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

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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., ≥ 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.

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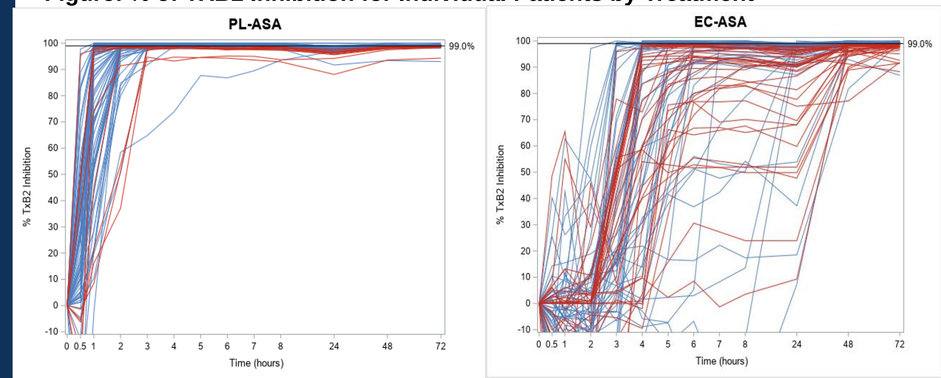
RESULTS

A total of 97 subjects were included. The median time to complete aspirin response (≥ 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
Acetylsalicylic acid			
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
Salicylic acid			
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
PD: Complete response			
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 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

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