#AHA22

Efficacy and Safety of Indobufen versus Aspirin after Coronary Drug-eluting Stent Implantation (OPTION): a randomized, open-label, non-inferiority trial

Junbo Ge, MD, FACC, FAHA

Department of Cardiology, Zhongshan Hospital

Fudan University

On behalf of the OPTION investigators

American Heart Association.

Disclosures

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Background

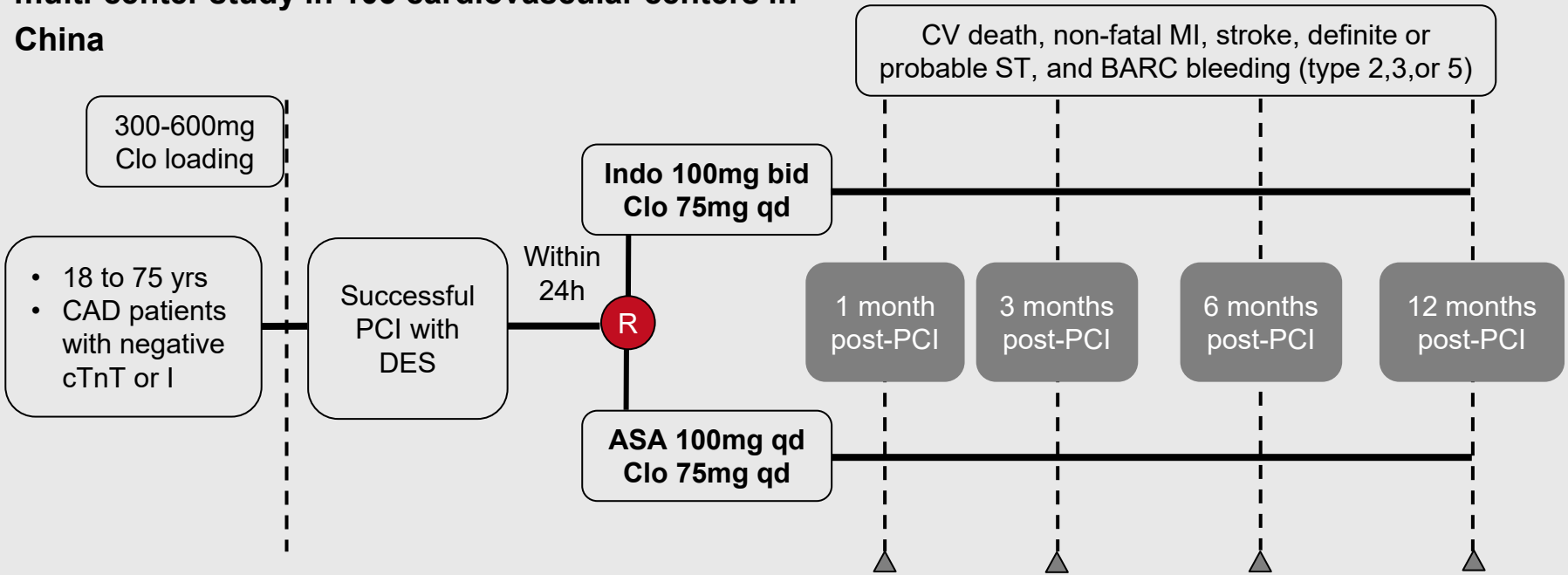
- Dual antiplatelet therapy (DAPT) with aspirin as a background therapy has become the standard care following PCI.
- Several unfavorable non-cardiac effects, such as allergy and intolerance, limit the use or adherence of aspirin in clinical practice.
- Indobufen is associated with a better platelet selectivity, tolerability and benefit/risk profile.
- Exploration of pharmacological alternatives to aspirin on top of a P2Y12 inhibitor is of great interest and clinical relevance.

Objective

- The OPTION trial was conducted to establish whether **indobufen-based DAPT** (indobufen 100mg twice a day plus clopidogrel 75mg/d for 12 months) is non-inferior to **conventional DAPT** (aspirin 100mg/d plus clopidogrel 75mg/d for 12 months) in patients with negative cardiac troponin undergoing coronary DES implantation.

Study design

- ✓ **a randomized, open-labeled, prospective, non-inferiority, multi-center study in 103 cardiovascular centers in China**



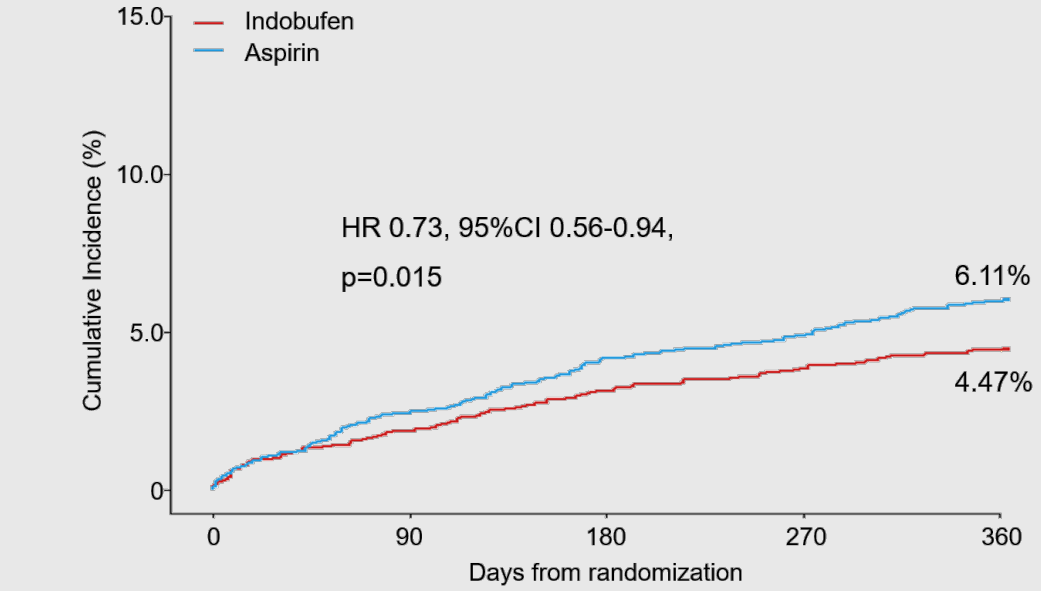
CAD= coronary artery disease, **PCI**= percutaneous coronary intervention, **DES**= drug-eluting stent, **Clo**= clopidogrel, **Indo**= indobufen, **ASA**=aspirin, **CV**= cardiovascular, **MI**= myocardial infarction, **ST**= stent thrombosis

Baseline characteristics of the ITT population

	Indobufen N= 2258	Aspirin N= 2293
Age, years	61.0±8.3	61.2±8.4
Male	1521 (67.4%)	1447 (63.1%)
BMI, kg/m^2	25.0±3.3	25.0±3.2
Hypertension	1517 (67.2%)	1542 (67.2%)
Diabetes mellitus	802 (35.5%)	768 (33.5%)
Hyperlipidemia	744 (33.0%)	734 (32.0%)
Current smoking	584 (25.9%)	541 (23.6%)
Previous myocardial infarction	137 (6.1%)	137 (6.0%)
Previous heart failure	128 (5.7%)	142 (6.2%)
Previous stroke	146 (6.5%)	108 (4.7%)
Previous gastrointestinal bleeding	13 (0.6%)	15 (0.6%)
ARC high bleeding risk	145 (6.4%)	137 (6.0%)
Creatinine clearance <60ml/min	294 (13.0%)	286 (12.5%)

	Indobufen N= 2258	Aspirin N= 2293
Clinical presentation		
Stable CAD	993 (44.0%)	990 (43.2%)
Unstable angina	1265 (56.0%)	1303 (56.8%)
PCI procedure		
Multivessel disease	1264 (56.0%)	1280 (55.8%)
No. of stents	1.51±0.77	1.53±0.79
Length of stents (mm)	37.8±23.1	38.5±24.7
Bifurcation target lesion	215 (9.5%)	210 (9.2%)
Complex-PCI	541 (24.0%)	583 (25.4%)
Medication		
Statin	2087 (92.4%)	2134 (93.1%)
β-blocker	1537 (68.1%)	1609 (70.2%)
ACEI or ARB	1303 (57.7%)	1347 (58.7%)
PPIs	1085 (48.0%)	1138 (49.6%)

The primary endpoint

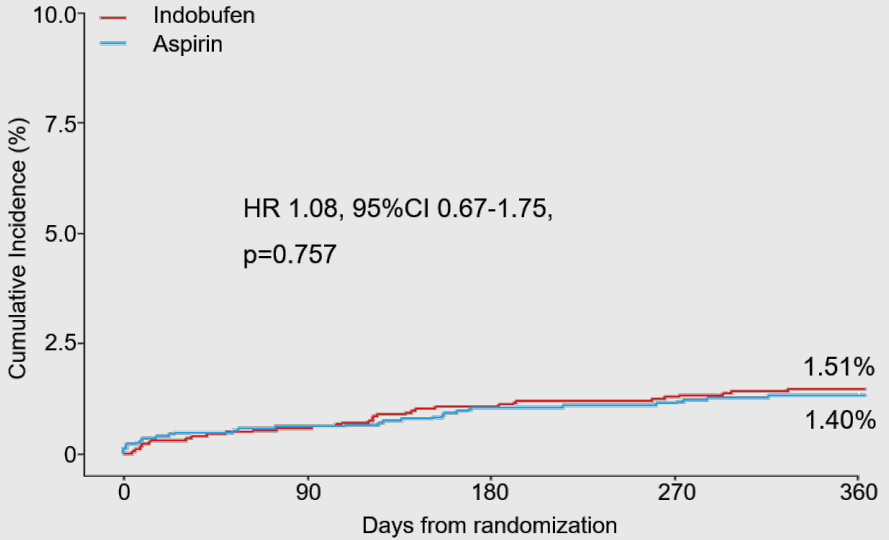


Number at risk

Indobufen	2258	2182	2147	2121	2108
Aspirin	2293	2207	2165	2144	2119

- a composite of CV death, nonfatal MI, ischemic stroke, definite or probable stent thrombosis, or BARC type 2, 3 or 5 bleeding at 1-year
- occurred in 101 (4.47%) patients in the indobufen-based DAPT group and 140 (6.11%) patients in the conventional DAPT group ($p_{noninferiority}<0.001$)

The secondary efficacy endpoint

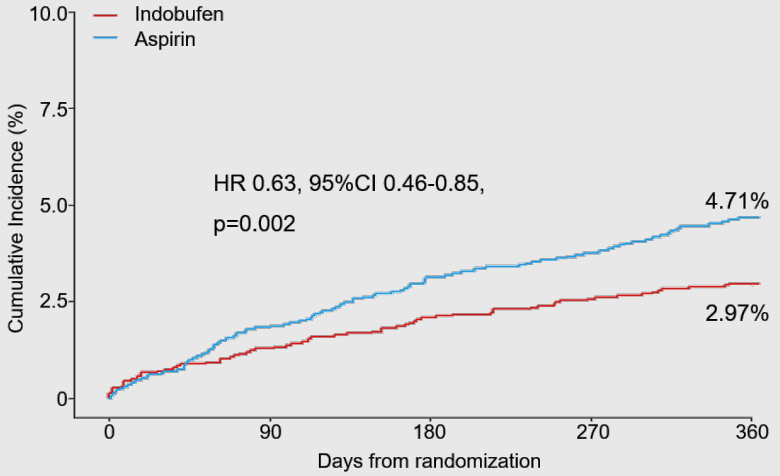


Number at risk

Indobufen	2258	2210	2189	2171	2167
Aspirin	2293	2250	2237	2227	2223

	Indobufen N= 2258	Aspirin N= 2293
CV death, nonfatal MI, ischemic stroke, ST	34 (1.51%)	32 (1.40%)
CV death	3 (0.13%)	4 (0.17%)
Nonfatal MI	9 (0.40%)	10 (0.44%)
Ischemic stroke	18 (0.80%)	19 (0.83%)
Definite or probable ST	5 (0.22%)	4 (0.17%)

The secondary safety endpoint



Number at risk

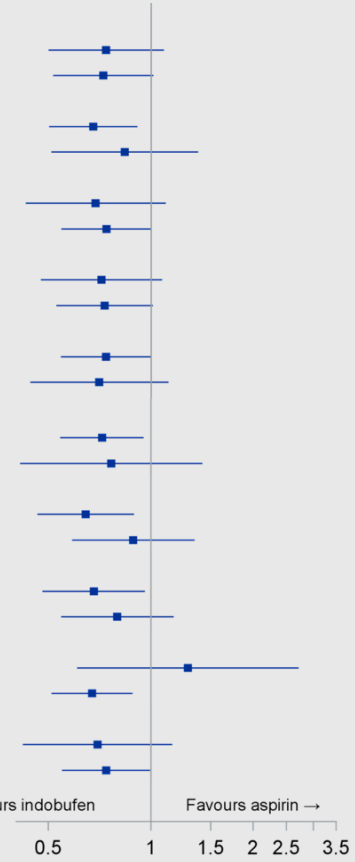
Indobufen	2258	2195	2169	2145	2136
Aspirin	2293	2219	2186	2167	2146

	Indobufen N= 2258	Aspirin N= 2293	P value
BARC type 2, 3, 5 bleeding	67 (2.97%)	108 (4.71%)	**0.002**
BARC type 3, 5 bleeding	29 (1.28%)	28 (1.22%)	0.84
BARC type 2 bleeding	38 (1.68%)	80 (3.49%)	**<0.001**
BARC type 3 bleeding	24 (1.06%)	24 (1.05%)	0.95
BARC type 5 bleeding	5 (0.22%)	4 (0.17%)	0.72

Subgroup analysis

- ✓ The beneficial effect of indobufen-based DAPT was consistent across all subgroups with no significant interaction.

	Indobufen	Aspirin	HR (95% CI)	P value for interaction
Age, year				0.94
≥65	43 (5.01)	62 (6.76)	0.74 (0.50,1.09)	
<65	58 (4.15)	78 (5.67)	0.72 (0.52,1.02)	
Sex				0.47
Male	74 (4.87)	103 (7.12)	0.68 (0.50,0.91)	
Female	27 (3.66)	37 (4.37)	0.84 (0.51,1.37)	
Current smoker				0.80
Yes	30 (5.14)	40 (7.39)	0.69 (0.43,1.10)	
No	71 (4.24)	100 (5.71)	0.74 (0.55,1.00)	
Diabetes				0.94
Yes	40 (4.99)	53 (6.90)	0.72 (0.47,1.08)	
No	61 (4.19)	87 (5.70)	0.73 (0.53,1.01)	
Hypertension				0.87
Yes	71 (4.68)	97 (6.29)	0.74 (0.54,1.00)	
No	30 (4.05)	43 (5.73)	0.71 (0.44,1.12)	
Creatinine clearance, ml/min				0.86
≥60	83 (4.23)	117 (5.83)	0.72 (0.54,0.95)	
<60	18 (6.12)	23 (8.04)	0.76 (0.41,1.42)	
Multivessel disease				0.23
Yes	59 (4.67)	92 (7.19)	0.64 (0.46,0.89)	
No	42 (4.23)	48 (4.74)	0.89 (0.59,1.34)	
PPI use				0.55
Yes	53 (4.88)	81 (7.12)	0.68 (0.48,0.96)	
No	48 (4.09)	59 (5.11)	0.80 (0.54,1.17)	
ARC-HBR				0.11
Yes	16 (11.03)	12 (8.76)	1.28 (0.61,2.72)	
No	85 (4.02)	128 (5.94)	0.67 (0.51,0.88)	
Complex-PCI				0.85
Yes	25 (4.62)	38 (6.52)	0.70 (0.42,1.16)	
No	76 (4.43)	102 (5.96)	0.74 (0.55,0.99)	



Conclusions

- Indobufen plus clopidogrel DAPT for 12 months is non-inferior in the 1-year composite of efficacy and safety outcomes compared to aspirin plus clopidogrel DAPT.
- There is no statistical difference regarding the 1-year efficacy composite (CV death, nonfatal MI, ischemic stroke, and definite or probable ST) between indobufen plus clopidogrel DAPT and conventional DAPT. The decreased BARC bleeding in indobufen group is mostly driven by a reduction of minor bleeding events.

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Indobufen or Aspirin on Top of Clopidogrel after Coronary Drug-eluting Stent Implantation (OPTION): a Randomized, Open-label, Endpoint-blinded, Non-inferiority Trial

Hongyi Wu, MD; Lili Xu, MD; Xin Zhao, MD; Huanyi Zhang, MB; Kang Cheng, MD; Xiaoyan Wang, MD; Manhua Chen, MB; Guangping Li, MD; Jiangnan Huang, MD; Jun Lan, MM; Guanghe Wei, MM; Chi Zhang, MD; Yinman Wang, MD; Juying Qian, MD; Junbo Ge, MD; on behalf of the OPTION investigators

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