were 71%, 67%, 66%, 64%, 63%, 60%, 52% and 23% respectively. The persistence-adherence index at two year was 66% for ARAs, 63% for amlodipine, 62% for β-blockers, 61% for other CCBs, 60% for ACE inhibitors, 51% for hydrochorothiazide, 50 % for other diuretics and 32% for chlorthalidone.

Conclusion: Persistence and adherence to treatment are essential to treatment success and varied substantially between the different therapeutic options. Results of this study indicate that, in a real life setting, patients are significantly less compliant to diuretics than to any other antihypertensive agents.

Key Words: Treatment Compliance, Antihypertensive Drugs, Drug Databases Analyses

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EFFECTIVE BLOOD-PRESSURE CONTROL WITH VALSARTAN/HCTZ COMBINATION THERAPY IN PATIENTS WITH MODERATE TO SEVERE SYSTOLIC HYPERTENSION: THE VALOR TRIAL

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Background: Increasing evidence shows that combination therapy with at least two antihypertensive agents is needed to achieve appropriate blood-pressure (BP) control in a large part of the hypertensive population. One of the most appealing combinations is that of adding a diuretic to an angiotensin-receptor blocker (ARB).

Methods: We studied the effects on sitting systolic BP of the combinations valsartan (V; an ARB) 160 mg + HCTZ 12.5 mg and V160 mg + HCTZ 25 mg od, compared with monotherapy V160 mg od. Treatment-naive and previously treated patients (N=767) with moderate to severe systolic hypertension (SBP ≥160 mm Hg and ≤200 mmHg) and with or without co-morbidities, were randomised (after a 2-week washout if previously treated and a 2 week placebo run-in period) to either V80 od (monotherapy group) or V160 od (combination groups) for 4 weeks, with force-tration to V160 mg, V160/HCTZ 12.5 od or V160/HCTZ 25 od for an additional 4 weeks. Endpoints were change in SBP between V160 and V160/HCTZ 25 and between V160/HCTZ 12.5 and V160; changes in DBP between groups, response rates and tolerability.

Results: As shown in the Table, all treatments were highly effective and there were additional SBP and DBP reductions in the combination groups. Responder rates were above 50% in all groups and reached 75% in the V160/HCTZ 25 group. Rates of adverse events did not differ significantly between monotherapy and combination therapies.

Conclusions: V160 mg od is safe and effective in patients with moderate to severe systolic hypertension. Adding HCTZ 12.5 or 25 mg provides significant additional reductions in systolic and diastolic BP and increases responder rates compared with V160 mg monotherapy, with maintained excellent tolerability.

Table 1

	V160	V160/HCTZ12.5	V160/HCTZ25
N	261	254	252
Male/female	130/131	141/113	140/112
Mean age	60.4 (10.6)	60.8 (11.5)	60.7 (11.6)
Baseline mean SBP/DBP	167.9 (8.0)/93.2 (8.9)	167.4 (8.3)/93.4 (9.6)	167.2 (7.9)/93.7 (8.8)
Mean change SBP/DBP	−20.7 (15.7)/−6.6 (8.9)	−27.9 (13.8) */−10.2 (7.7)*	−28.3 (13.1) */−10.1 (7.8)*
Response rate¥	56.9%	74.4%*	75%*
Any AE (monotherapy phase/combination phase)	37.3%/27.5%	32.1%/28.6%	32.8%/34.0%

*Values in brackets are ± SD. * P < 0.05 vs V160; ¥ SBP < 140 or decrease in SBP ≥20 mmHg and/or DBP<90 mmHg*

Key Words: Valsartan, Combination Therapy, Double-Digit Blood-Pressure Lowering Efficacy

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EFFECTS ON BLOOD PRESSURE, NITRIC OXIDE URINARY EXCRETION AND ON eNOS PROTEIN EXPRESSION BY NEVIBOLOL AND METOPROLOL IN SPONTANEOUSLY-HYPERTENSIVE RATS

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The acute effects of Nebivolol (NEB), a beta-blocker which activates the NO-pathway, and Metoprolol (MET) on nitric oxide (NOx) urinary excretion, blood pressure (BP) and on protein expression of endothelial nitric oxide synthase (eNOS) in thoracic/abdominal aortae were studied in spontaneously hypertensive rats (SHR). NOx excretion was studied by sampling urine every 12 h after i.p. inj. of NEB (30mg/kg) or MET (30mg/kg) at 7 and 19h. BP was measured by telemetry after i.p. inj. of NEB (3,10,30 mg/kg) or MET (1.98, 6.59, 30, 100 mg/kg) at 7 and 19h. Thoracic and abdominal aortae were withdrawn 24 hours after NEB (30 mg/kg) injection at 7h to determine eNOS protein expression by Western blot.

NEB significantly increased NOx excretion, most marked 12–24h after drug dosing, whereas MET had no effect. Effects of MET and NEB on BP were only dose-dependent when given at 19h: Max. was reached by MET after 30 min (−21mmHg) and by NEB after 3 hours (−30mmHg). NEB lowered BP for several days, MET only for some hours. eNOS protein expression was not affected by NEB: control vs NEB in thoracic (OD: 85.8 ± 18.3 and 94.2 ± 19.8, resp) in abdominal aortae (OD: 113.2 ±. 11.3 and 125.3 ± 11.7, resp). Thus, NEB in contrast to MET affected the NO-pathway by enhancing NOx production, eNOS protein expression was not influenced. Increased NOx excretion by NEB was completely prevented by the NO-synthase inhibitor L-NAME. The increased NOx excretion must be due to increased activity of eNOS. The two beta-blockers also vary in onset and duration of decreasing BP. The long-lasting effect of NEB may be due to active metabolites.

Support: Berlin-Chemie, Berlin, Germany

NOx urine excretion after Nebivolol and Metoprolol in SHR

	Drug dosing at 7h Urins sampling from 19-7h	ANOVA	Drug dosing at 19h Urine sampling from 7-19h	ANOVA
Control (n = 5)	0.9 +/− 0.1	p < 0.001†	0.5 +/− 0.1	p < 0.01†
NEB (n = 5)	4.9 +/− 1.0	p < 0.001‡	3.0 +/− 0.6	p < 0.01‡
MET (n = 5)	1.0 +/− 0.1		0.5 +/− 0.0	

Means +/− SEM, expressed as μmoles, † Control vs NEB, ‡ NEB vs MET

Key Words: Nebivolol and Metoprolol, Nitric Oxide, Spontaneously-Hypertensive Rats

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EFFECTS OF IRBESARTAN ON PLATELET AGGREGATION AND MARKERS OF INFLAMMATION IN HYPERTENSIVE PATIENTS WITH AND WITHOUT ATHEROSCLEROTIC CARDIOVASCULAR DISEASE

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Clinically evident atherosclerotic cardiovascular disease (ASCVD) is a pro-inflammatory state associated with increased platelet aggregability (PAGG) and activation of the renin angiotensin system.

Objectives: We hypothesize that: a) in hypertensive patients a selective angiotensin II AT_1 receptor antagonist Irbesartan (IRB) in addition to its hypotensive effect may also contribute to reduction of PAGG and of plasma markers of inflammation; b) these effects of IRB are different in patients with and without ASCVD.