

# Improved Pharmacologic Profile of a Novel Liquid Aspirin Formulation Compared with Enteric-Coated Aspirin: A Pooled Analysis of Two Randomized Crossover Studies

Bhatt DL,<sup>1</sup> Angiolillo DJ,<sup>2</sup> Steg PG,<sup>3</sup> Fan W,<sup>4</sup> Kimmelstiel C,<sup>5</sup> Mehran R,<sup>6</sup> Dangas GD,<sup>6</sup> Prats J,<sup>7</sup> Deliargyris EN.<sup>4</sup>

<sup>1</sup>Brigham and Women's Hospital Heart & Vascular Center, Boston, MA; <sup>2</sup>University of Florida College of Medicine, Jacksonville, FL; <sup>3</sup>Département de Cardiologie, Hôpital Bichat, Paris, France; <sup>4</sup>PLx Pharma, Sparta, NJ; <sup>5</sup>Division of Cardiology Tufts Medical Center, Boston, MA; <sup>6</sup>Wiener Cardiovascular Institute, Mount Sinai Hospital, New York, NY; <sup>7</sup>Elysis LLC, Carlisle, MA

## BACKGROUND

Enteric-coated aspirin (EC-ASA) is preferred over immediate release aspirin based on the presumption of lower gastrointestinal (GI) risk. However, studies show that not only EC-ASA does not lower GI risk, but also that it is limited by erratic absorption and high rates of non-responsiveness. This study compared the pharmacokinetic/pharmacodynamic (PK/PD) profile of EC-ASA to a novel pharmaceutical lipid-aspirin complex (PL-ASA) liquid formulation that is bioequivalent to immediate-release aspirin, and that has been specifically designed to reduce GI risk.

## METHODS

Two randomized, crossover studies in obese diabetic patients comparing PK/PD parameters after 3 doses of 325-mg of EC-ASA or PL-ASA were pooled at the patient level. The primary endpoint was time to complete aspirin response i.e.,  $\geq 99\%$  thromboxane B2 (TXB2) inhibition. Additional PK/PD analyses were also performed.

# A novel pharmaceutical lipid-aspirin complex (PL-ASA) administered in liquid-filled capsules has superior bioavailability and results in faster and more complete platelet inhibition compared with enteric-coated aspirin.

Bhatt DL, Angiolillo DJ, PG Steg et al. *J Am Coll Cardiol* March 24, 2020, 75 (11 Suppl 1) 29; DOI: 10.1016/S0735-1097(20)30656.  
For more information, contact Dr. Deepak L. Bhatt @ DLBhattMD@post.Harvard.edu

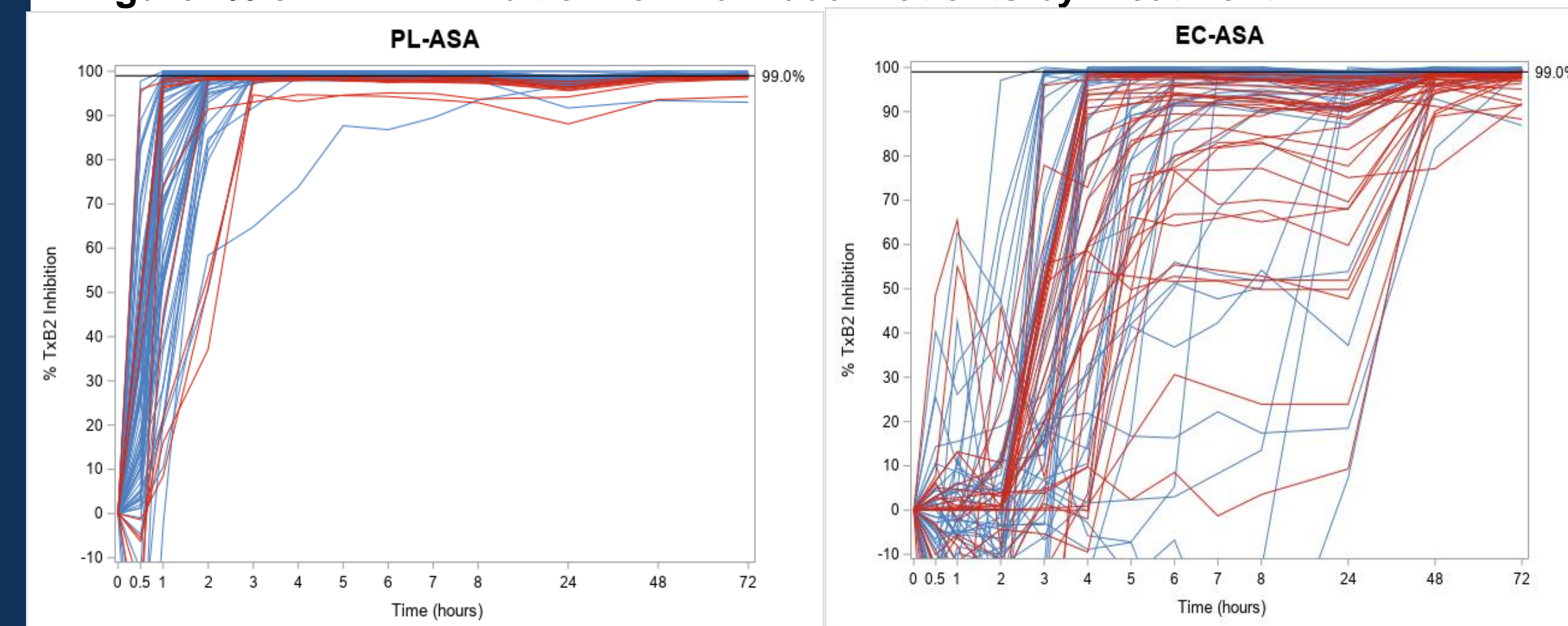
## RESULTS

A total of 97 subjects were included. The median time to complete aspirin response ( $\geq 99\%$  TXB2 inhibition) was significantly faster with PL-ASA (2.0 vs. 47.97 hours,  $p < 0.0001$ ). All drug absorption (PK) and platelet inhibition (PD) parameters were significantly better with PL-ASA, resulting in consistently higher incidence of aspirin response compared to EC-ASA (Table, Figure).

Table: PK/PD Parameters

PK (at 24 hours)	PL-ASA (N=92)	EC-ASA(N=91)	P-value
<b>Acetylsalicylic acid</b>			
$C_{max}$ (ng/mL)	2219.0	487.7	<0.0001
$AUC_{0-t}$ (ng x hr/mL)	2520.0	582.7	<0.0001
$T_{max}$ (hr)	1.2	3.7	<0.0001
<b>Salicylic acid</b>			
$C_{max}$ (ng/mL)	14829.4	8282.3	<0.0001
$AUC_{0-t}$ (ng x hr/mL)	76785.4	60148.8	0.0008
$T_{max}$ (hr)	2.0	6.1	<0.0001
<b>PD: Complete response</b>			
At 72 hours (3 doses)	82/92 (89.1%)	58/91 (63.7%)	<0.0001

Figure: % of TXB2 Inhibition for Individual Patients by Treatment



Blue lines = % TXB2 inhibition in individual patients who ever reached 99% inhibition by 72 hours after initiation of study drug.  
Red lines = % TXB2 inhibition in individuals who never reached 99% inhibition by 72 hours after initiation of study drug.

## CONCLUSION

PL-ASA has superior bioavailability resulting in faster and more complete platelet inhibition compared with EC-ASA.

The combination of improved absorption and more reliable antiplatelet effect compared with EC-ASA make PL-ASA a very attractive alternative to EC-ASA

## REFERENCE

Bhatt DL, Grosser T, Dong JF et al. Enteric Coating and Aspirin Nonresponsiveness in Patients With Type 2 Diabetes Mellitus. *J Am Coll Cardiol* 2017 Feb 14;69(6):603-612.

## DISCLOSURE INFORMATION

PLx Pharma Inc. was the sponsor. The content is solely the responsibility of the authors. Dr. Bhatt received research funding, and Drs. Angiolillo, Kimmelstiel, Steg, and Prats received consulting fees from PLx Pharma Inc; Dr. Deliargyris and Ms. Fan are employees of PLx. No other authors had conflicts.