Aspirin	**Total Nasal Symptoms Score (TNSS) Worksheet**	Participant ID: Participant Initials: Visit Date: Visit: Coordinator ID:

Test each nostril for stuffiness. Place finger to block end of right nostril. Try to breathe through the left nostril and determine severity of blockage/congestion. Then Repeat process to evaluate right nostril.

	None	A Little	Moderate	Quite a bit	Severe	Very Severe
1. Nasal Congestion (Left nostril)	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
2. Nasal Congestion (Right nostril)	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
3. Runny Nose	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
4. Itchy Nose	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
5. Sneezing	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
6. Itchy Eyes	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
7. Teary Eyes	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
8. Itchy Ears or Throat	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
9. Eye Redness	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

10. Total Score _____

Participant Initials: __ __ __

Date: __ __/__ __/20 __ __

Time __ __:__ __

Supplemental FIG. E1. Total Nasal Symptom Score (TNSS) questionnaire. The scores for items 1 and 2 are averaged, so that the final range is between 0-40 points.

$$inverselog_{10}\left(\frac{\left(2-(PrevTNSS-BaselineTNSS)\right)\times(log_{10}ProvocDose-log_{10}PrevDose)}{(MaxTNSS-BaselineTNSS)-(PrevTNSS-BaselineTNSS)}+(log_{10}PrevDose)\right)$$

→ *BaselineTNSS:* The patient's first morning TNSS score, prior to the administration of aspirin.

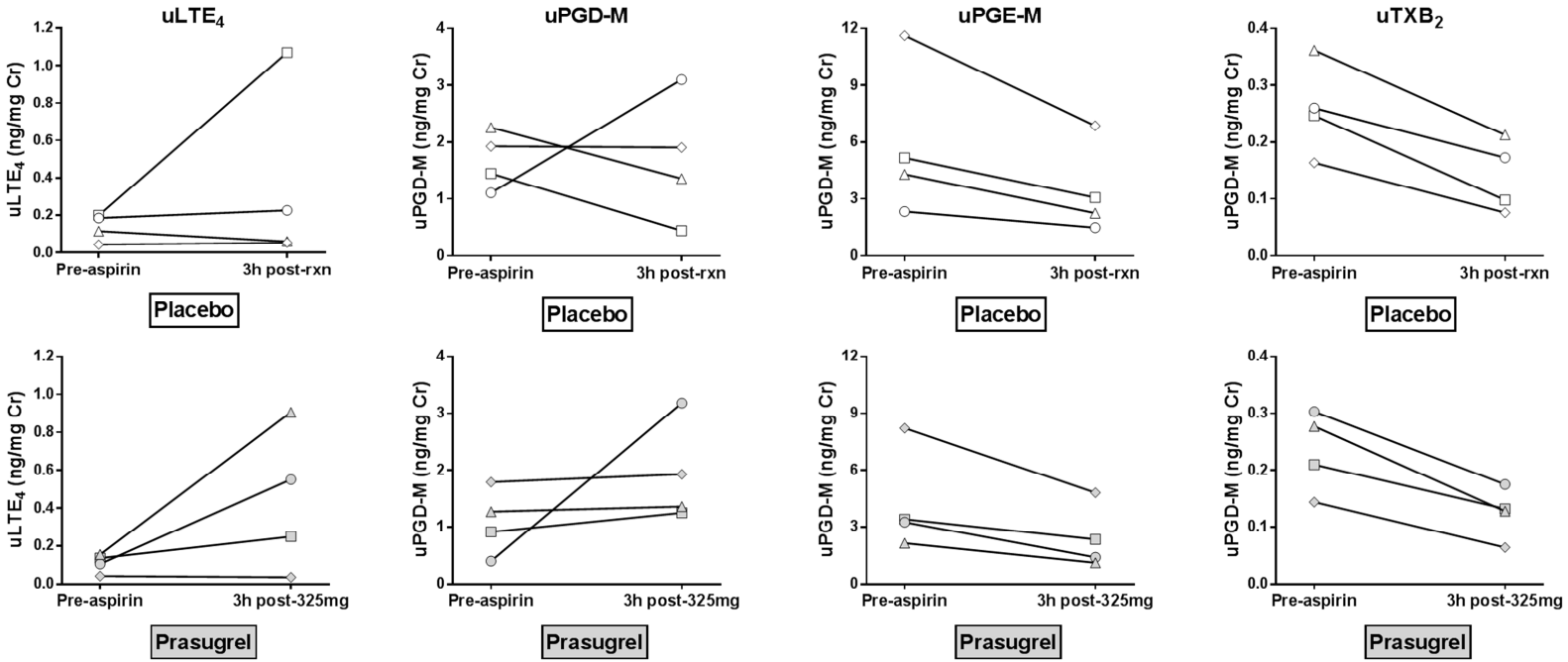
→ *ProvocDose:* The administered dose of aspirin that provoked the reaction (40.5, 81, 162, or 325)

→ *PrevDose:* The administered dose of aspirin that was given just previously to the dose of aspirin that provoked the reaction. In all cases, the *PrevDose* is ½ of the *ProvocDose*.

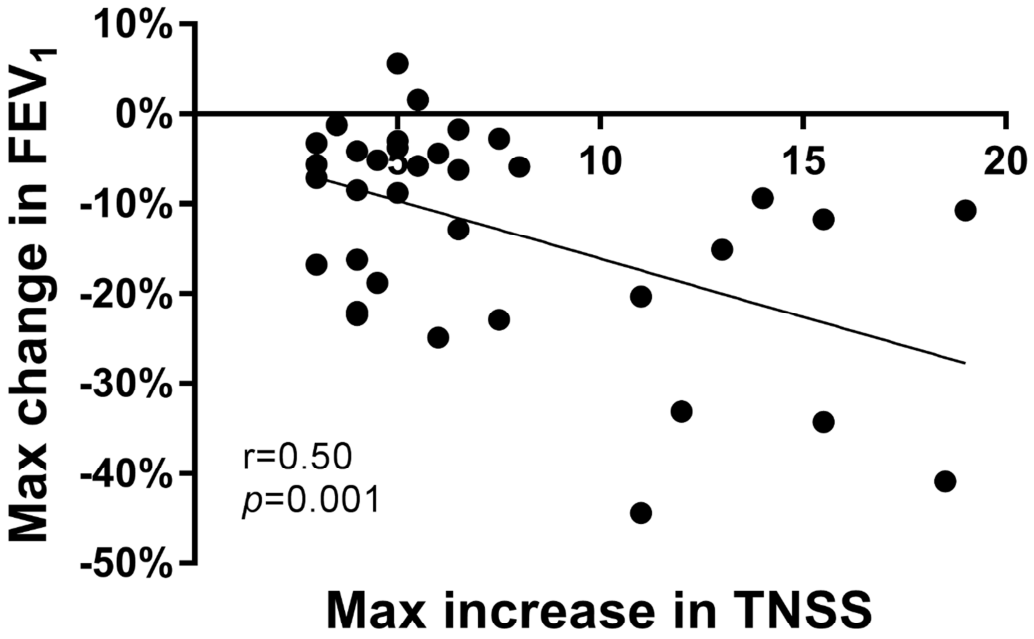
→ *PrevTNSS*: The patient's previous TNSS score that was taken after the *PrevDose* was given. For patients whose reaction was induced by the first dose of aspirin (40.5mg), the *PrevTNSS* was the *BaselineTNSS*, as there were no intervening TNSS questionnaires given.

→ *MaxTNSS*: The patient's maximum TNSS recorded during the 3-hour observation of reaction. All patients recorded a TNSS at 30-minute intervals during that 3-hour period, and so the *MaxTNSS* is the highest TNSS recorded at one of the following timepoints: Onset of reaction, 30 minutes post onset of reaction, 60 minutes post onset of reaction, 90 minutes post onset of reaction, 120 minutes post onset of reaction, 150 minutes post onset of reaction, 180 minutes post onset of reaction.

Supplemental FIG. E2. PD_2 Calculation (provocative dose of aspirin that would cause an increase in TNSS of 2 points during an aspirin challenge.


uLTE4
uPGD-M
uPGE-M
uTXB2
uLTE4 (ng/mg Cr)
uPGD-M (ng/mg Cr)
Pre-aspirin
3h post-rxn
3h post-325mg
Placebo
Prasugrel

Supplemental FIG. E3. Urinary eicosanoid levels are shown for the 4 prasugrel responders, before and 3 hours after the aspirin-induced reaction on the placebo arm (top row) and before and 3 hours after the 325mg dose of aspirin on the prasugrel arm (bottom row).


10%
0%
-10%
-20%
-30%
-40%
-50%
Max change in FEV1
5
10
15
20
r=0.50
p=0.001
Max increase in TNSS

Supplemental FIG. E4. Correlation between maximum change in FEV_1 and maximum increase in total nasal symptom score (TNSS) during aspirin-induced reactions on the prasugrel treatment arm is shown.

Supplemental Table E2. Results of logistical regression for association between genotype and response to prasugrel for selected SNPs. Genomic position is given relative to the reference human genome (GRCh37/hg19).

SNP	Position	Location	Alleles	MAF	Estimate	Std. Error	z value	Pr(>|z|)
rs6809699	151056598	Exon	A/C	0.143	18.467	3802.118	0.005	0.996
rs6785930	151056616	Exon	G/A	0.429	0.523	0.867	0.603	0.547
rs2046934	151057642	Intron	G/A	0.130	17.467	2465.326	0.007	0.994
rs9848789	151058963	Intron	C/T	0.089	0.114	1.012	0.113	0.910
rs7615865	151073033	Intron	T/C	0.214	1.105	1.144	0.966	0.334
rs1491978	151080070	Intron	C/T	0.196	0.939	1.132	0.830	0.407
rs7634096	151087637	Intron	C/T	0.143	-0.432	1.082	-0.399	0.690
rs7637803	151089226	Intron	C/T	0.125	-0.256	1.060	-0.242	0.809
rs3732765	151090424	Intron	G/A	0.286	0.089	0.784	0.113	0.910
rs11708287	151090863	Intron	A/C	0.286	0.089	0.784	0.113	0.910
rs9859538	151090963	Intron	G/A	0.339	0.285	0.679	0.420	0.674
rs12497065	151096112	Intron	T/C	0.278	0.136	0.776	0.175	0.861
rs12497089	151096164	Intron	T/A	0.259	0.243	0.761	0.319	0.750
rs17283010	151097391	Intron	G/A	0.278	0.136	0.776	0.175	0.861
rs12489121	151098519	Intron	A/G	0.321	-0.119	0.752	-0.159	0.874
rs6787801	151099741	Intron	A/G	0.446	0.343	0.804	0.427	0.670
rs9289836	151100121	Intron	C/T	0.339	0.285	0.679	0.420	0.674
rs3821663	151100677	Intron	T/G	0.286	0.089	0.784	0.113	0.910
rs11713504	151100956	Intron	A/G	0.278	0.136	0.776	0.175	0.861
rs10935840	151101083	Intron	A/G	0.278	0.136	0.776	0.175	0.861
rs7429509	151101167	Intron	C/T	0.321	0.416	0.721	0.577	0.564
rs12488803	151101358	Intron	T/G	0.250	0.296	0.756	0.392	0.695
rs10935841	151101691	Intron	C/T	0.286	0.089	0.784	0.113	0.910
rs12485508	151101746	Intron	C/T	0.286	0.089	0.784	0.113	0.910
rs1491974	151102452	Intron	A/G	0.464	0.205	0.759	0.270	0.787
rs4603933	151103070	Upstream	T/G	0.125	17.403	2465.326	0.007	0.994

MAF - minor allele frequency
Std. Error - standard error

Supplemental Table E3. Adverse events.

	Placebo arm	Prasugrel arm	P-value
Total adverse events reported	25	36	
Bruising	3	12	0.006
Upper respiratory infection/sinusitis	5	7	0.75
Worsening of asthma	5	4	1
Muscle injury/myalgia	2	0	0.49
Headache	2	2	0.49
Throat infection	1	1	1
Accidental ingestion of NSAID	1	0	1
Systemic reaction to aspirin challenge	1	0	1
Skin rash	1	1	1
Conjunctivitis	0	1	1
Ear Infection	0	1	1
Finger tingling/Numbness	0	1	1
Joint stiffness	0	1	1
Light-headedness	1	0	1
Lower leg edema	0	1	1
Mood change	1	0	1
Spider bite	1	0	1
Stomach pain	1	0	1
Urinary tract infection	0	1	1
Viral gastroenteritis	0	1	1

All events that occurred after randomization through two weeks after the second aspirin challenge were included. Data listed is number of participants reporting each type of adverse event.

Supplemental Table EI. Demographic/clinical and laboratory characteristics of the 5 responders and the 35 non-responders. Clinical and laboratory values are at the pre-aspirin baseline following each of the treatment arms. Data are mean ±SE.

	Prasugrel "responders" (n = 5)		**Prasugrel "nonresponders" (n = 35)**		**p-value (responder vs nonresponder)**	
	Placebo	**Prasugrel**	**Placebo**	**Prasugrel**	**Placebo**	**Prasugrel**
Age (y)	44 ± 4		47 ± 2		0.946	
Sex (female)	3 of 5		19 of 35		0.834	
FEV1 (L)	2.74 ± 0.26	2.74 ± 0.30	3.19 ± 0.14	3.16 ± 0.15	0.178	0.258
FEV1 predicted (%)	84.5 ± 5.4	84.0 ± 6.6	93.1 ± 2.3	92.2 ± 2.2	0.206	0.294
FeNO (ppb)	39.6 ± 8.9	39.2 ± 9.1	54.1 ± 8.4	45.9 ± 4.7	0.258	0.533
Blood AEC (/µL)	640 ± 166	500 ± 148	500 ± 62	435 ± 50	0.464	0.696
Blood eosinophils (%)	8.4 ± 1.7	7.2 ± 1.5	7.1 ± 0.7	6.4 ± 0.7	0.499	0.619
ACQ-7	0.93 ± 0.24	0.74 ± 0.11	0.77 ± 0.38	0.70 ± 0.11	0.495	0.865
TNSS, baseline	2.3 ± 0.7	5.4 ± 2.0	3.2 ± 0.7	3.2 ± 0.6	0.342	0.343
TNSS, max during rxn	5.7 ± 0.7	3.5 ± 1.2	10.8 ± 1.4	10.6 ± 0.9	0.002	0.0007
PD_2	82 ± 18	650	78 ± 18	66 ± 10	0.881	
$uLTE_4$ (ng/mg Cr)	0.14 ± 0.03	0.10 ± 0.14	0.44 ± 0.13	0.75 ± 0.28	0.041	0.026
uPGD-M (ng/mg Cr)	1.73 ± 0.20	1.48 ± 0.45	2.37 ± 0.26	2.54 ± 0.33	0.067	0.234
uPGE-M (ng/mg Cr)	5.36 ± 1.64	4.31 ± 1.05	7.97 ± 1.25	6.94 ± 0.87	0.443	0.264
$uTXB_2$ (ng/mg Cr)	0.26 ± 0.03	0.33 ± 0.10	0.38 ± 0.03	0.31 ± 0.02	0.022	0.811