

Cardiovascular Events During Differing Hypertension Therapies in Patients With Diabetes

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Objectives The aim of this study was to determine which combination therapy in patients with hypertension and diabetes most effectively decreases cardiovascular events.

Background The ACCOMPLISH (Avoiding Cardiovascular Events Through COMBination Therapy in Patients Living With Systolic Hypertension) trial compared the outcomes effects of a renin-angiotensin system blocker, benazepril, combined with amlodipine (B+A) or hydrochlorothiazide (B+H). A separate analysis in diabetic patients was pre-specified.

Methods A total of 6,946 patients with diabetes were randomized to treatment with B+A or B+H. A subgroup of 2,842 diabetic patients at very high risk (previous cardiovascular or stroke events) was also analyzed, as were 4,559 patients without diabetes. The primary end point was a composite of cardiovascular death, myocardial infarction, stroke, hospitalization for angina, resuscitated arrest, and coronary revascularization.

Results In the full diabetes group, the mean achieved blood pressures in the B+A and B+H groups were 131.5/72.6 and 132.7/73.7 mm Hg; during 30 months, there were 307 (8.8%) and 383 (11.0%) primary events (hazard ratio [HR]: 0.79, 95% confidence interval [CI]: 0.68 to 0.92, $p = 0.003$). For the diabetic patients at very high risk, there were 195 (13.6%) and 244 (17.3%) primary events (HR: 0.77, 95% CI: 0.64 to 0.93, $p = 0.007$). In the nondiabetic patients, there were 245 (10.8%) and 296 (12.9%) primary events (HR: 0.82, 95% CI: 0.69 to 0.97, $p = 0.020$). In the diabetic patients, there were clear coronary benefits with B+A, including both acute clinical events ($p = 0.013$) and revascularizations ($p = 0.024$). There were no unexpected adverse events.

Conclusions In patients with diabetes and hypertension, combining a renin-angiotensin system blocker with amlodipine, compared with hydrochlorothiazide, was superior in reducing cardiovascular events and could influence future management of hypertension in patients with diabetes. (Avoiding Cardiovascular Events Through COMBination Therapy in Patients Living With Systolic Hypertension [ACCOMPLISH]; NCT00170950) (J Am Coll Cardiol 2010;56:77-85) © 2010 by the American College of Cardiology Foundation

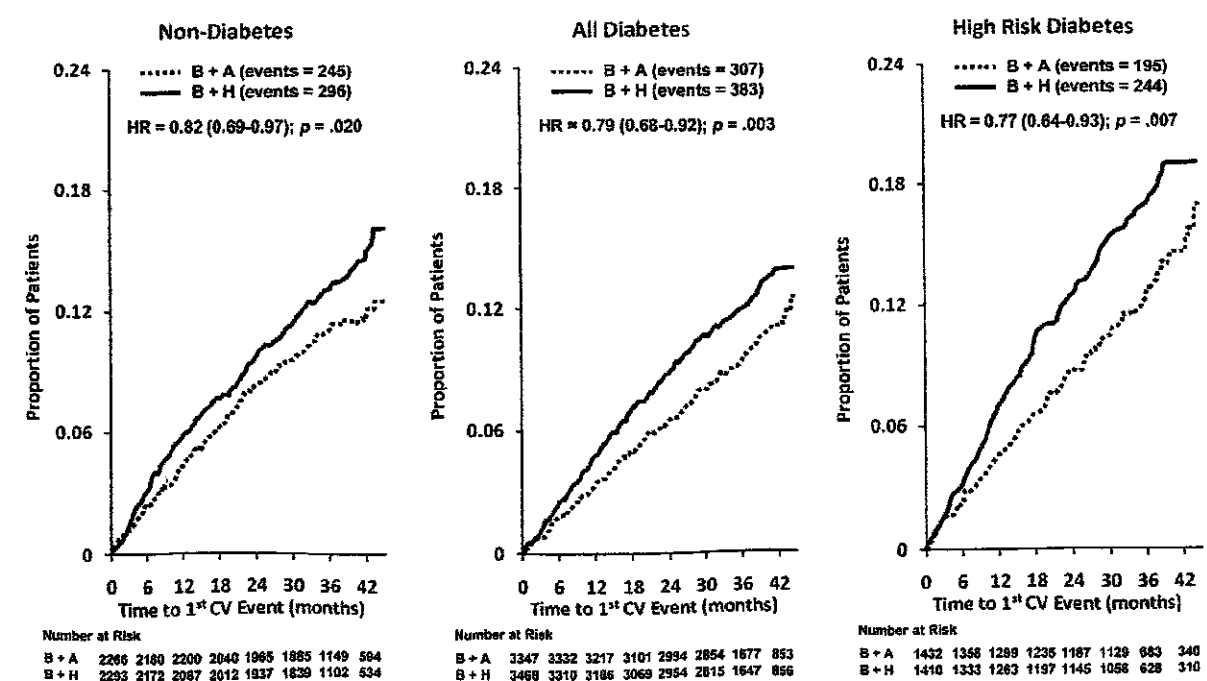


Figure 2 Time to First Events in Major Patient Subgroups

Kaplan-Meier curves for time to the first primary composite end point in patients without diabetes, with diabetes, and with high-risk diabetes (as defined in the text). CV = cardiovascular; HR = hazard ratio; other abbreviations as in Figure 1.

Table 1 Baseline Characteristics of Patient Subgroups

Characteristic	No Diabetes	All Diabetes	High-Risk Diabetes
Patients	4,559	6,946	2,842
Sex			
Male	3,009 (66%)*	3,954 (57%)	1,830 (64%)*
Female	1,550 (34%)*	2,992 (43%)	1,012 (36%)*
Age (yrs)	69.8 (7.0)*	67.5 (6.6)	66.9 (7.2)*
≥65 yrs	3,344 (73%)*	4,296 (62)	1,688 (59)*
Race			
Caucasian	4,075 (89%)*	5,537 (80%)	2,277 (80%)
Black	374 (8%)*	1,042 (15%)	429 (15%)
BP (mm Hg)			
Systolic	145.6 (18.6)	145.2 (18.1)	144.8 (18.3)
Diastolic	81.1 (10.8)*	79.3 (10.6)	78.7 (10.8)*
Heart rate (beats/min)	67.9 (10.7)*	72.0 (10.9)	71.0 (10.8)*
Body mass index (kg/m ²)	29.0 (5.3)*	32.2 (6.5)	32.2 (6.4)
Fasting blood glucose (mg/dl)	101.0 (17.2)*	144.7 (51.5)	146.4 (55.8)*
eGFR (ml/min)	76.5 (19.8)*	80.6 (22.2)	78.5 (23.4)*
Previous coronary artery disease	3,298 (72%)*	2,016 (29%)	2,016 (71%)*
Previous stroke	941 (21%)*	557 (8%)	557 (20%)*
Chronic kidney disease	867 (19%)*	1,210 (18%)	617 (22%)*
Left ventricular hypertrophy	760 (17%)*	761 (11%)	396 (14%)*
BP medications			
0†	128 (3%)*	193 (3%)*	59 (2%)*
1†	1,010 (22%)*	1,581 (23%)*	452 (16%)*
≥2	3,421 (75%)*	5,172 (75%)*	2,331 (82%)*
Lipid-lowering therapy	3,346 (73%)*	4,476 (64%)	2,192 (77%)*
Beta-blocker therapy	2,859 (58%)*	2,823 (41%)	1,582 (56%)*
Antiplatelet therapy	3,573 (79%)*	3,872 (56%)	2,106 (74%)*

Values are absolute numbers (%) or mean (SD). *Significant difference from the all diabetes cohort. †Significant difference from the non-high-risk members of the all diabetes cohort. BP = blood pressure; eGFR = estimated glomerular filtration rate.

Table 2 Comparison of Hypertension Treatment Steps in Patients With Diabetes

Characteristic	B+A	B+H
Patients	3,478	3,468
Benazepril 40 mg/day	2,246 (65)	2,179 (63)
Amlodipine 5 mg/day or HCTZ 12.5 mg/day	637 (18)	634 (18)
Amlodipine 10 mg/day or HCTZ 25 mg/day	1,796 (52)	1,731 (50)
1 additional drug	854 (25)	836 (24)
≥2 additional drugs	598 (17)	603 (17)
Intensification of diabetes therapy	1,496 (43)	1,551 (45)

Values are absolute numbers (%). The types of additional antihypertensive drugs allowed in the study are described in the text. Intensification of diabetes therapy after randomization included initiating drug therapy, increasing drug doses, and adding drugs. None of the differences between the treatment groups was significant. B+A = benazepril plus amlodipine; B+H = benazepril plus hydrochlorothiazide; HCTZ = hydrochlorothiazide.

Abbreviations and Acronyms

ACE = angiotensin-converting enzyme

B+A = benazepril plus amlodipine

B+H = benazepril plus hydrochlorothiazide

HR = hazard ratio

RAS = renin-angiotensin system

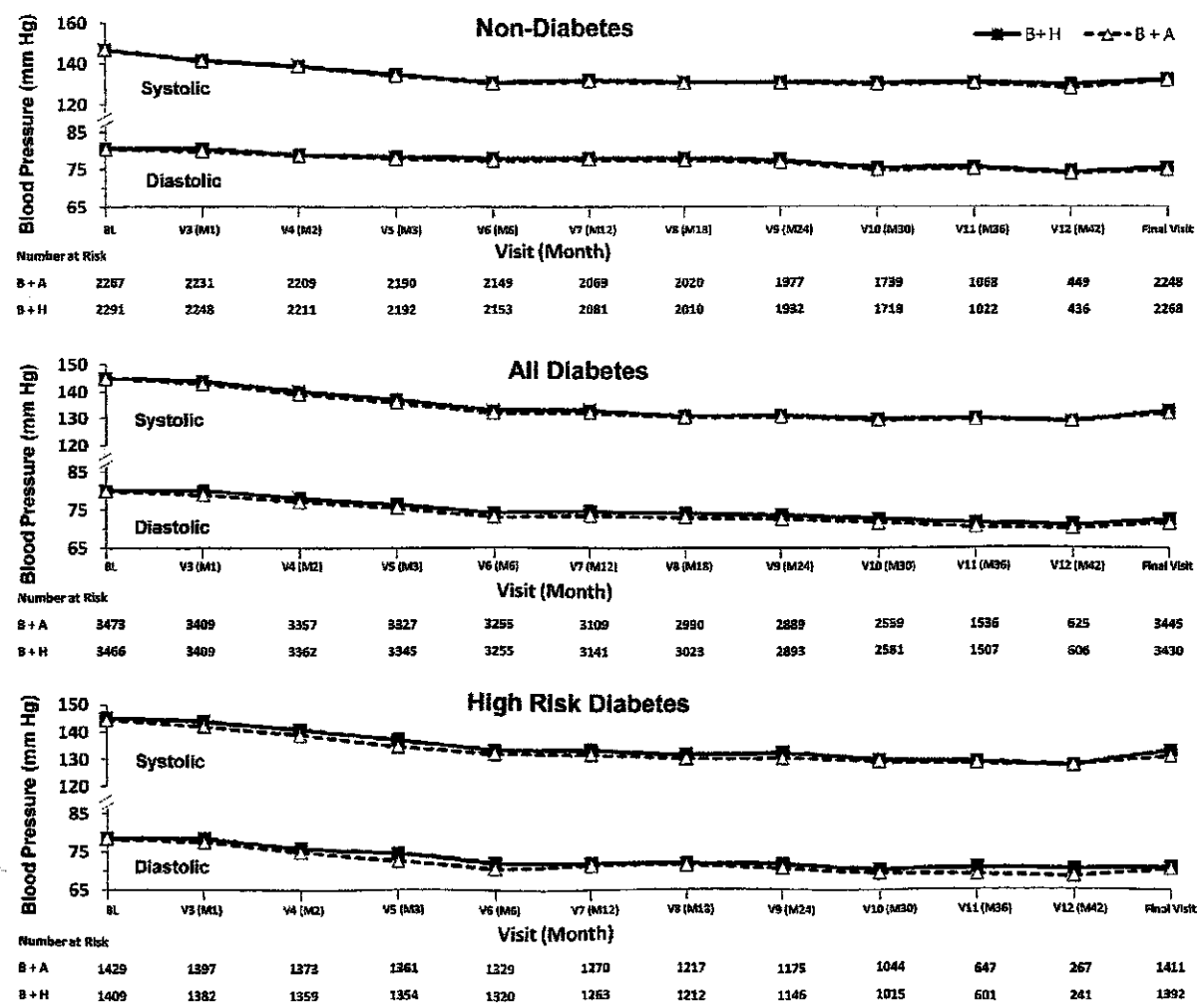


Figure 1 Mean Blood Pressure Values in Patient Subgroups During the Trial

Systolic and diastolic blood pressures during a 42-month period in patients without diabetes, with diabetes, and with high-risk diabetes (as defined in the text) during the ACCOMPLISH (Avoiding Cardiovascular Events Through COMBination Therapy in Patients Living With Systolic Hypertension) trial. Baseline blood pressures and patient numbers are given in Table 1. B+A = benazepril + amlodipine; B+H = benazepril + hydrochlorothiazide.