

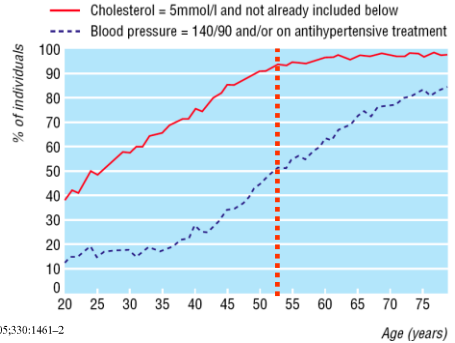
Direkte Reninhemmung

Neue Perspektiven in der Kombinationstherapie



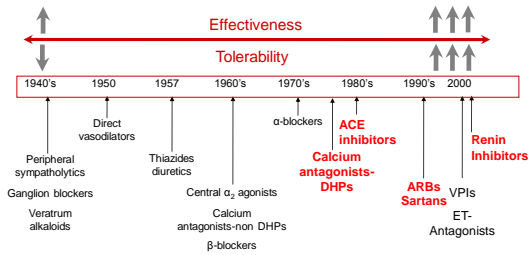
Georg Noll
Kardiologie, UniversitätsSpital Zürich
georg.noll@uzh.ch

Prävalenz der Hypertonie und Hypercholesterinämie

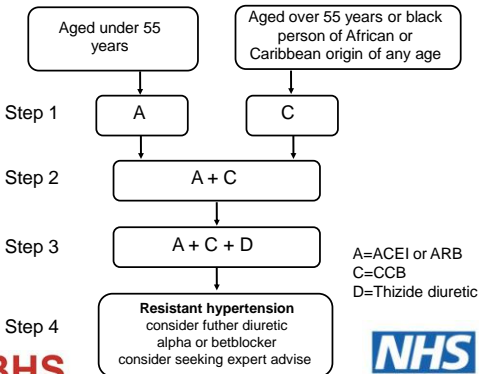
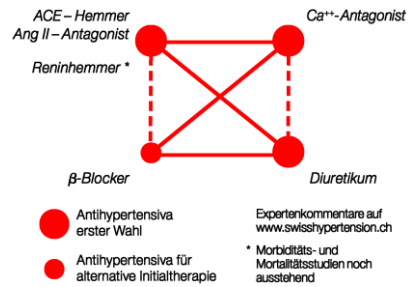


BMJ 2005;330:1461-2

Development of Antihypertensive Therapies



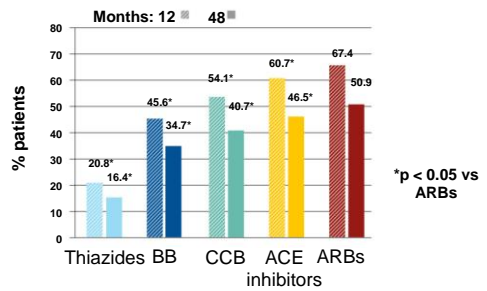
Therapie der arteriellen Hypertonie



NICE 2011



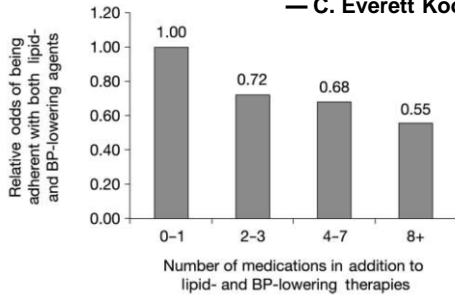
Continuation with initially prescribed antihypertensive class



Unger T. et al.; Drugs 64: 2731-2739; 2004

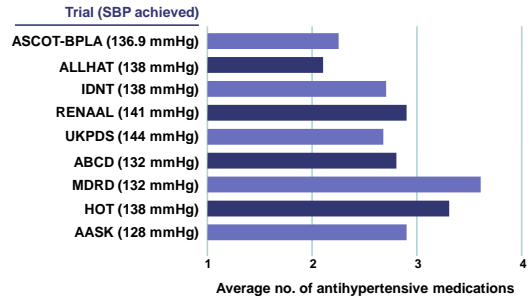
Drugs don't work in patients who don't take them.

— C. Everett Koop, M.D.



Chapman Circulation 2003

Multiple Antihypertensive Agents are Needed to Reach BP Goal



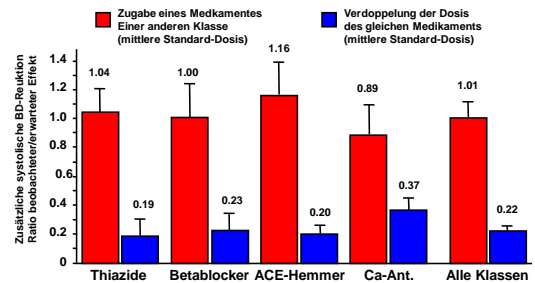
Reproduced from Am J Med 116(5A), Bakris et al. pp. 30S-8. Copyright © 2004, with permission from Elsevier; Dahlöf et al. Lancet 2005;366:895-906

Behandlungsrichtlinien der SGH 2009

	SYSTOLISCH 140-159 und/oder DIASTOLISCH 90-99 mmHg	SYSTOLISCH > 160 und/oder DIASTOLISCH > 100 mmHg
Keine Endorganschäden und Co-Morbidität	Monotherapie	Monotherapie oder Kombinationstherapie
Vorhandene Endorganschäden oder Co-Morbidität	Monotherapie oder Kombinationstherapie	Kombinationstherapie

www.swisshypertension.ch

Kombinations- vs Monotherapie für die BD-Reduktion: Metaanalyse von 11'000 Pts/42 Studien



Wald DS et al: Am J Med 2009

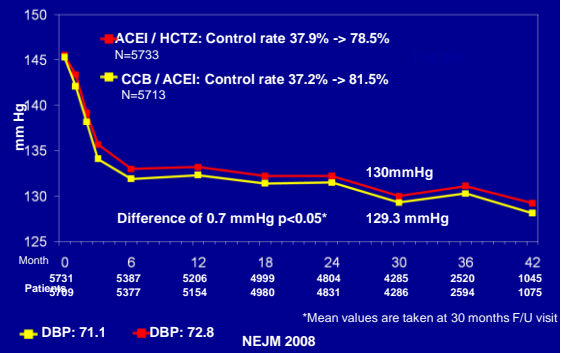
Baseline Characteristics

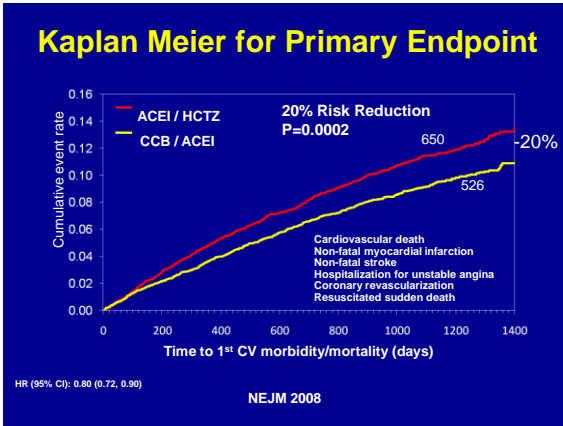


- 50% of patients were obese
- 60% of patients had Diabetes mellitus
- 97% of patients were treated previously for HT
- 74% of patients were treated with ≥ 2 antihypertensives
- Age: 68.4 years
- 78% of patients on ACEI or ARB
- 67% of patients on lipid-lowering agents
- 63% of patients on anti-platelet therapy
- Mean LDL 101.6 mg/dl
- Only 37.5% of patients were controlled to <140/90 mmHg

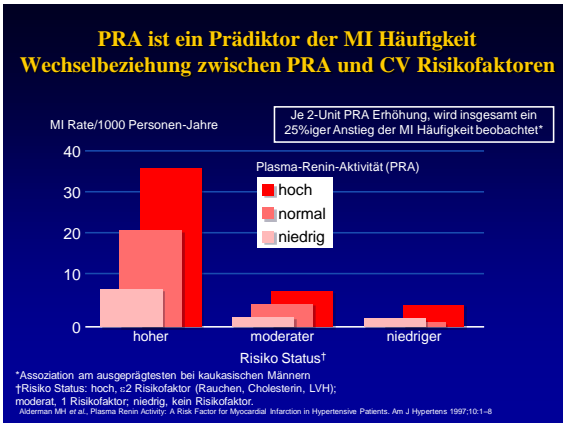
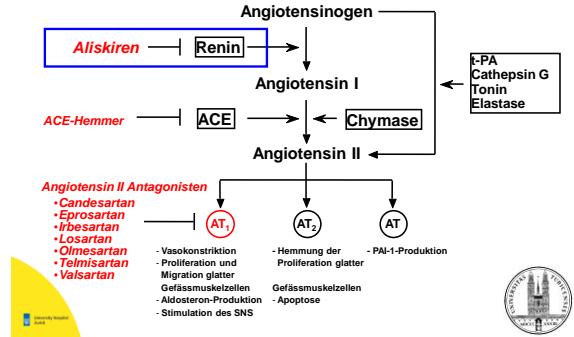
NEJM 2008

ACCOMPLISH: Systolic Blood Pressure

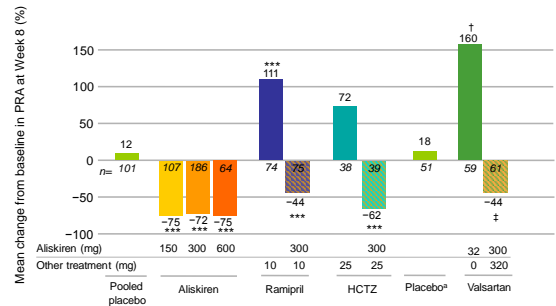




Das Renin-Angiotensin-System

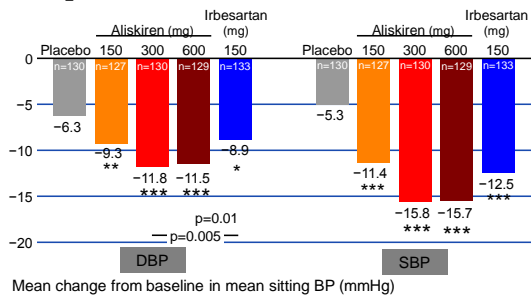


Aliskiren neutralisiert den PRA-Anstieg induziert durch Renin-stimulierende Substanzen



Taylor A, et al. 2007 (Pooled analysis)

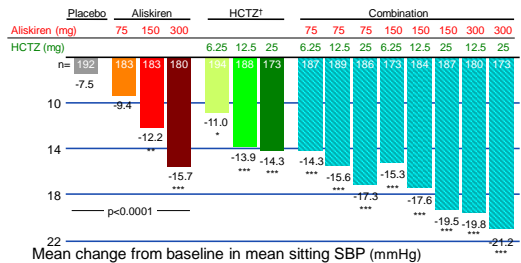
Aliskiren monotherapy provides dose-dependent reductions in DBP and SBP



*p<0.02 vs placebo; **p<0.005; ***p<0.0005 vs placebo

Gradman AH et al. Circulation. 2005

Aliskiren provides additional SBP lowering when combined with HCTZ



*Overall significance of HCTZ effect not tested
Pairwise comparisons: *p<0.05; **p<0.001; ***p<0.0001 vs. placebo; p<0.05 vs. each component monotherapy

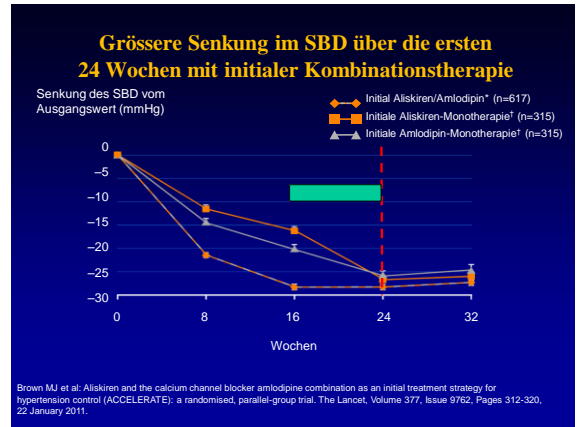
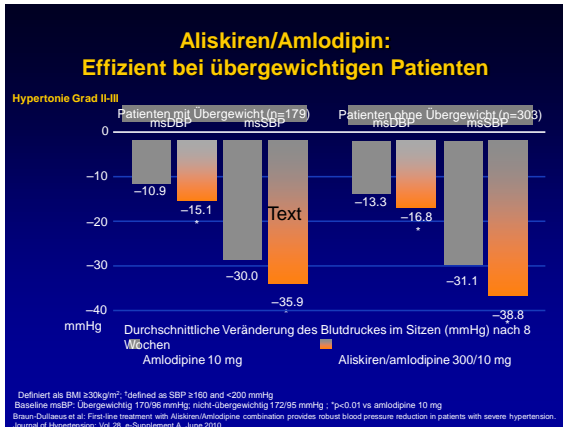
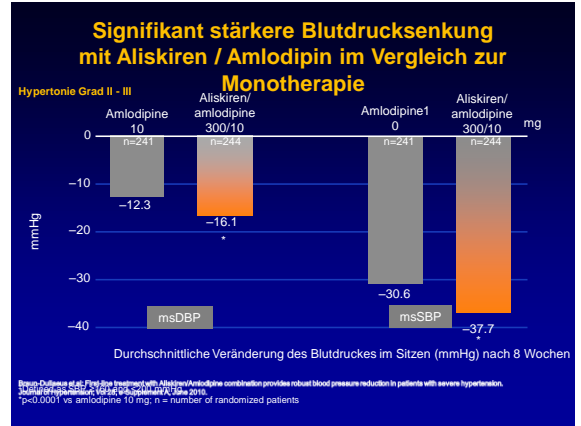
Vitelli A, Chrysant SG, Calhoun D, et al. Renin inhibition with aliskiren provides additive antihypertensive efficacy when used in combination with hydrochlorothiazide. J Hypertens 2007;25:217-226.

Tolerability of Aliskiren Monotherapy

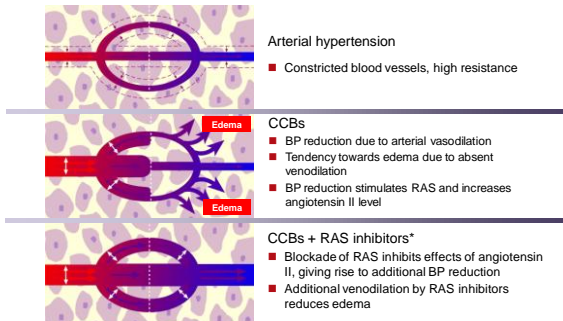
	Placebo n = 781	Aliskiren 75 mg n = 478	Aliskiren 150 mg n = 774	Aliskiren 300 mg n = 768	Aliskiren 600 mg n = 296	All aliskiren n = 2316
Any SAE, n (%)	5 (0.6)	3 (0.6)	3 (0.4)	4 (0.5)	1 (0.3)	11 (0.5)
Any AE, n (%)	314 (40.2)	193 (40.4)	290 (37.5)	309 (40.2)	130 (43.9)	922 (39.8)
Discontinuations due to AE, n (%)	27 (3.5)	8 (1.7)	12 (1.6)	20 (2.6)	5 (1.7)	45 (1.9)
Adverse events, reported by 22% of patients for aliskiren monotherapy overall, n (%)						
Headache	68 (8.7)	31 (6.5)	42 (5.4)*	44 (5.7)*	15 (5.1)	132 (5.7)**
Nasopharyngitis	45 (5.8)	34 (7.1)	33 (4.3)	29 (3.8)	5 (1.7)**	101 (4.4)
Diarrhea	9 (1.2)	6 (1.3)	9 (1.2)	18 (2.3)	28 (9.5)*	61 (2.6)*

AE, adverse event; SAE, serious adverse event. *p<0.05; **p<0.01; †p<0.0001 vs placebo

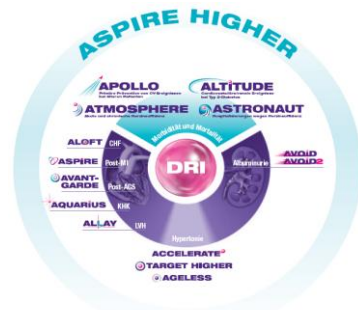
Weir MR, et al: Eur Heart J 2006



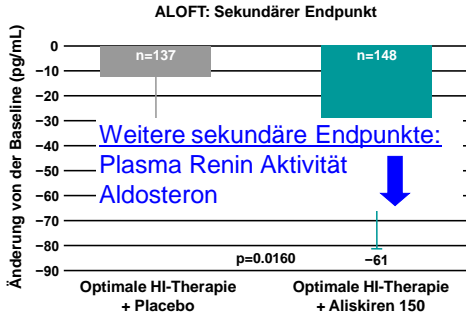
Complementary Effects of a CCB/RAS Inhibitor: Reduction of CCB-associated Edema



ASPIRE HIGHER: Ein umfangreiches Morbiditäts- und Mortalitätsstudienprogramm mit über 35'000 Patienten

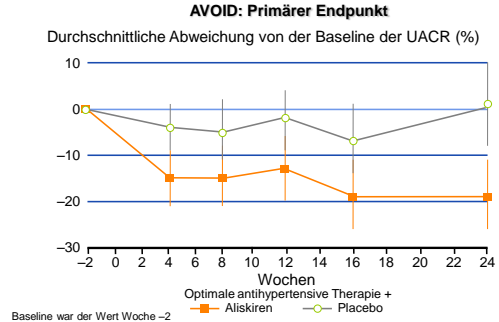


Effekt von Aliskiren auf BNP Level



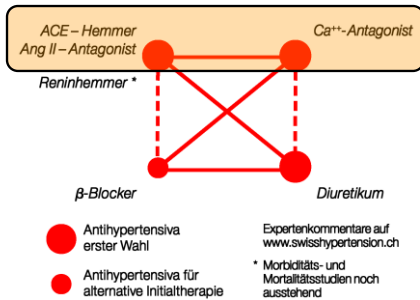
McMurray JJ, et al. Effects of the oral direct renin inhibitor aliskiren patients with asymptomatic heart failure. Circ Heart Fail 2008; 1:17-24
Rasilez® ist in der Schweiz nicht zur Behandlung der Herzinsuffizienz zugelassen.

Einfluss von Aliskiren auf Albuminurie bei diabetischer Nephropathie

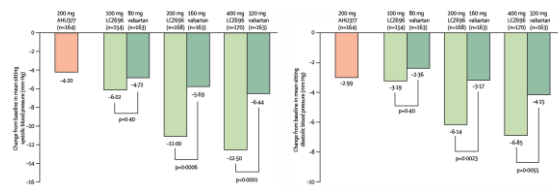


Paving et al. Aliskiren combined with losartan in type 2 diabetes and nephropathy. N Engl J Med 2008; 23: 2433-2446

Therapie der arteriellen Hypertonie



Blood Pressure Reduction by LCZ696



Ruilope L. et al, Lancet 2010

Take Home Messages

- Kombinationstherapie ist bei vielen Hypertonikern nötig
- Kombination RAS-Hemmer mit Kalziumantagonist ist die beste Zweierkombination
- Direkte Reninhemmung mit Aliskiren allein oder in Kombination führt zu einer starken Blutdrucksenkung und ist gut verträglich