptive statistics. A total of 810 patients enrolled; 807 were included in the safety population (men, 55.5%; white, 65.8%; with diabetes, 17.1%) and 60.4% completed open-label treatment. The most frequent reason for discontinuation was insufficient therapeutic response (did not meet BP goal; 8.4%); 6.5% of patients discontinued due to an AE. AEs were experienced by 59.2% of patients and were mostly mild or moderate in severity. The most common AEs were headache (5.7%), nasopharyngitis (5.0%), upper respiratory tract infection (4.6%), dizziness (4.3%), and bronchitis (3.0%). Only 1 out of 19 (2.4%) patients who experienced a serious AE had an event (bradycardia) deemed related to study medication. Three (0.4%) deaths occurred during the study; none was considered related to study medication. Mean baseline DBP/SBP was 158/100mmHg; mean ± SD changes from baseline in trough seated DBP and SBP at week 52 (observed cases) were -19.0 ± 8.7 mmHg and -25.5 ± 15.9 mmHg, respectively. A total of 76% Neb/Val-treated and 58% Neb/Val/HCTZ-treated completers achieved BP goal. In conclusion, long-term treatment with nebivolol and valsartan in adults with hypertension was safe and well tolerated.