Reduced gastric injury with a novel, liquid lipid-aspirin formulation: results from a pooled, patient level analysis of two randomized endoscopy studies In healthy volunteers*

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OBJECTIVES

Aspirin (acetylsalicylic acid), can lead to gastrointestinal mucosal injury through disruption of its protective phospholipid bilayer; GI injury is higher at the time of initiation of aspirin therapy.

A liquid formulation using a novel pharmaceutical lipid aspirin complex (PL-ASA, Vazalore™. PLx Pharma, Sparta NJ) has been designed to prevent the disruption of the protective mucosal bilayer without delaying absorption.

The current analysis aimed to determine rates of endoscopically detected gastroduodenal erosions and ulcers after 7 days of either immediate release aspirin (IR-ASA) or the novel PL-ASA liquid formulation with a similar antiplatelet effect as IR-ASA.

METHODS

Study Design:

Data from two randomized, single-blind, multicenter active control studies comparing upper GI damage after 7 days of 325 mg PL-ASA or IR-ASA in healthy volunteers not taking gastroprotection and who had a negative baseline endoscopy were pooled at the patient level.

Endpoints:

The primary endpoint was the composite of >5 erosions and/or ≥1 ulcer (≥3 mm deep) assessed at the site and subsequently by a blinded central reviewer on day 7. Secondary endpoints included the incidence of ulcers, and GI mucosal injury scoring.

RESULTS

A total of 451 subjects were randomized (mean age 57 years, 47% males). Of these, 441 completed the 7-day endoscopy and represent the full analysis set. (Table 1).

Table 1: Demographics of Study Population

(n)	PL-ASA (n=221)	IR-ASA (n = 230)
Age, mean ± SD	56.2 ± 5.83	57.5 ± 6.09
Male, % (n)	48.4% (107)	44.8% (103)
Female, % (n)	51.6% (114)	55.2% (127)
Ethnicity		
White, % (n)	69.2% (153)	67.4% (155)
African American, % (n)	21.3% (47)	23.5% (54)
Asian, % (n)	1.8% (4)	1.3% (3)
Hispanic, % (n)	5.0% (11)	4.8% (11)
Other, % (n)	2.7% (6)	3.0% (7)
Height (centimeters), mean ± SD	170.6 ± 10.22	170.7 ± 9.95
Weight (kilograms), mean ± SD	79.5 ± 14.25	78.6 ± 13.15
Body Mass Index (kg/m^2), mean ± SD	27.1 ± 3.12	26.9 ± 3.32
Subjects Completed 7-day endoscopy, n	218	223

Table 2: GI Mucosal Injury Composite Scores at baseline and Day 7

	PL-ASA (n=218)	IR-ASA (n=223)
Baseline GI score (based on FAS), % (n)		
0	62.4% (136)	61.4% (137)
1	27.1% (59)	27.8% (62)
2	9.2% (20)	9.9% (22)
3	0.9% (2)	0.9% (2)
4	0.5% (1)	0
Day 7 GI score (based on FAS), % (n)		
0	8.7% (19)	7.2% (16)
1	17.0% (37)	7.2% (16)
2	48.6% (106)	46.6% (104)
3	11.5% (25)	12.6% (28)
4	14.2% (31)	26.5% (59)
P-value (CAT-test)	0.0004	

FAS=full analysis set; CAT-test =Cochran-Armitage Trend test

GI Mucosal Injury Score key	Grade 2: >10 petechiae or 1-5 erosions
Grade 0: No injury	Grade 3: 6-10 erosions
Grade 1: 1 - 10 petechiae	Grade 4: >10 erosion and/or ≥1 ulcer

- PL-ASA significantly reduced the primary endpoint by 34% compared with IR-ASA (25.7% vs. 39.0%, p=0.0032) (figure).
- For ulcers, there was a 61% reduction with PL-ASA (6.0% vs. 15.2%, p=0.0018) (figure). The mean number of gastric erosions per patient was also reduced with PL-ASA (2.8 ± 7.3 vs. 4.2 ± 7.5, p<0.0001), while erosions in the duodenum were not different (1.4 ± 7.1 vs. 0.9 ± 2.3, p=0.45).
- The incidence of endpoints was similar whether site-reported or adjudicated.

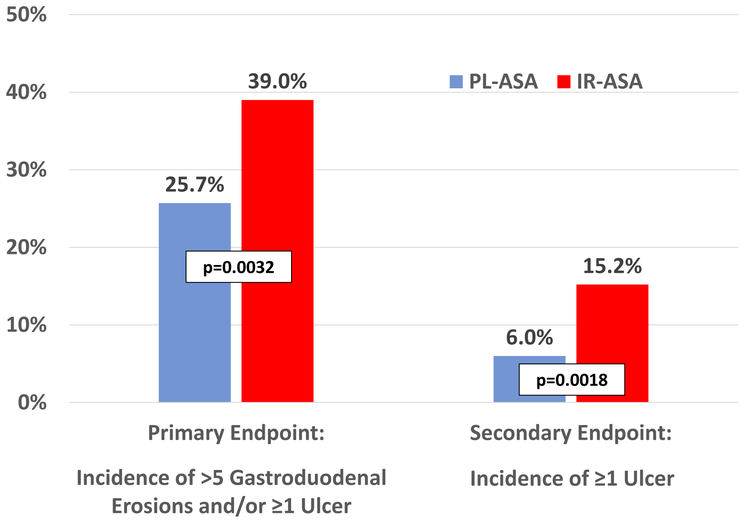

Figure: Primary and secondary endpoints at Day 7

DISCUSSION

Every year about 1.6 million patients will experience either a myocardial infarction (MI) or stroke in the US[1].

Aspirin is a central part of acute MI and stroke treatment protocols.

Aspirin use in the acute setting has a significant risk for gastrointestinal toxicity that is not reduced by the use of enteric-coated aspirin [2].

The novel PL-ASA liquid capsules reduced rates of GI injury at 7 days compared with IR-ASA.

The combination of reliable platelet inhibition [3] with less acute GI injury makes PL-ASA an attractive new aspirin therapy option.

References

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Declaration of Interest

PLx Pharma Inc. Sparta, NJ USA sponsored the studies.

Drs. Bhatt, Scheiman, Angiolillo, Steg and Dangas have received consulting fees from PLx Pharma Inc. Dr. Prats is a consultant to PLx Pharma Inc. Dr. Deliargyris is a former employee and Ms. Fan is a current employee of PLx Pharma Inc.

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