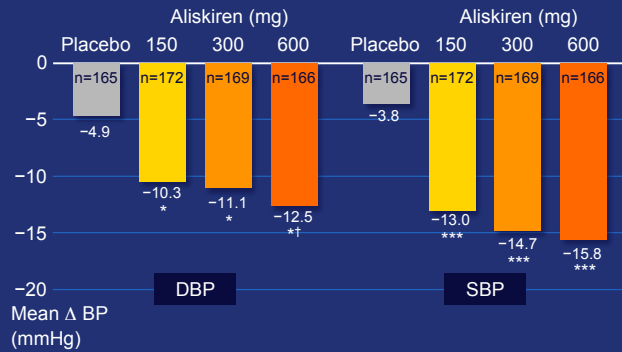


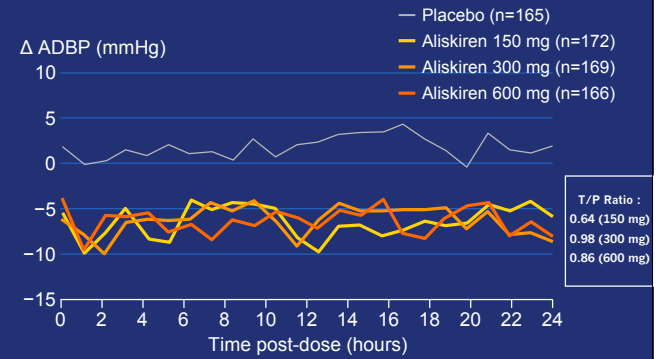
### Aliskiren monotherapy offers dose-dependent reductions in DBP and SBP



\*p<0.0001 vs placebo; \*\*\*p<0.0001 vs placebo  
†p<0.05 for aliskiren 600 mg compared with aliskiren 150 mg

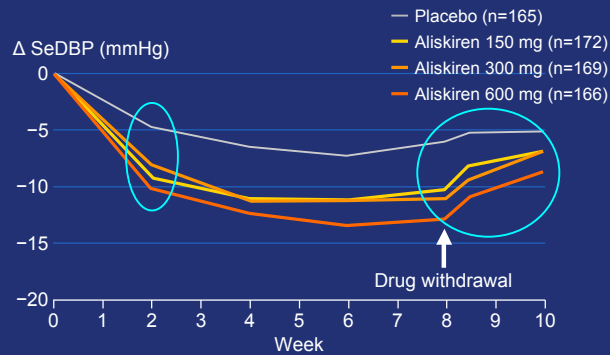
Oh BH, et al. 2006

### Significant reductions in mean ambulatory BP are sustained over 24 hours



Mitchell L, et al. 2006

### Aliskiren demonstrates onset of BP response by Week 2 and some persistence of effect after withdrawal



Herron J, et al. 2006 (Study 2308)

### Aliskiren, HCTZ and combination trial Multifactorial study design (2204)

8 weeks' double-blind treatment

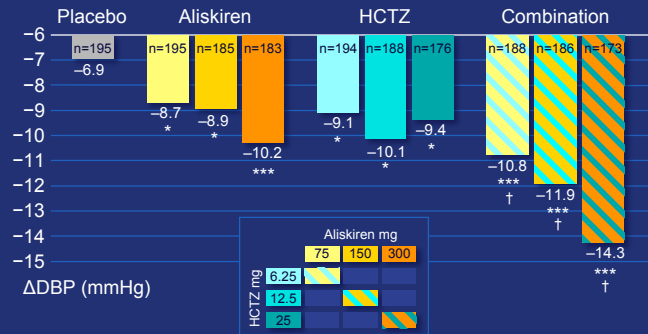
	Placebo	Aliskiren 75 mg	Aliskiren 150 mg	Aliskiren 300 mg
Placebo	n=195	n=195	n=185	n=183
HCTZ 6.25 mg	n=194	n=188	n=176	—
HCTZ 12.5 mg	n=188	n=193	n=186	n=181
HCTZ 25 mg	n=176	n=186	n=188	n=173

Placebo run-in period: 2–4 weeks

- Design:** Randomized, placebo-controlled, multifactorial study
- Primary objective:** Overall superiority of aliskiren to placebo on DBP  
Efficacy of HCTZ combinations compared with monotherapies
- Secondary objective:** SBP, responder rates, dose response
- Population:** 2776 patients ≥18 years with mild-moderate essential hypertension (DBP 95–109 mmHg)

Villamil A, et al. 2006 (Study 2204)

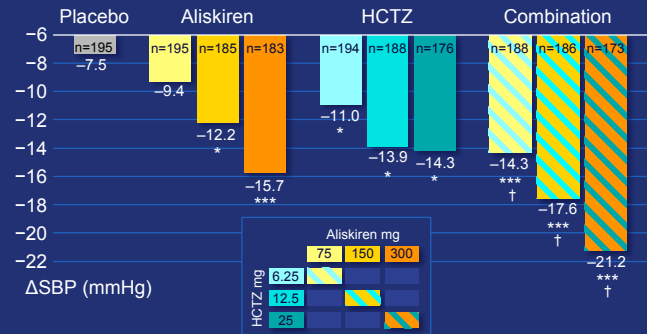
### Aliskiren and HCTZ combination provides additional DBP lowering



\*p<0.05; \*\*\*p<0.0001 vs placebo  
†p<0.05 vs each component monotherapy

Villamil A, et al. 2006

### Aliskiren and HCTZ combination provides additional SBP lowering

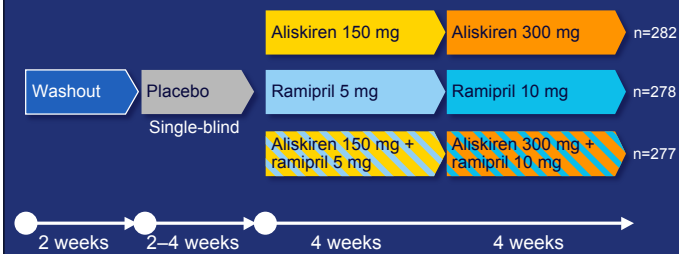


\*p<0.05; \*\*\*p<0.0001 vs placebo  
†p<0.05 vs each component monotherapy

Villamil A, et al. 2006

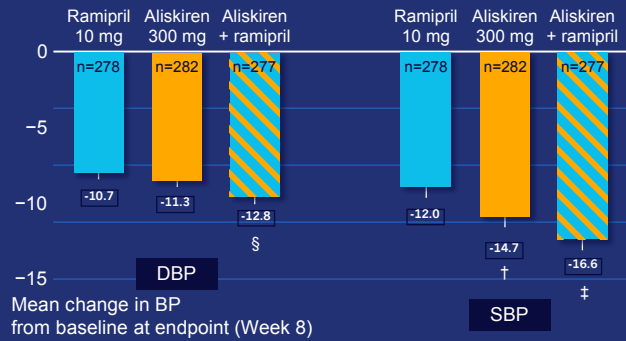
### Aliskiren in combination with ramipril Study 2307

Randomized, double-blind, parallel group, dose escalation study in 837 patients with hypertension and diabetes



Uresin Y, et al. 2006 (Study 2307)

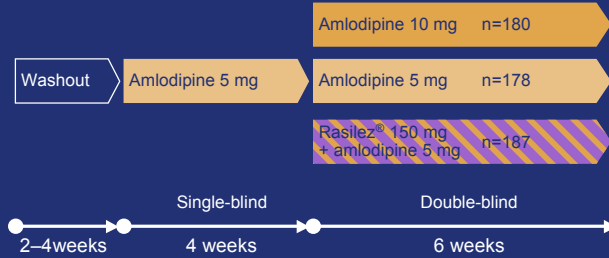
### Aliskiren /ramipril combination provided significantly greater reductions in BP than either drug as monotherapy



§p<0.05 vs ramipril and aliskiren alone; †p<0.05; ‡p<0.005 vs ramipril

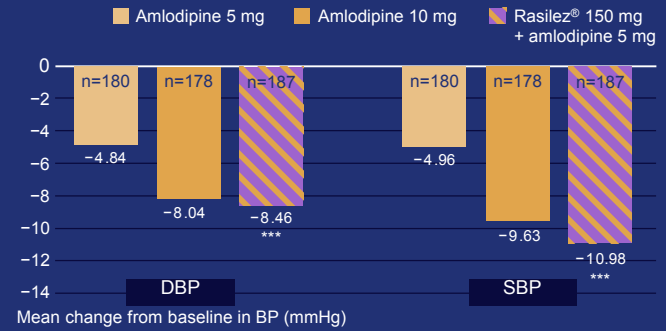
Uresin Y, et al. 2006 (Study 2307)

## Aliskiren in non responders to amlodipine Study 2305



Munger M, et al. WCC 2006 (Study 2305)

## Aliskiren significantly improves BP control when added to amlodipine 5 mg



\*\*\*p<0.001 vs amlodipine 5 mg

Munger M, et al. WCC 2006 (Study 2305)

## Aliskiren /amlodipine combination has less oedema than increasing amlodipine

	Aliskiren 150 mg + amlodipine 5 mg	Amlodipine 5 mg	Amlodipine 10 mg
AEs, %	31.6	28.5	30.9
Oedema, %	2.1	3.4	11.2
GI, %	5.9	4.5	2.8
Diarrhoea, %	1.6	0.6	1.1
SAEs	2 Diverticulitis Hyperglycaemic coma	1 Myocardial ischaemia	2 Myocardial ischaemia Eye haemorrhage
AE discontinuations	5	3	5

Novartis, data on file 2005 (Study 2305)

## Summary of aliskiren preclinical data

- Aliskiren demonstrates organ protective effects in animal models
  - Renoprotection comparable to ACEi and ARBs
  - LVH reductions comparable to ARBs
  - Atherogenesis prevention
- Aliskiren may affect the renin receptor (pathophysiological relevance of (pro)renin receptor still unknown...)
  - Upcoming preclinical studies will address key questions such as :
    - Does the (pro)renin receptor play a role in pathogenesis of CV disease ?
    - What is the effect of aliskiren on (pro)renin receptor function ?
    - Can aliskiren block the enzymatic activity of (pro)renin ?

## Aliskiren High specificity for human renin

Renin isoform	IC <sub>50</sub> (nM)
Human	0.6
Marmoset	2
Dog	7
Rabbit	11
Guinea pig	63
Rat	80
Pig	150
Cat	8500

- Aliskiren has a high specificity for human renin and is thus challenging to study in animal models
- Animal model developed to test human renin inhibitors: *double TransGenic Rat (dTGR)*
  - expresses genes for human renin and human angiotensinogen
  - animals develop severe hypertension and end-organ damage

## Aliskiren is the most effective\* antihypertensive due to direct renin inhibition

### \*Multidimensional

- Monotherapy provides double-digit BP reductions
- Consistent additive BP lowering
- Superior BP reductions versus ACEi
- Durability and persistence of control; no rebound
- Strong evidence supporting suppression of the Renin System
- Excellent safety profile with important differences
- Exciting, innovative outcome program

FYI only – not to be presented