

# PRECISION-ABPM

**Prospective Randomized Evaluation of Celecoxib Integrated Safety versus Ibuprofen Or Naproxen Ambulatory Blood Pressure Measurement Trial**



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# Declaration of interest

Study Sponsor: Pfizer

Executive committee members agreed not to accept any financial payments related to NSAIDs from any manufacturer of NSAIDs throughout the duration of the trial, including the trial's sponsor

Served on Steering Committees/Speakerbureau for:

Abbott, Bayer, Biotronik, Cardioventis, Fresenius, Merck, Novartis, Servier, Zoll

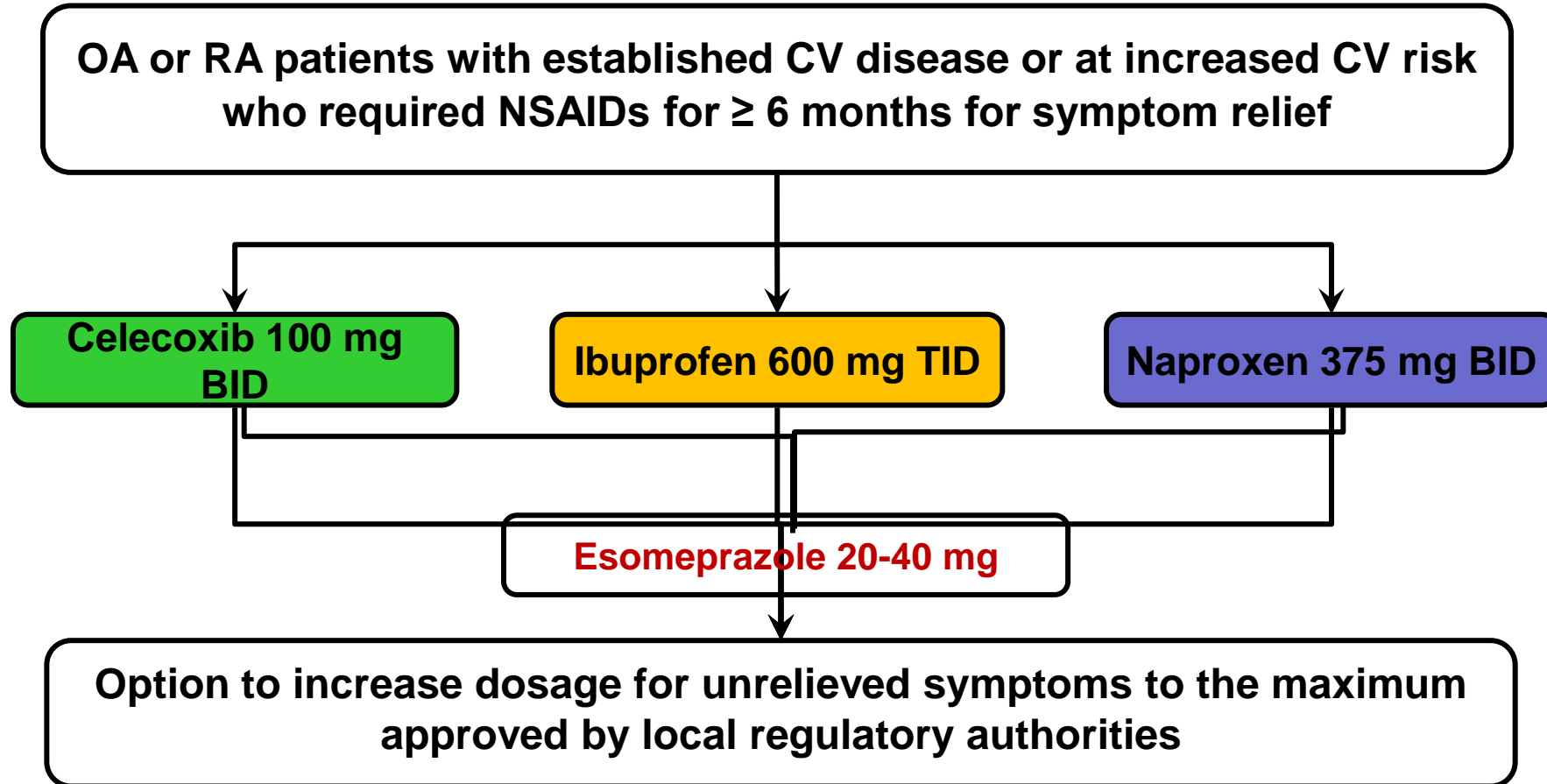
# PRECISION-ABPM: Background

- Non-steroidal anti-inflammatory drugs (NSAIDs) are amongst the most widely prescribed drugs in the world with more than 100 million prescriptions in the United States and Europe
- NSAIDs reduce pain and inflammation through the suppression of prostaglandin synthesis, by inhibiting the enzyme cyclooxygenase (COX), but may also exert cardiovascular off-target effects
- One fourth of the worlds population aged over 35 years has arthritis
  - of these, almost half have *or are at high risk of* cardiovascular disease, particularly hypertension

# PRECISION-ABPM: Objective

- Even relatively small changes in blood pressure may impact cardiovascular morbidity and mortality
- Current labeling of all NSAIDs include warnings regarding potential risk of cardiovascular events and increase in blood pressure
- Therefore, the primary objective of PRECISION-ABPM was to compare the COX-2 inhibitor **celecoxib** vs two widely used non-selective NSAIDs, **naproxen** and **ibuprofen**, in patients with arthritis and either known CAD or at relatively high cardiovascular risk
- Primary endpoint was the change from baseline in 24-hour mean systolic blood pressure after 4 months treatment

# PRECISION-ABPM: **Treatments**



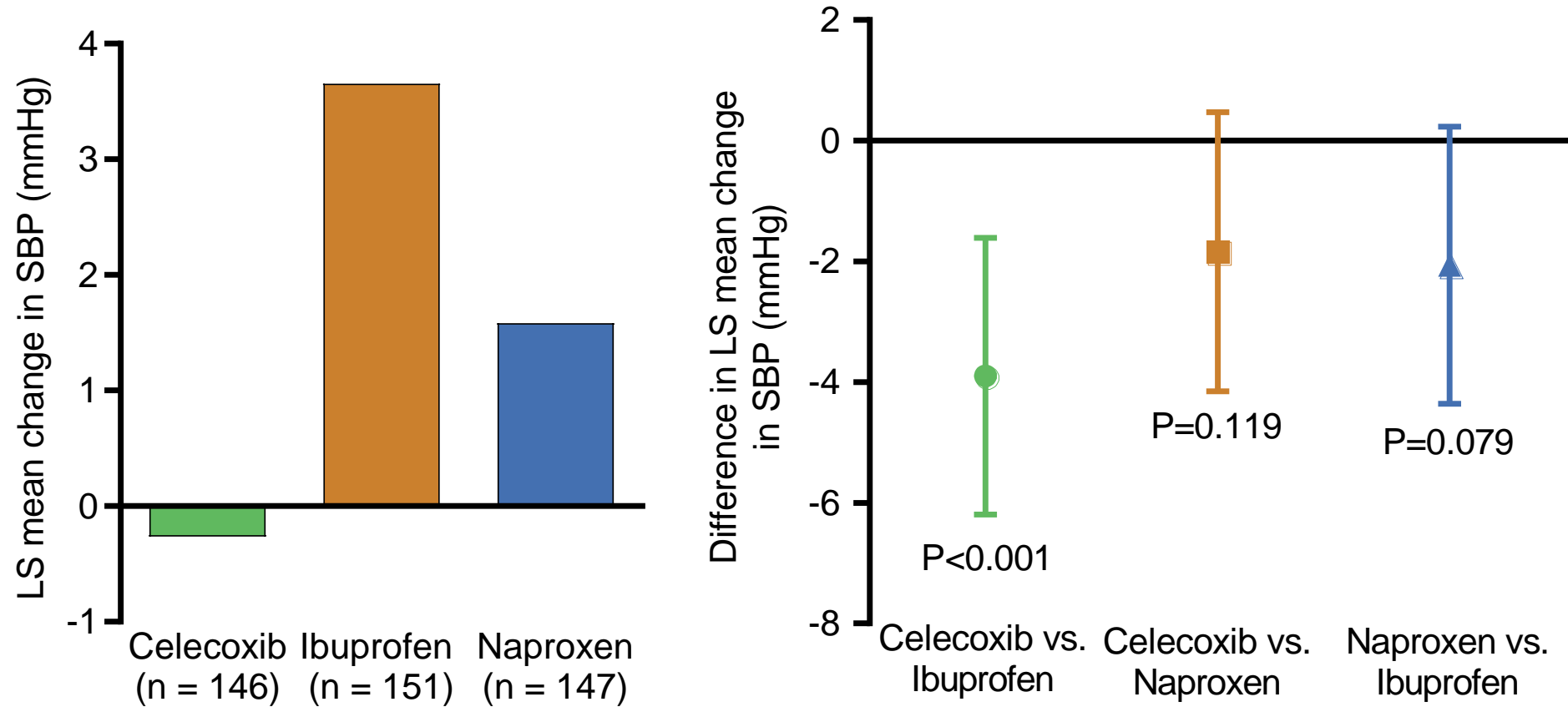
# PRECISION-ABPM: Patient Baseline Characteristics

Characteristics	Celecoxib (100-200mg BID) n = 146	Ibuprofen (600-800mg TID) n = 151	Naproxen (375-500mg BID) n = 147
Age, years	62.1 ± 10.1	61.9 ± 9.7	61.4 ± 10.3
Sex m/f, %	70/76	72/79	63/84
Race: White/Black/Other, %	81/13/6	80/17/3	81/16/2
BMI, kg/m <sup>2</sup>	32.6 ± 7.0	32.7 ± 6.9	31.9 ± 6.6
OA/RA, %	92/8	91/9	94/6
Baseline aspirin, %	49	49	46
Blood pressure			
Systolic BP, mmHg	125.1 ± 9.41	125.5 ± 10.63	125.3 ± 9.93
Diastolic BP, mmHg	74.6 ± 7.43	74.2 ± 8.72	74.8 ± 7.52
Laboratory tests			
HbA1c, %	7.6 ± 1.92	7.4 ± 1.63	7.5 ± 2.08
Creatinine, mg/dL	0.9 ± 0.21	0.9 ± 0.23	0.9 ± 0.20
eGFR, mL/min/1.73m <sup>2</sup>	79.8 ± 18.28	79.8 ± 18.25	79.6 ± 18.16

# PRECISION-ABPM: Co-Medication

Characteristics	Celecoxib (100-200mg BID) n = 146	Ibuprofen (600-800mg TID) n = 151	Naproxen (375-500mg BID) n = 147
Study Drug (mean dose/day)	208 (34)	2031 (237)	852 (98)
Any concomitant medication, %	85	89	87
Agents acting on the RAAS, %	59	67	59
Beta-Blocker, %	29	35	34
Ca Channel Blockers, %	23	22	22
Diuretics,%	32	41	32
Peripheral Vasodilators, %	8	3	5

# PRECISION-ABPM: Change in Ambulatory 24-h Systolic Blood Pressure from Baseline at 4 Months

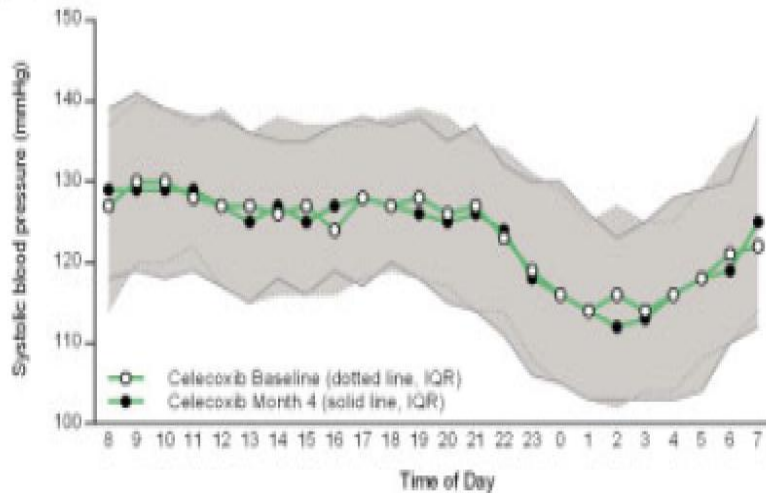


LS, least squares. SBP, systolic blood pressure



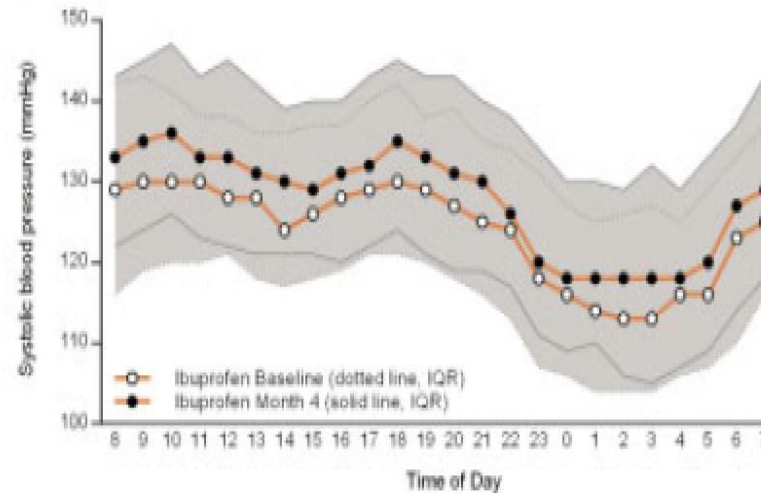
# PRECISION-ABPM: Hourly Ambulatory Systolic BP Over 24 Hours at Baseline and at 4 Months

## Celecoxib



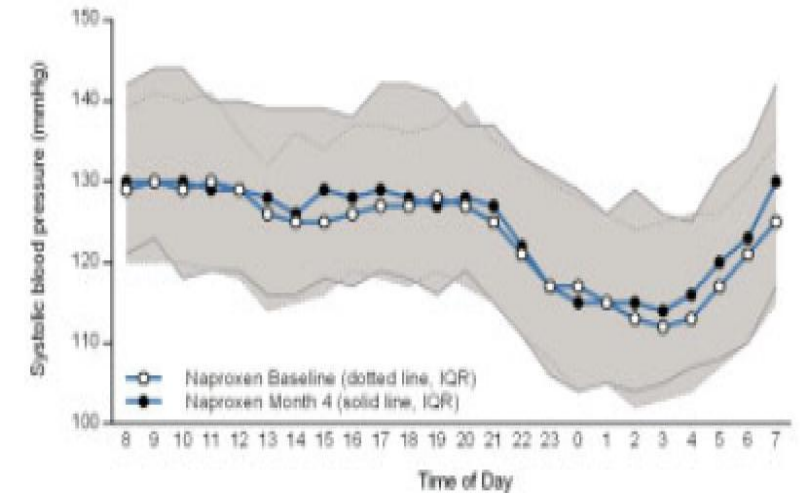
$\Delta$  at month 4  $p=0.80$

## Ibuprofen



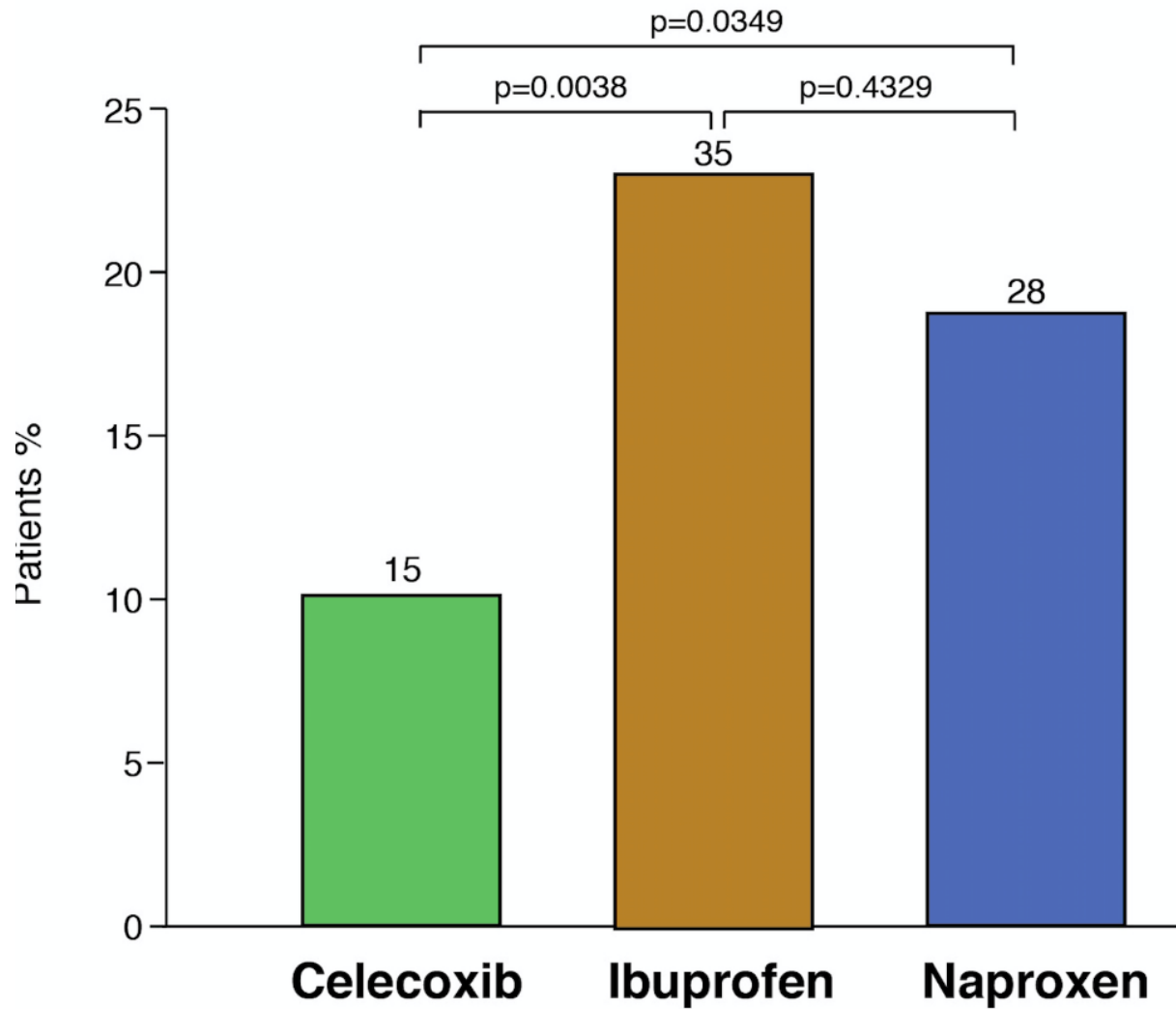
$\Delta$  at month 4  $p<0.001$

## Naproxen



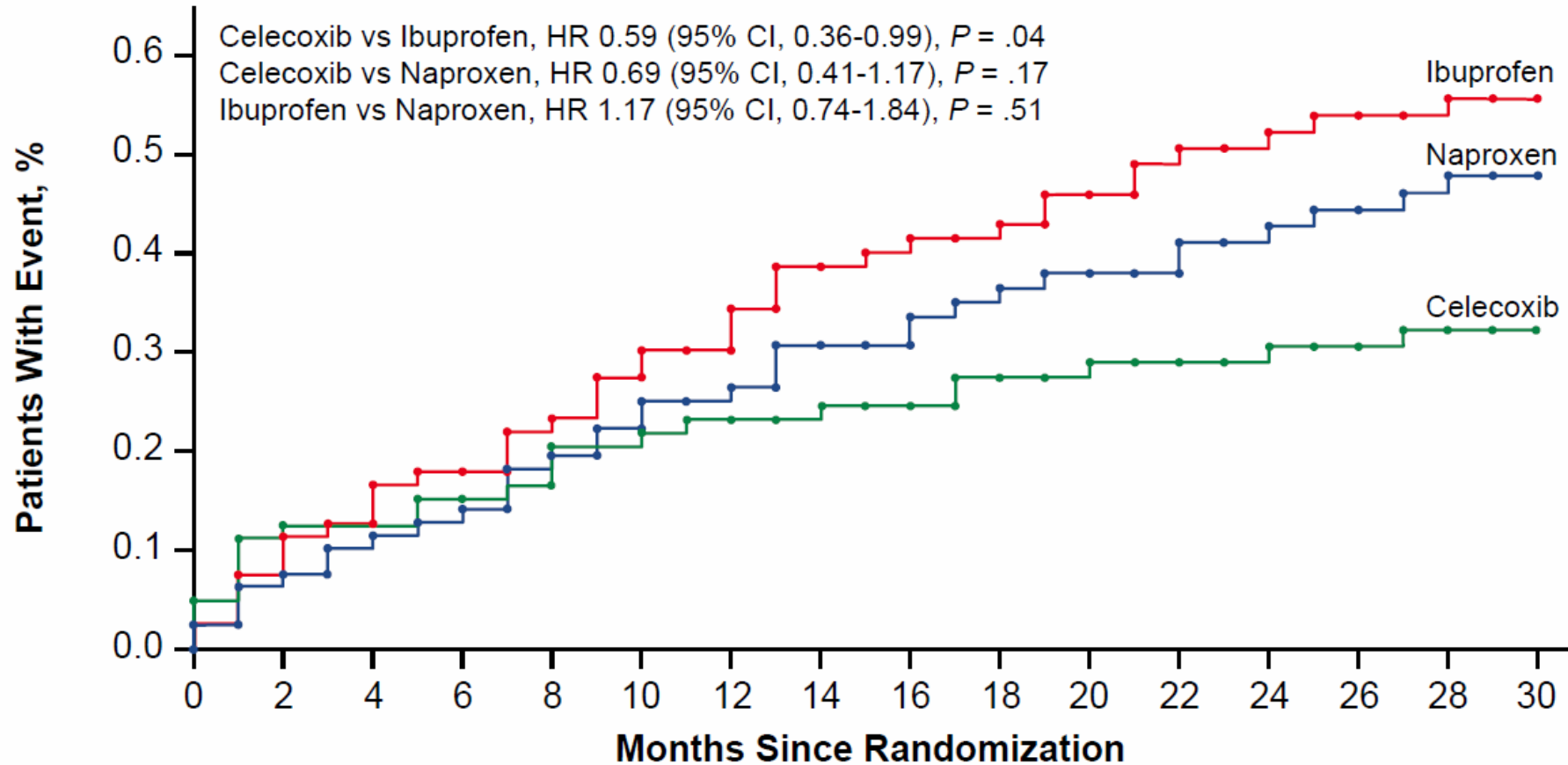
$\Delta$  at month 4  $p=0.12$

# PRECISION-ABPM: Patients with Baseline Normotensive Blood Pressure Who Developed Hypertension at 4 months



New hypertension defined as mean 24-hour SBP  $\geq$  130 and/or DBP  $\geq$  80 mmHg

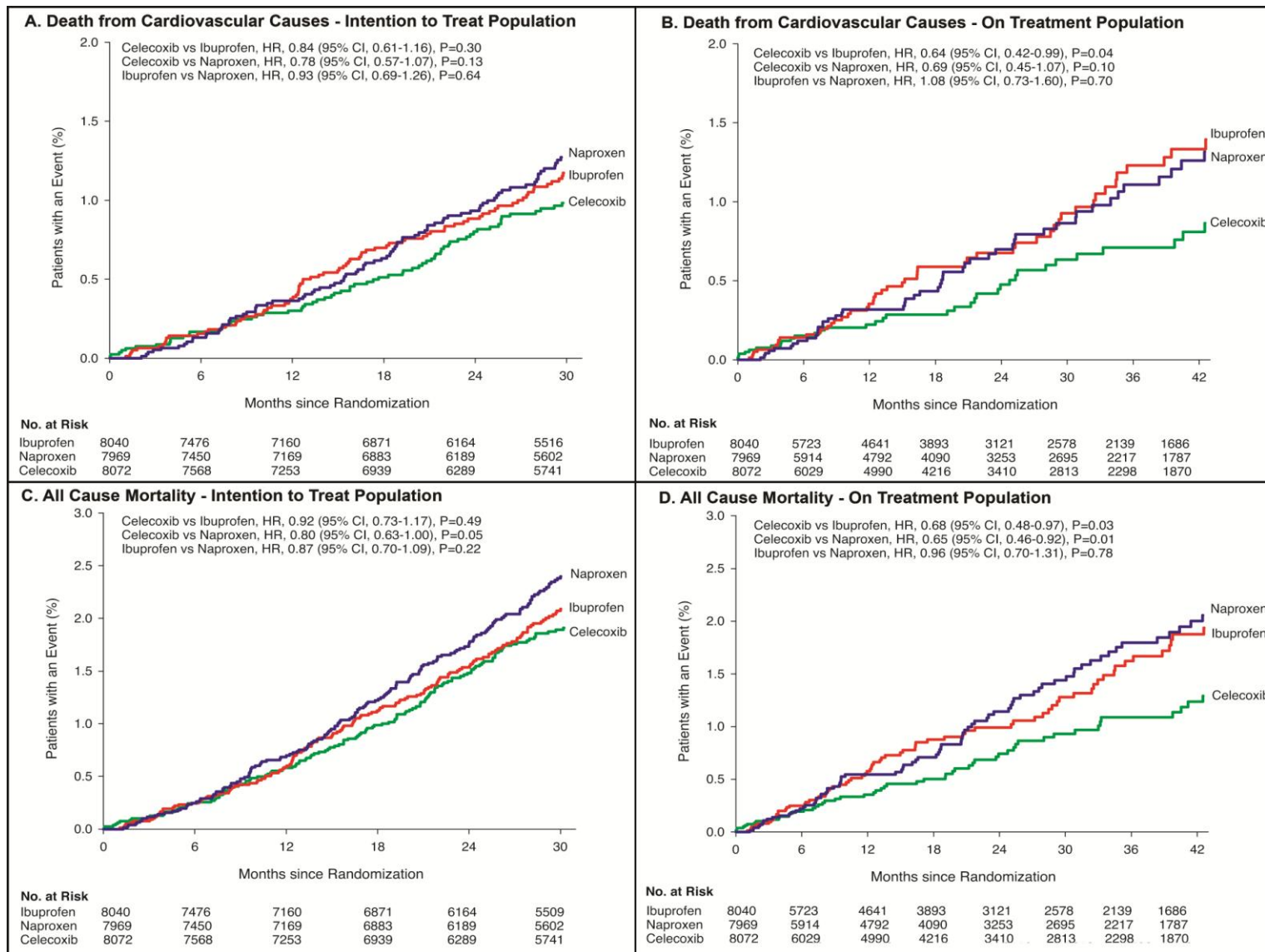
# PRECISION: Time to First Hospitalization for Hypertension



**No. at Risk:**

Celecoxib	8072	7841	7674	7558	7456	7317	7236	7082	7013	6908	6639	6446	6240	5990	5832	5673
Ibuprofen	8040	7797	7599	7458	7347	7218	7135	7002	6931	6830	6536	6331	6105	5833	5704	5544
Naproxen	7969	7772	7607	7439	7360	7223	7145	7020	6942	6847	6537	6358	6148	5874	5713	5543

# PRECISION: Cardiovascular and All Cause Mortality



# PRECISION-ABPM: **Limitations**

- Regulatory restrictions limited the dose of celecoxib to 200 mg daily for osteoarthritis patients who comprised the majority enrolled; however, symptom relief was similar with all 3 NSAIDs
- The results reflect the relative safety of these 3 drugs, but provide no information about the other currently-marketed NSAIDs
- These data do not provide conclusive evidence regarding the safety of intermittent treatment or use of low-dose over-the-counter preparations
- No direct inferences are possible regarding the effects of NSAIDs compared with placebo

# PRECISION-ABPM: **Conclusions**

- Prescription-strength Ibuprofen was associated with a significant increase of systolic blood pressure, and a higher incidence of new-onset hypertension when compared with the COX-2 selective inhibitor celecoxib
- PRECISION-ABPM adds to the evidence about the adverse cardiovascular effects of NSAIDs, particularly ibuprofen, and confirms that they should be used only after consulting a healthcare professional
- Clinicians need to weigh the potential hazards of worsening blood pressure control and its clinical sequelae against the arthritis-mitigating benefits associated with the use of NSAIDs, particularly ibuprofen

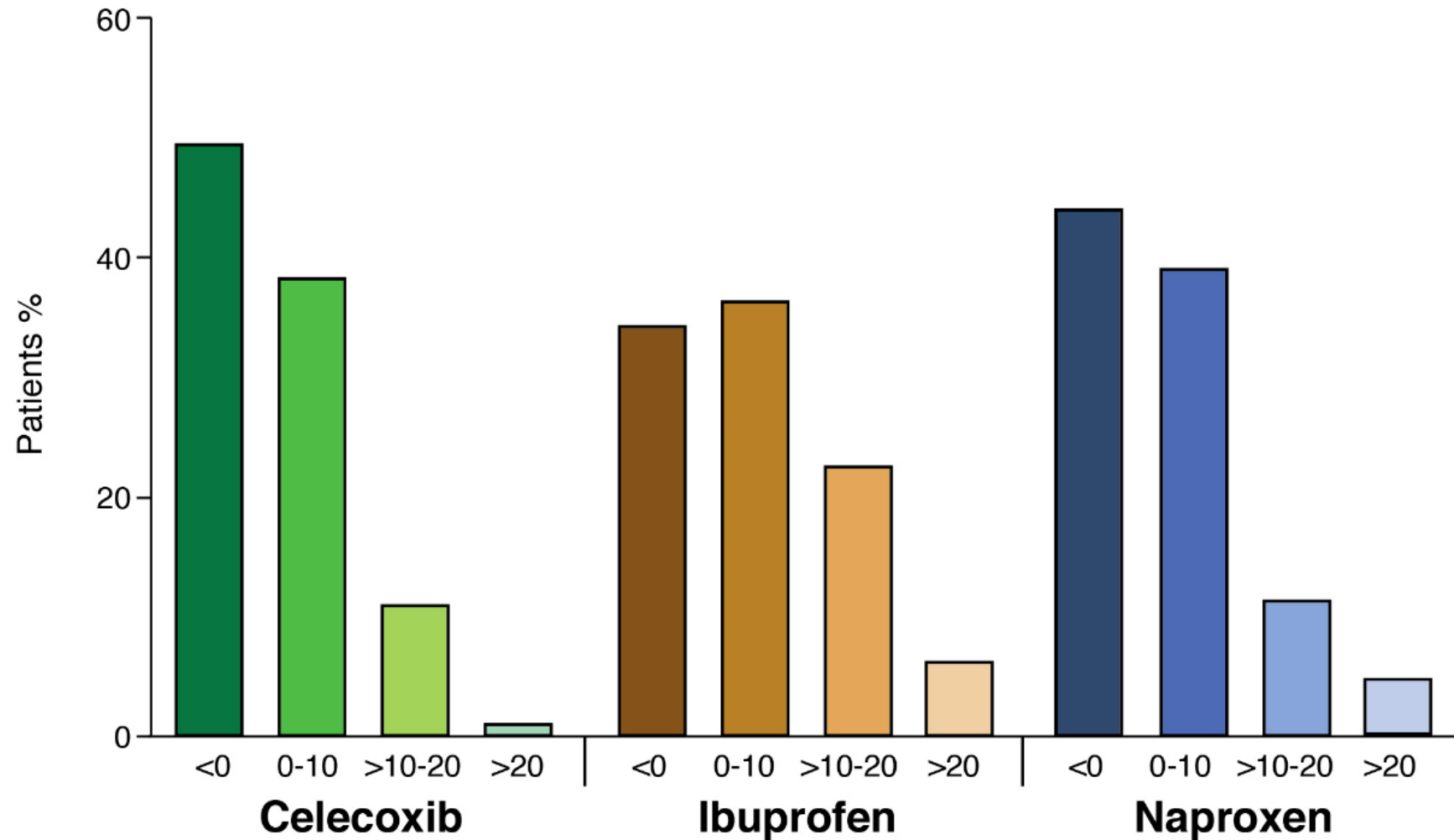
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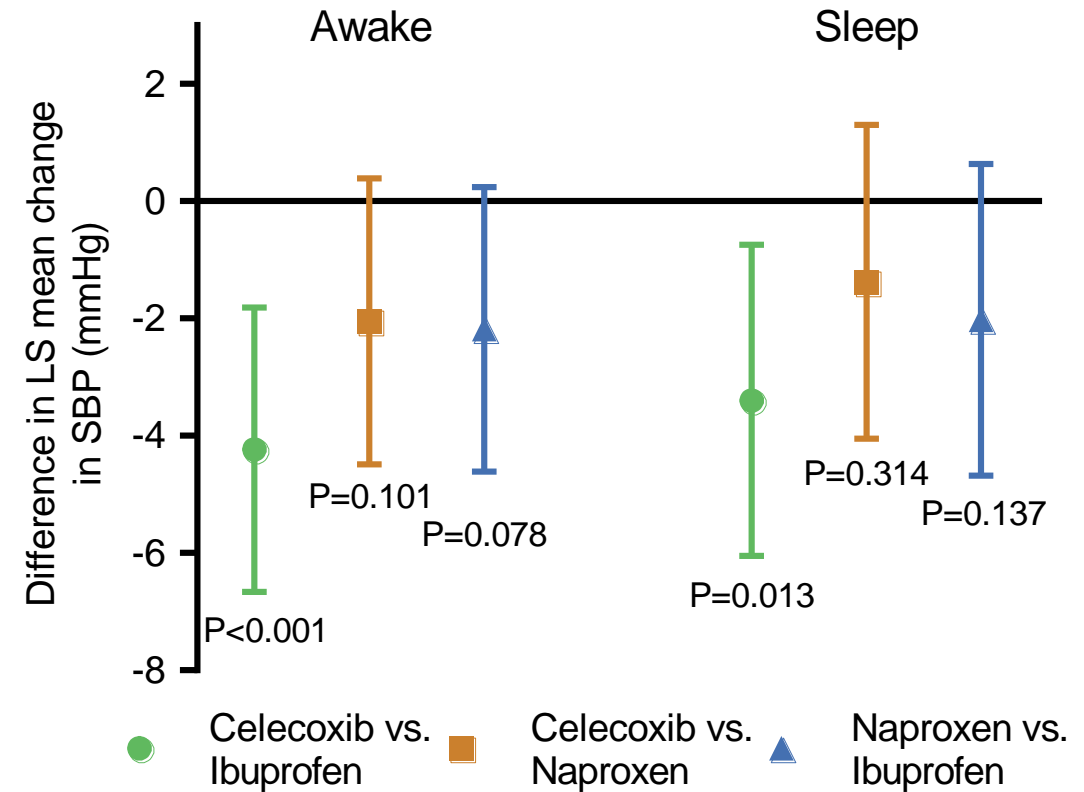
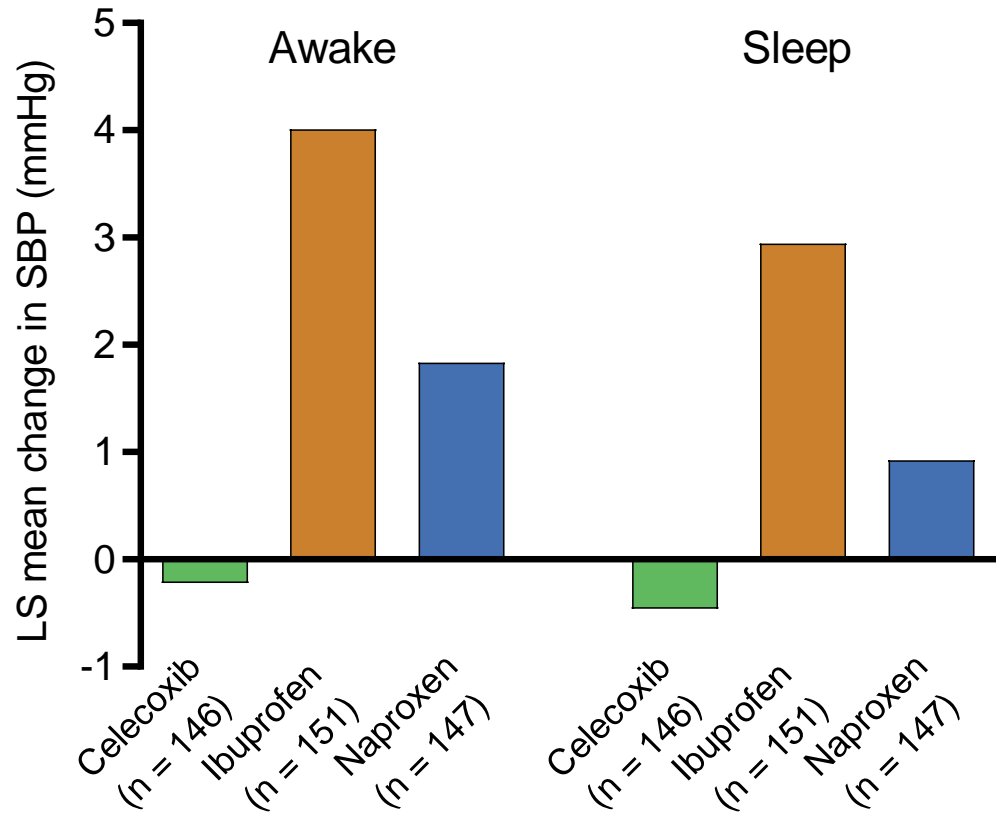


# PRECISION-ABPM: Distribution of Changes from Baseline in Ambulatory Systolic BP at 4 Months



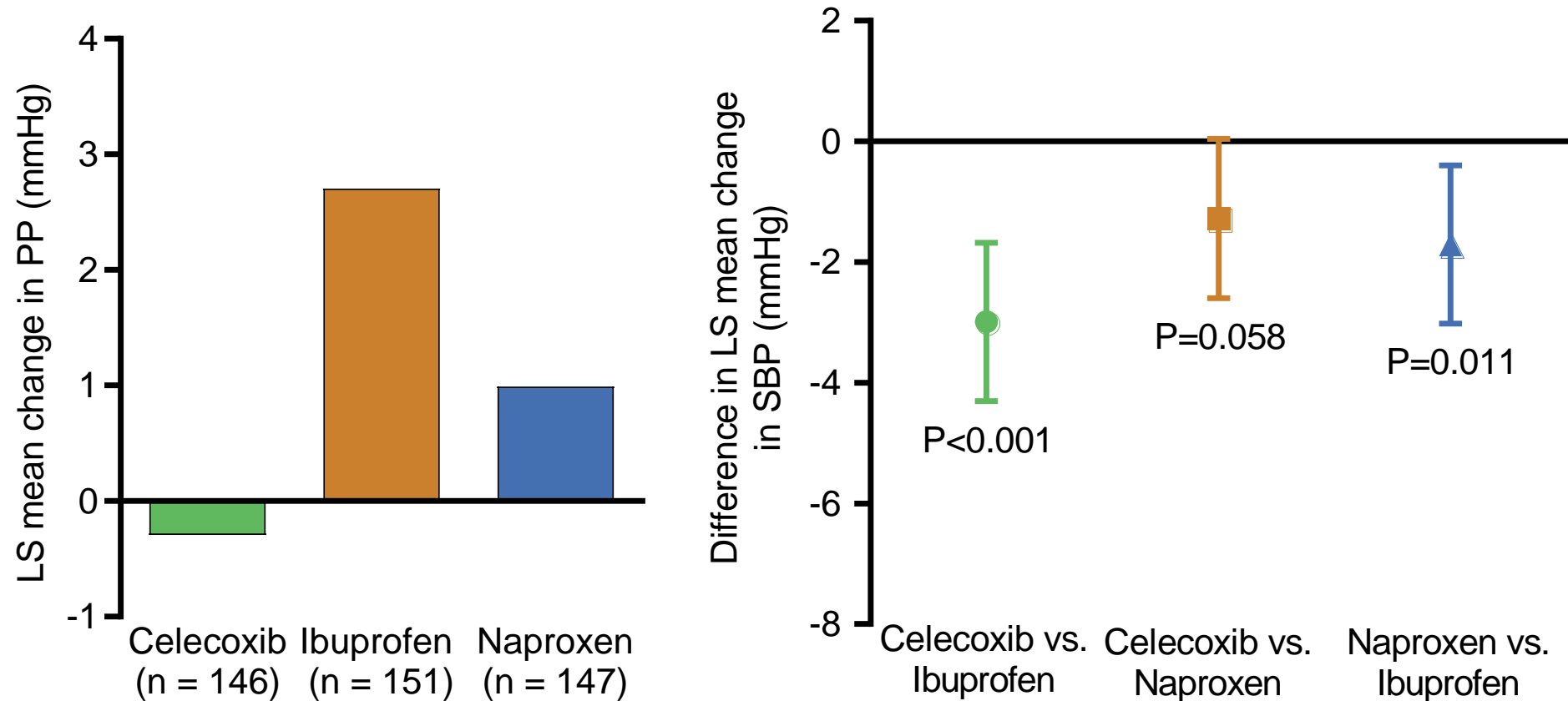


# PRECISION-ABPM: Change in Awake and Sleep Systolic Blood Pressure from Baseline at 4 Months



LS, least squares. SBP, systolic blood pressure.

# PRECISION-ABPM: Change in Mean 24-h Pulse Pressure from Baseline at 4 Months



LS, least squares. PP, pulse blood pressure

# PRECISION: Gastrointestinal and Renal Events

