

SA-12

## Concomitant Medications (1/2) Phase 2 and Phase 3 OA Studies up to 13 Weeks

n (%)	Placebo (N = 1114)	Naproxcinod 375 mg <i>bid</i> (N = 598)	Naproxcinod 750 mg <i>bid</i> (N = 1470)	Naproxen 500 mg <i>bid</i> (N = 1175)
<i>Any prior and concomitant medications</i>	856 (76.8)	396 (66.2)	1157 (78.7)	893 (76.0)
Anilides (acetaminophen)	260 (23.3)	116 (19.4)	529 (36.0)	424 (36.1)
HMG CoA reductase inhibitors	180 (16.2)	97 (16.2)	186 (12.7)	143 (12.2)
Platelet Agg Inhibitors Excl. Heparin	158 (14.2)	93 (15.6)	178 (12.1)	121 (10.3)
Proton pump inhibitors	137 (12.3)	72 (12.0)	133 (9.0)	96 (8.2)
Thyroid Hormones	93 (8.3)	52 (8.7)	124 (8.4)	95 (8.1)
Other Antiinfl./Antirheumatic, NS	79 (7.1)	49 (8.2)	103 (7.0)	79 (6.7)
Selective Serotonin Reuptake Inh.	78 (7.0)	46 (7.7)	84 (5.7)	53 (4.5)
Calcium	74 (6.6)	43 (7.2)	90 (6.1)	65 (5.5)
Natural And Semisynthetic Estrogens	61 (5.5)	32 (5.4)	89 (6.1)	72 (6.1)
Calcium in Combinations	52 (4.7)	31 (5.2)	42 (2.9)	36 (3.1)
Other Antihistamines For Systemic Use	51 (4.6)	39 (6.5)	44 (3.0)	40 (3.4)
Biguanides	49 (4.4)	26 (4.3)	55 (3.7)	42 (3.6)
Other Lipid Modifying Agents	44 (3.9)	42 (7.0)	41 (2.8)	45 (3.8)
Other Antidepressants	44 (3.9)	31 (5.2)	38 (2.6)	36 (3.1)

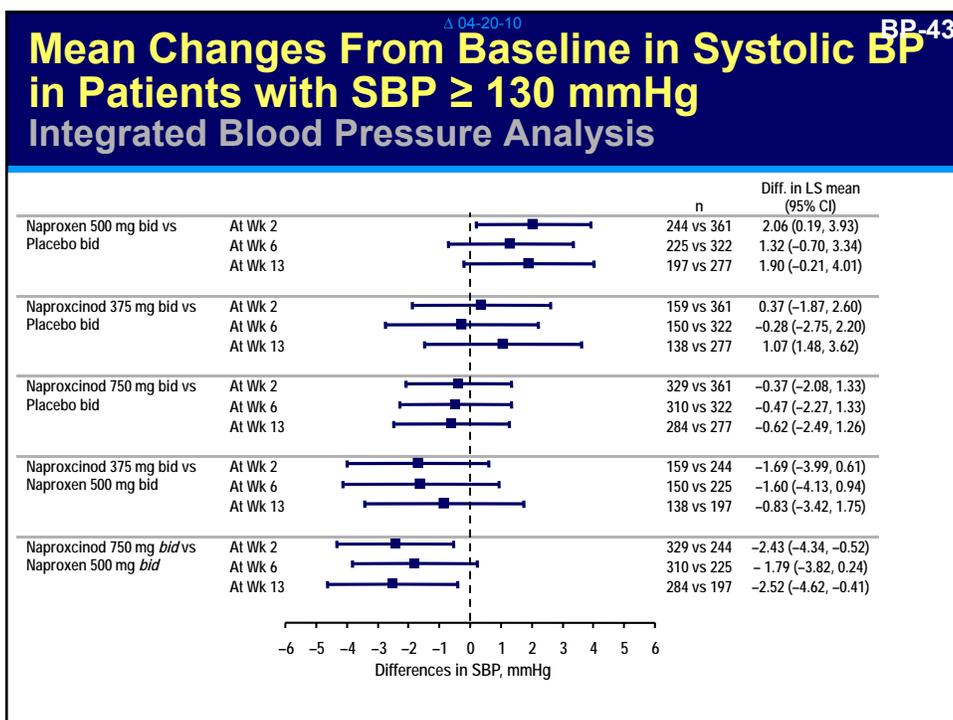
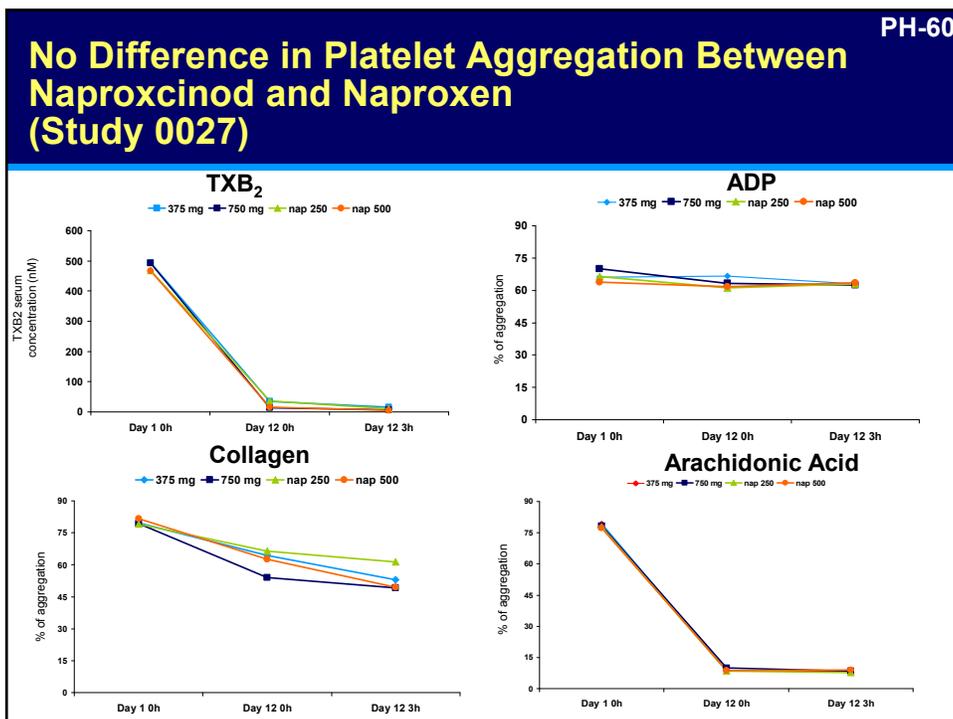
PR-35

## Rescue Pain Medication Intake Phase II and Phase III Studies

Phase III: LS mean average daily rescue medication (wk 13)	Placebo <i>bid</i>	Naproxcinod		Naproxen 500 mg <i>bid</i>
		375 mg <i>bid</i>	750 mg <i>bid</i>	
Study 301	1.77	1.33	1.43	1.34
Study 302	1.40	1.32	0.83	1.03
Study 303	1.83	NA	1.35	1.38

Phase II: mean average daily rescue medication (wk 6)	Placebo <i>bid</i>	Naproxcinod		Naproxen 500 mg <i>bid</i>
		375 mg <i>bid</i>	750 mg <i>bid</i>	
Study 0010	1.4	0.6	0.9	0.8
Study 0017	1.8	NA	0.9	NA



BP-106

△ 05-03-10

### Blood Pressure Related AEs by Age Group: BP Decreased

All Placebo OA controlled Studies

PT	Age group	Placebo <i>bid</i>	Naproxcinod 375 mg <i>bid</i>	Naproxcinod 750 mg <i>bid</i>	Naproxen 500 mg <i>bid</i>
Hypotension	<65 yo	1 (0.1)	0	6 (0.6)	2 (0.3)
	≥65 yo	0	0	3 (0.6)	0
	≥75 yo	0	0	1 (1.1)	0
BP decreased	<65 yo	0	0	3 (0.3)	0
	≥65 yo	0	0	1 (0.2)	0
	≥75 yo	0	0	1 (1.1)	0
Orthostatic hypotension	<65 yo	0	3 (0.7)	4 (0.4)	2 (0.3)
	≥65 yo	0	1 (0.5)	0	0
	≥75 yo	0	0	0	0
Presyncope	<65 yo	0	0	0	0
	≥65 yo	0	0	1 (0.2)	0
	≥75 yo	0	0	0	0
Syncope	<65 yo	2 (0.3)	1 (0.2)	2 (0.2)	1 (0.1)
	≥65 yo	0	0	2 (0.4)	1 (0.3)
	≥75 yo	0	0	0	0
Dizziness	<65 yo	17 (2.4)	10 (2.5)	33 (3.3)	18 (2.3)
	≥65 yo	7 (1.8)	5 (2.6)	14 (2.9)	6 (1.5)
	≥75 yo	3 (3.6)	3 (7.1)	3 (3.3)	1 (1.6)

SA-106

### Summary of Adverse Events By Age

All OA Placebo-Controlled Studies Up to 13 Weeks

AGE GROUP	Placebo <i>N</i>	Naproxcinod 375 mg <i>bid</i> <i>N</i>	Naproxcinod 750 mg <i>bid</i> <i>N</i>	Naproxen 500 mg <i>bid</i> <i>N</i>
<b>AGE GROUP &lt;65</b>	<i>N=722</i>	<i>N=408</i>	<i>N=994</i>	<i>N=778</i>
Any AE	359 (49.7)	210 (51.5)	566 (56.9)	469 (60.3)
Cardiac AE	7 (1.0)	3 (0.7)	14 (1.4)	9 (1.2)
Vascular AE	17 (2.4)	15 (3.7)	27 (2.7)	19 (2.4)
GI AE	120 (16.6)	78 (19.1)	261 (26.3)	213 (27.4)
<b>AGE GROUP ≥65</b>	<i>N = 394</i>	<i>N = 193</i>	<i>N = 478</i>	<i>N = 397</i>
Any AE	195 (49.5)	91 (47.2)	264 (55.2)	213 (53.7)
Cardiac AE	8 (2.0)	1 (0.5)	10 (2.1)	5 (1.3)
Vascular AE	7 (1.8)	6 (3.1)	13 (2.7)	8 (2.0)
GI AE	80 (20.3)	31 (16.1)	116 (24.3)	102 (25.7)