



Avoiding Cardiovascular Events through COMbination Therapy in Patients Living with Systolic Hypertension

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Presenter Disclosure Information

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Disclosure Information...

The following relationships exist related to this presentation:

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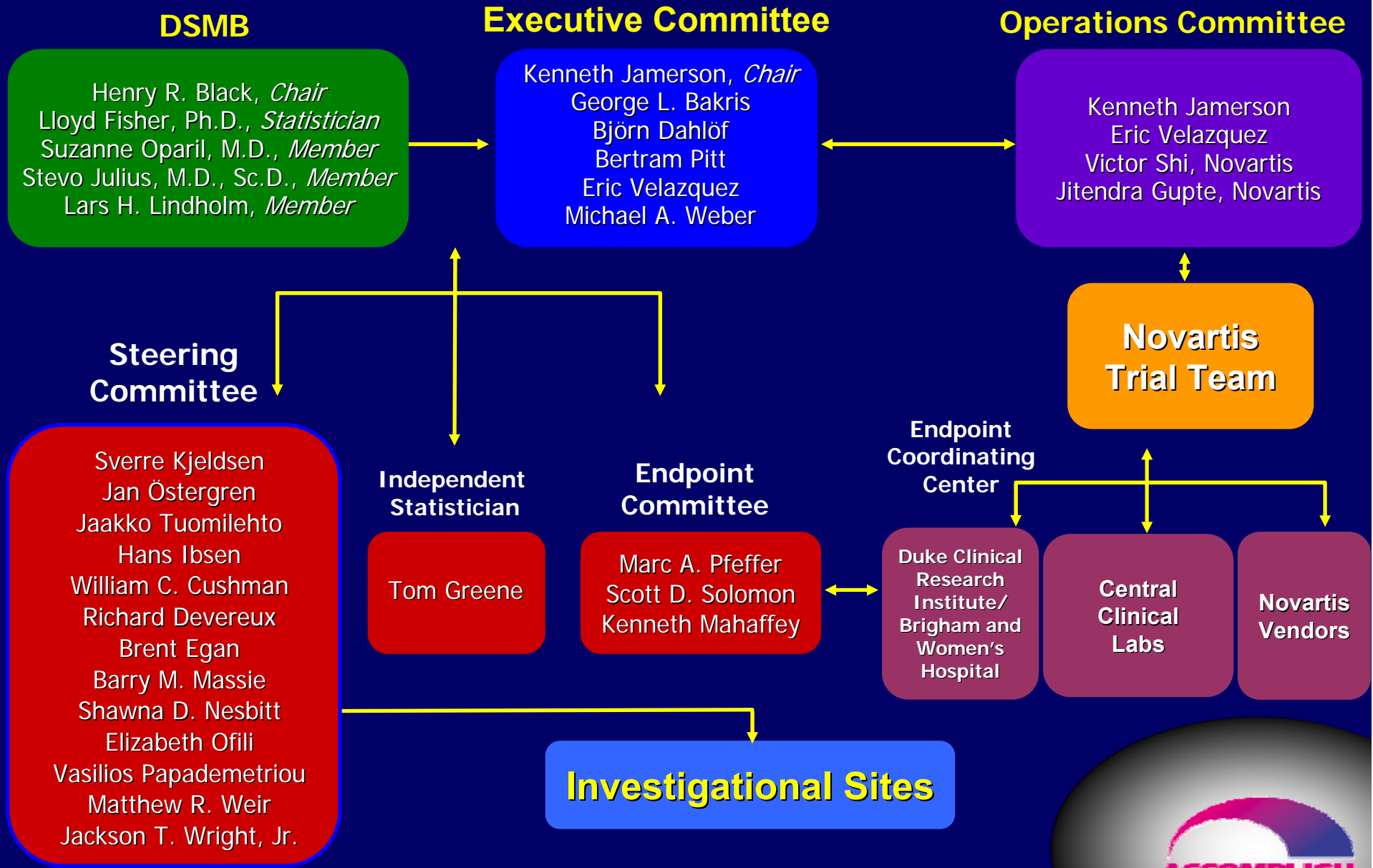
Avoiding Cardiovascular Events through COMbination Therapy in
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The following relationships exist related to this presentation:

Collectively, the authors have consulted for most pharmaceutical entities that manufacture cardiovascular products globally. Specifically, all authors have significant consultant, speaker, advisory, and research agreements with the trial sponsor, Novartis.

ACCOMPLISH Organizational Structure



BACKGROUND



ACCOMPLISH: A Novel Hypertension Trial

- **Traditional approach to hypertension management:**
 - **Initiate monotherapy then sequentially add medications to achieve target BP**
- **ACCOMPLISH:**
 - **Initiate single tablet combination therapy in high-risk hypertension**
 - **Specific combinations may confer target organ protection in addition to their BP-lowering effects**



ACCOMPLISH Hypothesis

ACCOMPLISH will test a new strategy for the treatment of hypertension – the first outcomes trial to compare initial therapy with two different combinations

The combination of benazepril and amlodipine will reduce cardiovascular morbidity and mortality in patients with high-risk hypertension by 15% when compared to the combination of benazepril and HCTZ



Primary Endpoint

Cardiovascular Mortality and Morbidity, defined as:

- Cardiovascular death
- Non-fatal myocardial infarction
- Non-fatal stroke
- Hospitalization for unstable angina
- Coronary revascularization procedure (PCI or CABG)
- Resuscitated sudden death

Targeted Population for Recruitment into the ACCOMPLISH Study

- Men or women age ≥ 55 years
- SBP ≥ 160 mmHg or currently on antihypertensive therapy
- Evidence of cardiovascular or renal disease or target organ damage



ACCOMPLISH Patients Were Receiving Significant Medical Management at Baseline

- **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**

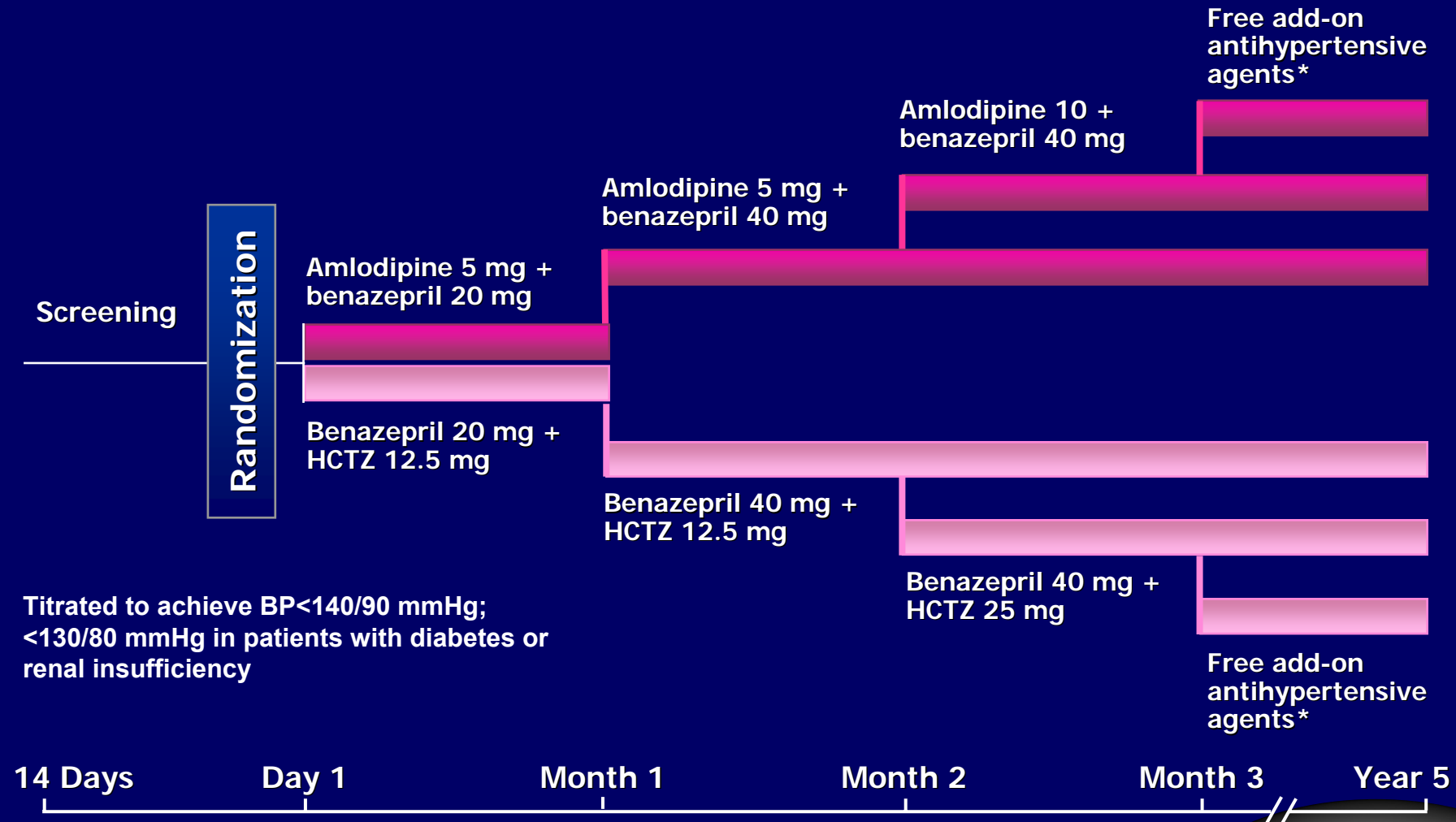


Baseline Traits of the ACCOMPLISH Cohort

- 50% of patients were obese
- 60% of patients had Diabetes Mellitus
- 97% of patients were treated previously for hypertension
- 74% of patients were treated with ≥ 2 antihypertensive agents
- **Only 37.5% of patients were controlled to $<140/90$ mmHg**



ACCOMPLISH: Design



Titrated to achieve BP < 140/90 mmHg;
< 130/80 mmHg in patients with diabetes or
renal insufficiency

*Beta blockers; alpha blockers; clonidine; (loop diuretics).

Jamerson KA et al. *Am J Hypertens.* 2003;16(part2)193A



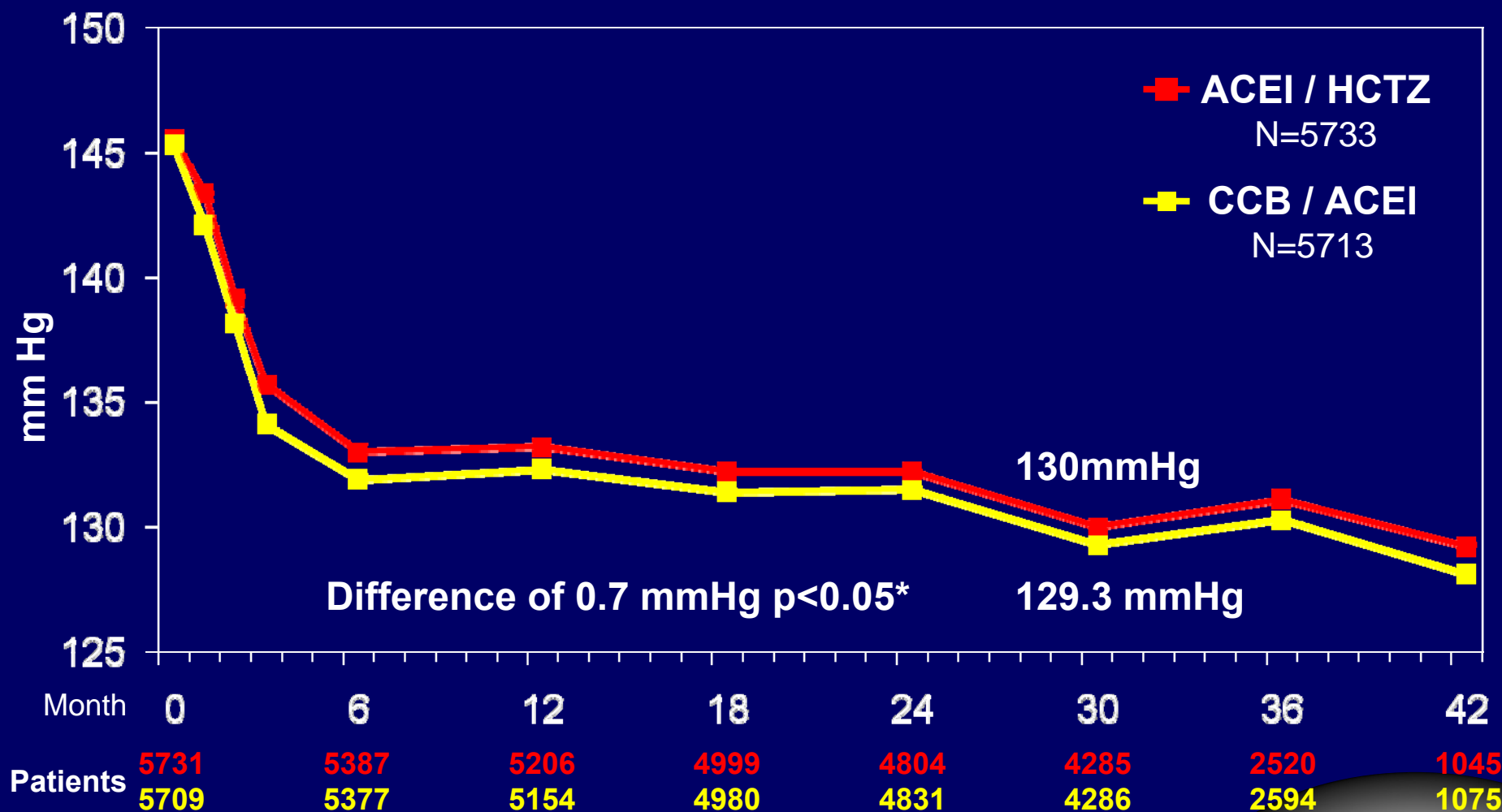
Baseline Demographics

	ACEI / HCTZ N=5741 (%)	CCB / ACEI N=5721 (%)
Gender		
Male	3509 (61.1)	3436 (60.1)
Female	2226 (38.8)	2283 (39.9)
Race		
Caucasian	4789 (83.4)	4814 (84.1)
Black	699 (12.2)	675 (11.8)
Asian	27 (0.5)	22 (0.4)
Other	220 (3.8)	208 (3.6)
Age		
Mean (years)	68.3	68.4
< 70	3407 (59.3)	3367 (58.9)
≥ 70	2328 (40.6)	2351 (41.1)
Region		
Nordic countries*	1676 (29.2)	1677 (29.3)
United States	4059 (70.7)	4042 (70.7)

*Denmark, Finland, Norway or Sweden



Systolic Blood Pressure Over Time

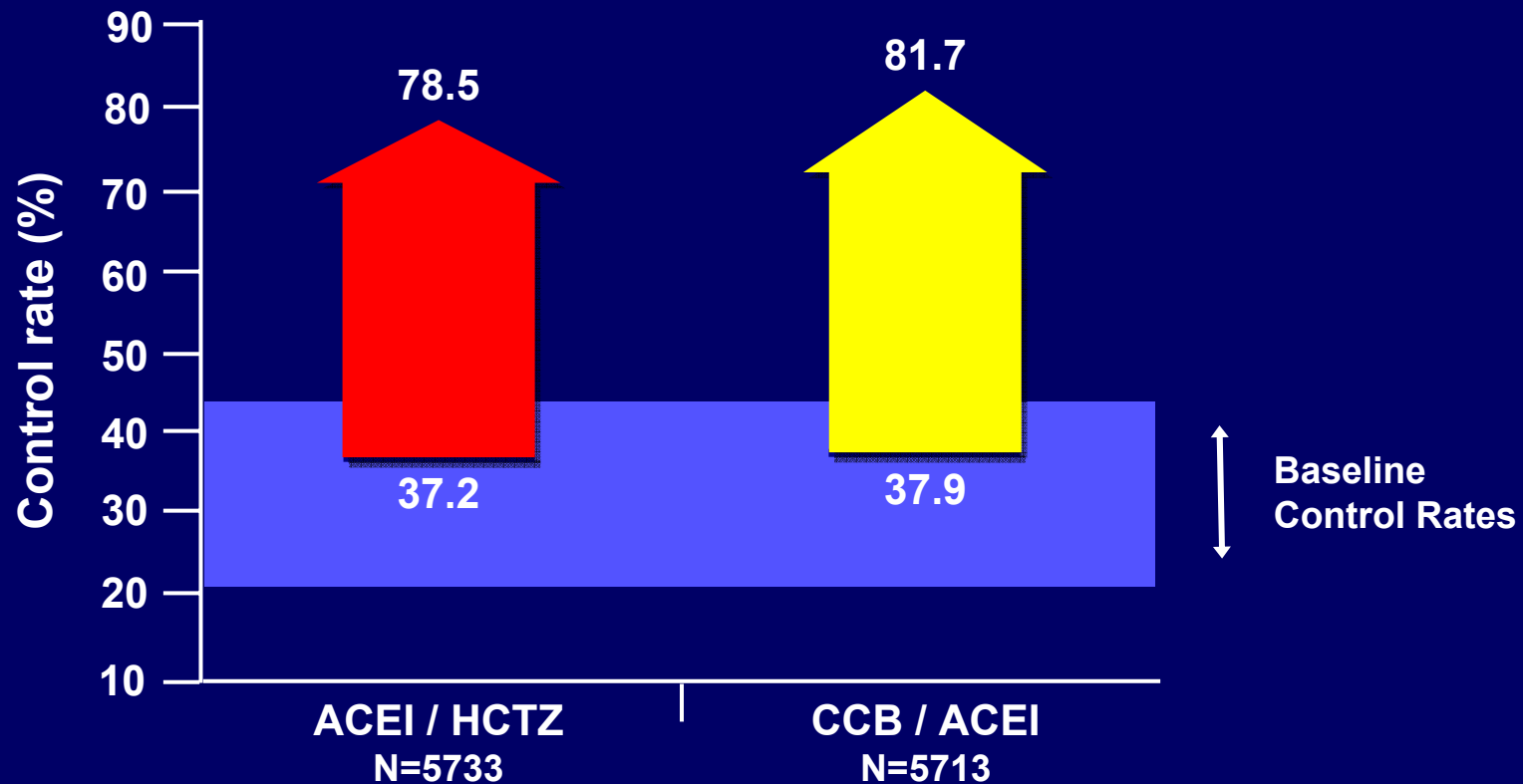


*Mean values are taken at 30 months F/U visit

■ DBP: 71.1 ■ DBP: 72.8



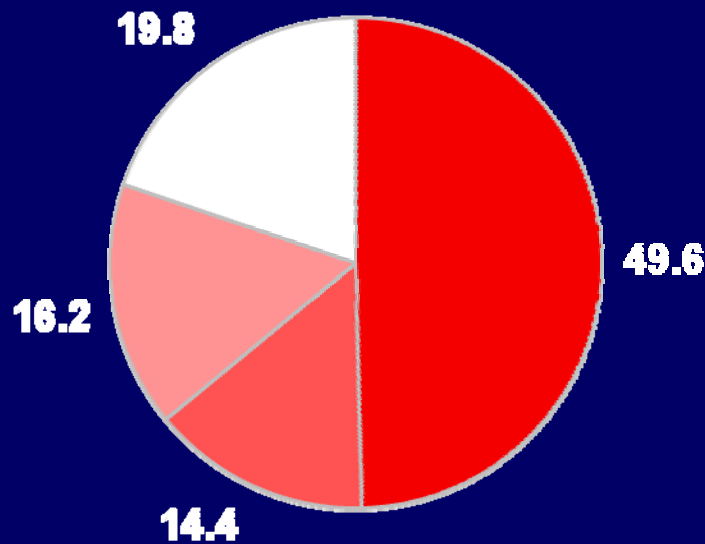
ACCOMPLISH: Exceptional Control Rates with Initial Combination Therapy



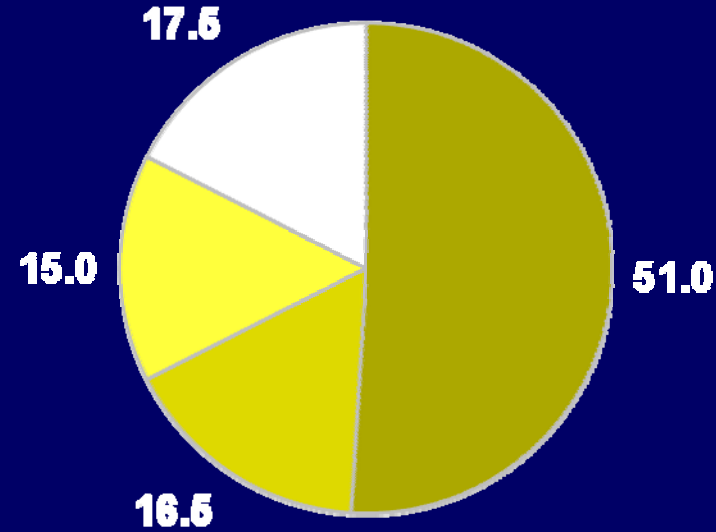
P<0.001 at 30 months follow-up
Control defined as <140/90 mmHg



Low Pill Burden in ACCOMPLISH



ACEI / HCTZ
N=5733



CCB / ACEI
N=5713

- Study Medication Only
- Study + 1 Add-on
- Study + ≥ 2 Add-on
- Drug Interruption

- Study Medication Only
- Study + 1 Add-on
- Study + ≥ 2 Add-on
- Drug Interruption

Includes patients receiving beta blockers, alpha blockers, clonidine, loop diuretics. The number of patients with free add-on antihypertensive agents only include those patients who has reached dose level 3.

At 30 month follow-up

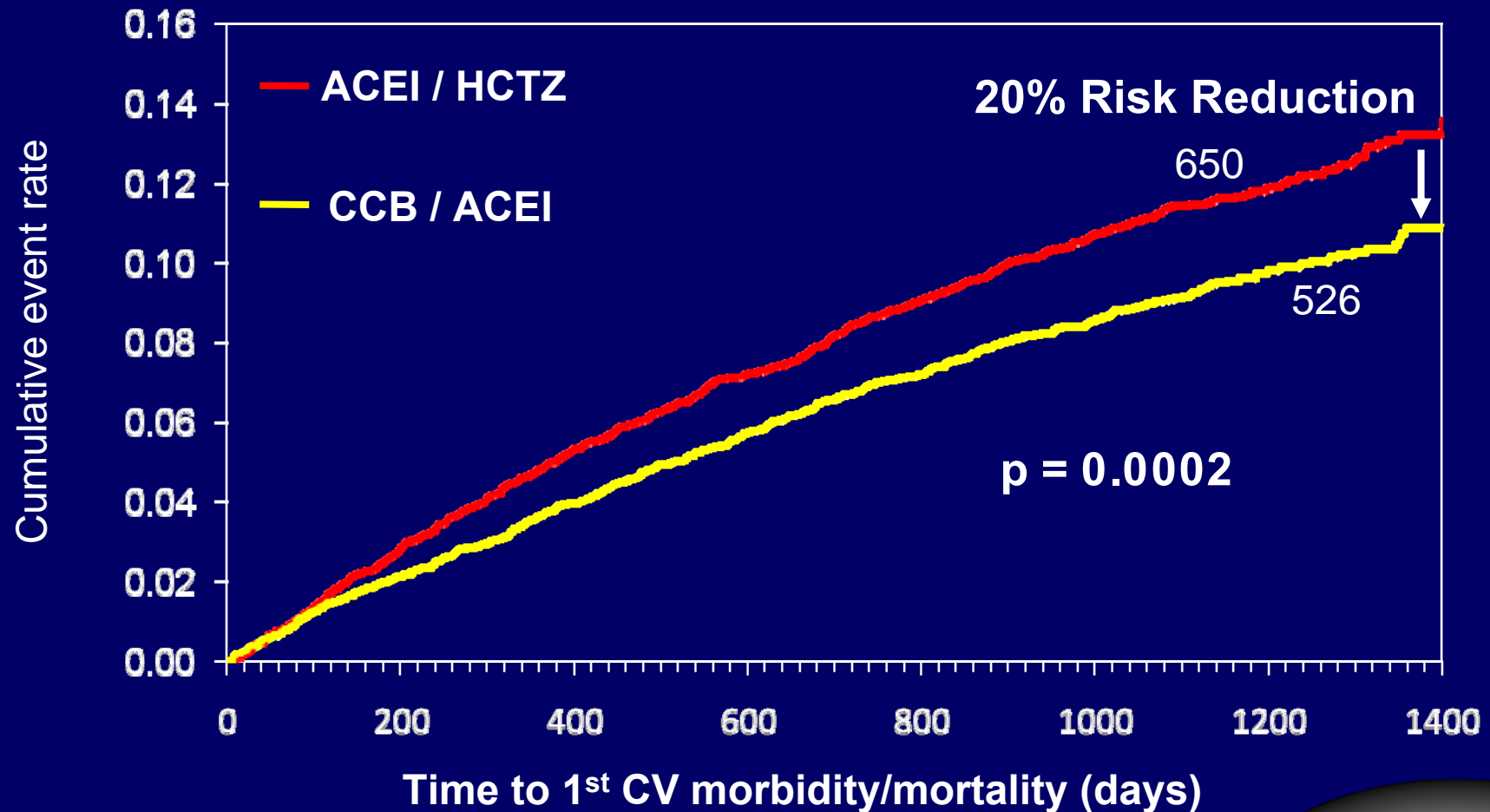


DSMB Oct 17 2007

- Pre-specified efficacy boundary was crossed with 60% of the expected trial information
- Executive Committee accepted the recommendation
- Last patient last visit was Jan 24, 2008
- Total of 1176 unique patients with events
- 95.3% of primary events are adjudicated



Kaplan Meier for Primary Endpoint



HR (95% CI): 0.80 (0.72, 0.90)

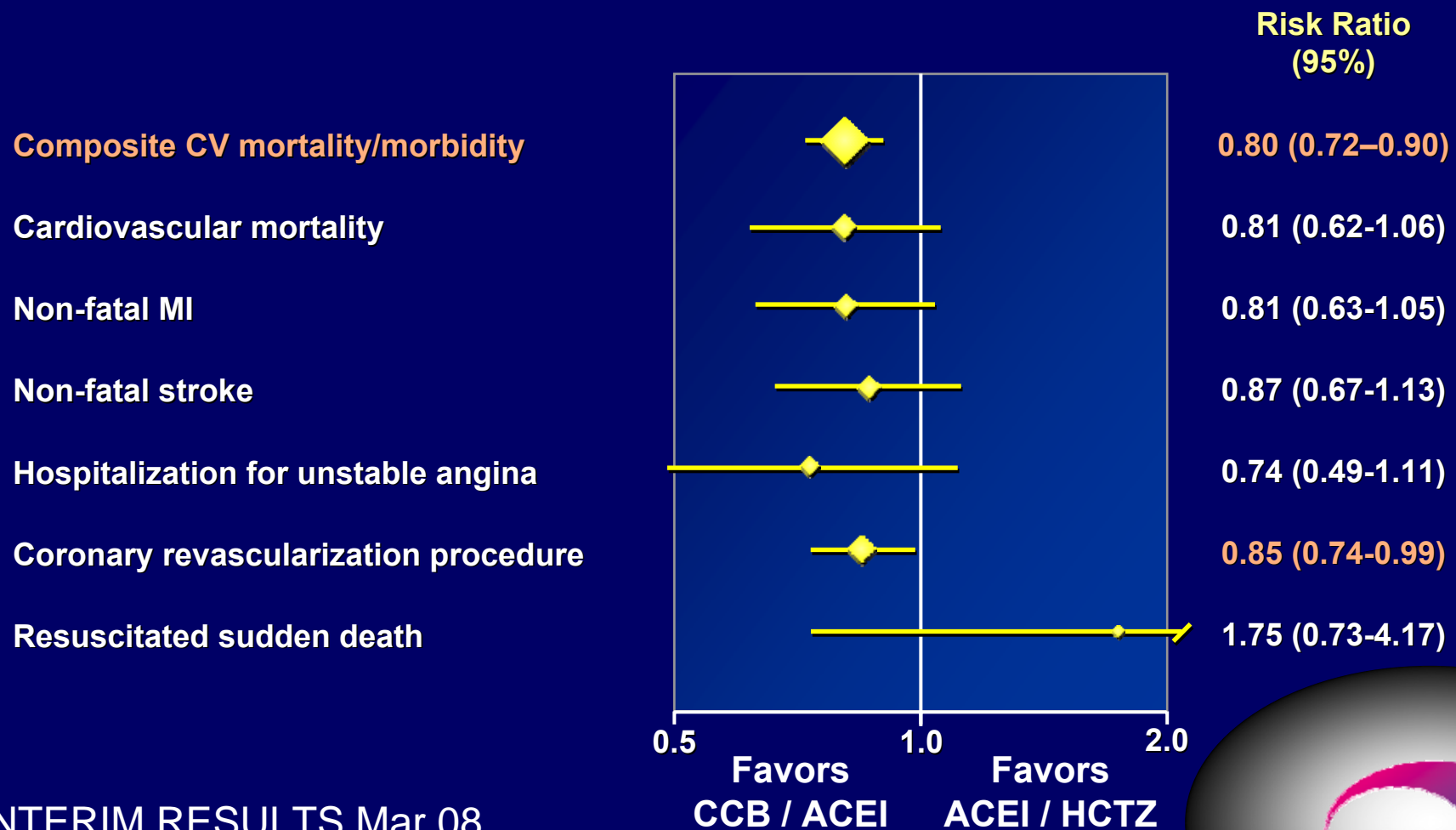
INTERIM RESULTS Mar 08



Primary Endpoint and Components

Incidence of adjudicated primary endpoints, based upon cut-off analysis date 3/24/2008

(Intent-to-treat population)



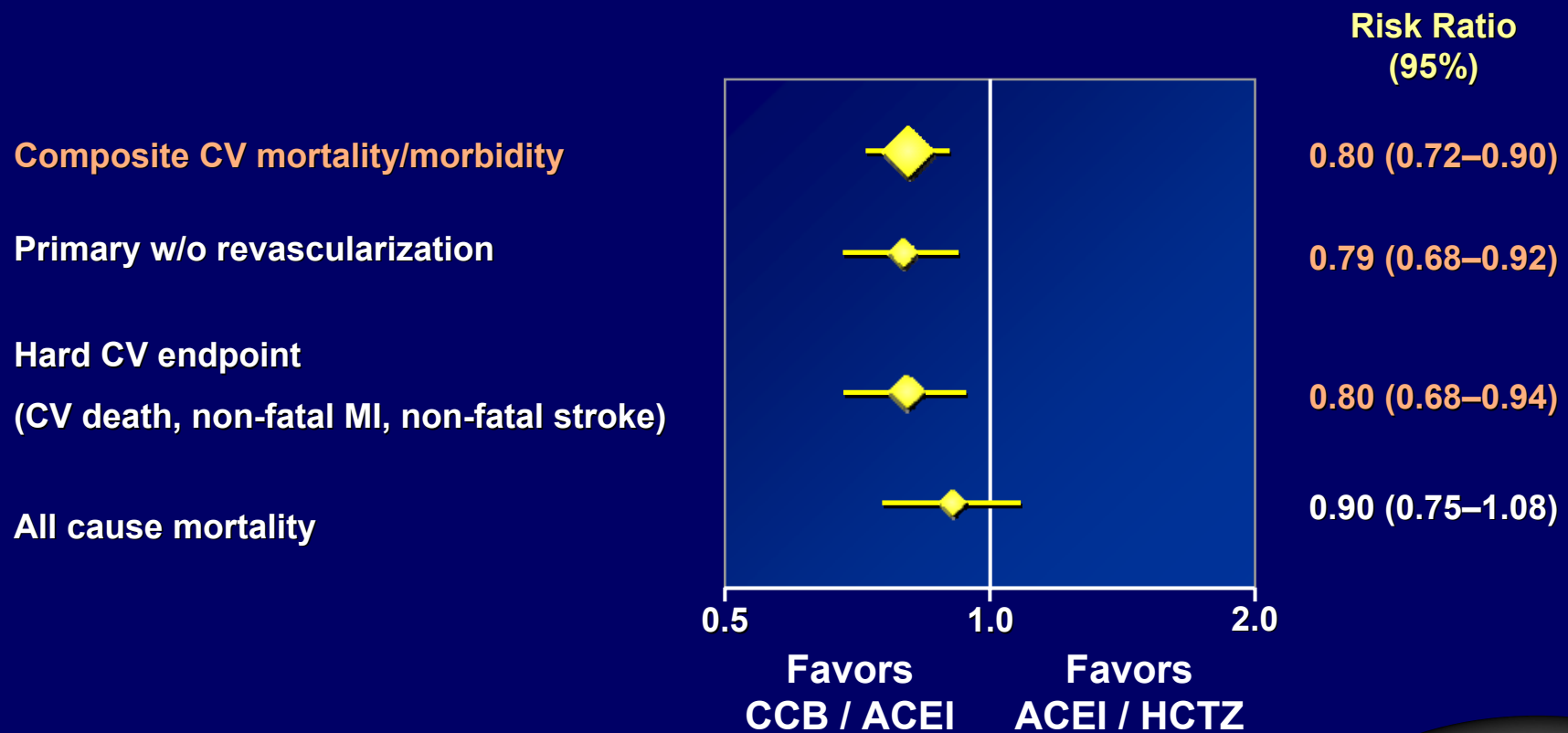
INTERIM RESULTS Mar 08



Primary and Other Endpoints

Incidence of adjudicated primary endpoints, based upon cut-off analysis date 3/24/2008

(Intent-to-treat population)



INTERIM RESULTS Mar 08



Summary

- Single tablet combination therapy was initiated in 11,462 high risk hypertensive patients
- After mean follow-up of 39 months,
 - The combination of ACEI / CCB was superior to ACEI / diuretic
 - CV morbidity / mortality was reduced by 20% (p=0.0002)
 - Hard CV Endpoint (CV death, stroke and MI) was reduced by 20% (p=0.007)



Summary (cont'd)

- Prior to study entry, 97% of patients were on antihypertensive medication, 74% receiving ≥ 2 therapies
- After mean follow up of 30 months,
 - Overall BP control rates increased from 37% to 80%
 - Mean SBP decreased from 145 to <130 mmHg
 - 50% of participants required only one tablet



Conclusions

ACCOMPLISH achieved exceptional BP control with combination therapy providing a new option for cardiovascular risk reduction to millions of patients with hypertension.

The results of ACCOMPLISH provide compelling evidence for initial combination therapy with ACEI / CCB and challenge current diuretic-based guidelines.

