

The logo for GLASSY features the word "GLASSY" in a white, bold, sans-serif font. The letter "A" is replaced by a stylized blue graphic consisting of a thick blue line that forms a large, open loop around the letter "S", with a smaller loop extending downwards from the bottom of the "S".

GLASSY

NCT01813435

**Ticagrelor Monotherapy Beyond
One Month Versus Conventional
Therapy On Adjudicated Ischemic
And Bleeding Endpoints
Following Drug Eluting Stent
Implantation. Primary Results of
the GLOBAL LEADERS
Adjudication Sub-Study
(GLASSY)**

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on behalf of GLASSY Investigators

Declaration of Interest

Dr. Valgimigli reports grants and personal fees from Abbott, personal fees from Chiesi, personal fees from Bayer, personal fees from Daiichi Sankyo, personal fees from Amgen, grants and personal fees from Terumo, personal fees from Alvimedica, grants from Medicure, grants and personal fees from Astrazeneca, personal fees from Biosensors, personal fees from Idorsia, outside the submitted work.

Background

- Dual antiplatelet therapy (DAPT) mitigates the risks of cardiac and, to lesser extent, cerebrovascular ischemic events.
- However, prolonged DAPT carries a heightened major bleeding risk.
- P2Y₁₂ inhibitor monotherapy might limit bleeding risk and retain the ischemic benefits of prolonged DAPT and provide long-term greater ischemic protection than aspirin alone.
- In GLOBAL LEADERS ticagrelor with 1-mo aspirin did not reduce the composite of death or Q-MI as compared to 1-year DAPT followed by aspirin*.

Background ii

- By design, all clinical endpoints in the GLOBAL LEADERS study were investigator reported (IR) without central adjudication.

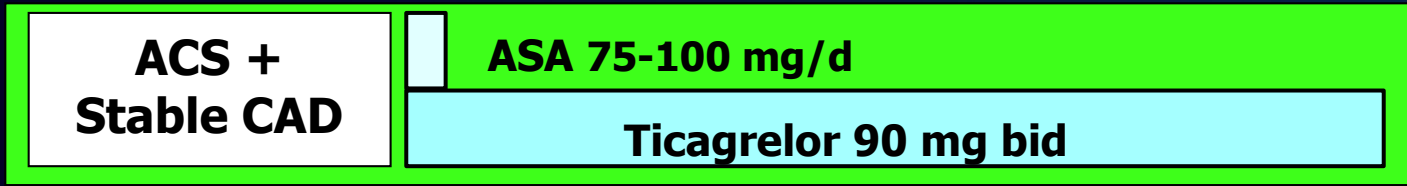
*“The FDA considers the adjudication process to be a critically important component of good clinical study practice”**

- The current study was designed to prospectively implement an independent central adjudication process of both reported events and potential unreported event triggers to further assess the impact of this novel experimental treatment in a large stratified sample of patients included in the GLOBAL LEADERS trial.

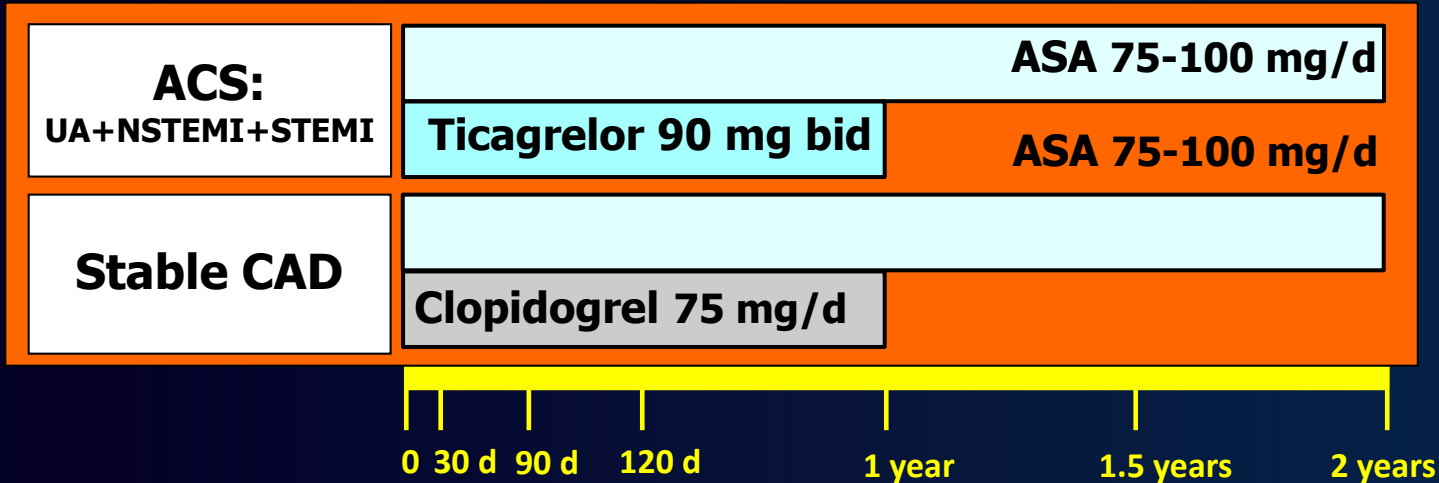
GLOBAL LEADERS design



Experimental arm



Control arm



**“All-comers”
PCI population
N = 15,991
1:1 Randomisation,
open-label design,
130 centers
worldwide**

**Any type of lesions:
Left main, SVG, CTO
bifurcation, ISR, etc.**

**Unrestricted use of
DES (number, length)**

Randomization was also stratified by site

To assess the comparative effectiveness of the experimental treatment strategy as compared to conventional 12-month DAPT followed by aspirin on the:

- **Primary efficacy EP of CEC-adjudicated all-cause death, non-fatal MI, non-fatal stroke or urgent TVR**
(*non-inferiority and if met superiority*)
- **Primary safety EP of CEC-adjudicated BARC 3 or 5 bleeding**
(*superiority*)

Under the assumptions that the co-primary *Efficacy* and *Safety EPs* would occur, respectively at 11% and 5% in the control group, 7,186 patients would yield:

> 85% power to detect non-inferiority for the co-primary efficacy EP with a NI margin at 1.22 on a relative scale ($\approx 2.4\%$ ARD), 1-sided type I error of 2.5%.

80% power to assess the superiority for the co-primary efficacy EP, assuming 20% RRR with two-sided alpha of 2.5%.

> 80% power to detect a 33% RRR in the experimental arm for the co-primary safety endpoint (BARC 3 or 5 bleeding) with two-sided alpha error at 2.5%.

GLASSY – PARTICIPATING SITES AND FUNDS



The study was sponsored by the European Institute of Clinical Research (ECRI), a nonprofit organization, and received grant support from the department of cardiology at Bern university hospital, Bern, Switzerland and from the Swiss National Science Foundation (SNSF) Project number: IZSEZO_180403.

Germany

Bad Nauheim, PI: C. Hamm
Essen, PI: C. Naber

United Kingdom

Blackburn, PI: S. Gard

The Netherlands

Rotterdam, PI: D. Diletti
Amsterdam, PI: T. Slagboom

Belgium

Hasselt, PI: E. Benit
Bonheiden, PI: L. Janssens
Chaleroi, PI: A. Aminian
Genk, PI: M. Vrolix

Switzerland

Bern, PI: S. Windecker

20 Top enrolling
sites (N= 7, 585)

Poland

Chrzabow, PI: A. Zurakowski
Krakov, PI: K. Zmudka
Dabrowa Gornicza, PI: P. Buszan
PAKS Kozle, PI: J. Prokopczuk

Austria

Vienna, PI: K. Huber

Italy

Pavia, PI: M. Ferrario
Ferrara, PI: C. Tumscitz
Terni, PI: M. Dominici
Arezzo, PI: L. Bolognese

Bulgaria

Sofia, PI: I. Petrov

GLASSY – STUDY DESIGN



GLASSY
7,585

**Global
Leaders Trial**
15,991

CRF based screening

Investigator reported events
Event triggers based on prespecified logics

Source documents collection/translation

CEC process

Formal adjudication of IR and triggered EPs

CHAIR:

E. MC FADDEN

CO-CHAIR:

S. LEONARDI

MEMBER:

R. PICCOLO

PROJECT LEADER:

A. FRANZONE

GLASSY – PARTICIPANTS VS NON PARTICIPANTS

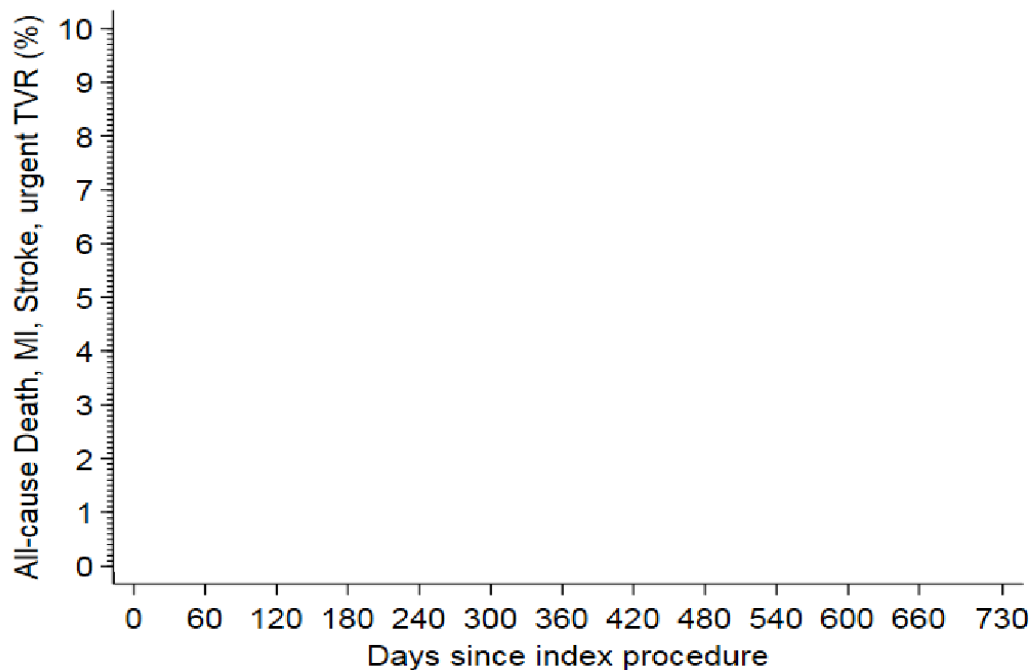
Clinical characteristics	Glassy (20 sites) N=7,585	Not Glassy (110 sites) N= 8,383	P-value*
Age	64.9±10	64.2±10	0.41
Female sex	1799 (23.7)	1915 (22.8)	0.33
Hypertension	5492 (73)	6223 (74)	0.70
Diabetes mellitus	1822 (24)	2216 (26)	0.47
Renal failure (eGFR < 60 ml/min)	1005 (13)	1166 (14)	0.83
Peripheral Vascular disease	553 (7)	452 (5)	0.03
Current smoker	2186 (29)	1983 (24)	0.007
Previous MI	1762 (23)	1948 (23)	0.91
Previous PCI	2522 (33)	2699 (32)	0.53
Previous CABG	443 (6)	500 (6)	0.62
Stable CAD	3745 (49)	4736 (56)	0.048
Multivessel treatment	1098 (14)	1248 (15)	0.65
Previous major bleeding	48 (0.6)	50 (0.6)	0.78
Statin at dis.	6954 (92)	7747 (93)	0.78
Heart failure with ACEi or ARB at dis.	469 (84)	465 (83)	0.51
Heart failure with betablocker at dis.	130 (83)	181 (82)	0.88

*: Mixed-models p-values, accounting for a random effect of hospital identifier

Clinical outcomes according to GLASSY inclusion

Subgroups	Experimental Intervention Group N = 7980	Control Group N = 7988	Rate Ratio [Exp./Reference*] (95% CI)	Rate ratio (95% CI)		p-value	p-value for interaction
				0.25	0.5 1.0 2.0		
All-cause mortality or New Q-wave MI or equivalent LBBB							0.741
GLASSY	151/3794	179/3791	0.84 (0.68-1.04)			0.114	
No GLASSY	154/4186	174/4197	0.88 (0.71-1.10)			0.266	
All-cause mortality							0.343
GLASSY	111/3794	136/3791	0.81 (0.63-1.04)			0.105	
No GLASSY	113/4186	117/4197	0.97 (0.75-1.25)			0.805	
New Q-wave MI or equivalent LBBB							0.395
GLASSY	43/3794	48/3791	0.89 (0.59-1.35)			0.585	
No GLASSY	41/4186	59/4197	0.70 (0.47-1.04)			0.072	
BARC 3 or 5 Bleeding							0.896
GLASSY	82/3794	86/3791	0.95 (0.70-1.29)			0.760	
No GLASSY	81/4186	83/4197	0.98 (0.72-1.33)			0.907	
BARC 3 bleeding							0.965
GLASSY	77/3794	81/3791	0.95 (0.70-1.30)			0.753	
No GLASSY	73/4186	78/4197	0.94 (0.68-1.30)			0.712	
BARC 5 bleeding							0.388
GLASSY	12/3794	10/3791	1.20 (0.52-2.78)			0.668	
No GLASSY	10/4186	14/4197	0.72 (0.32-1.62)			0.424	

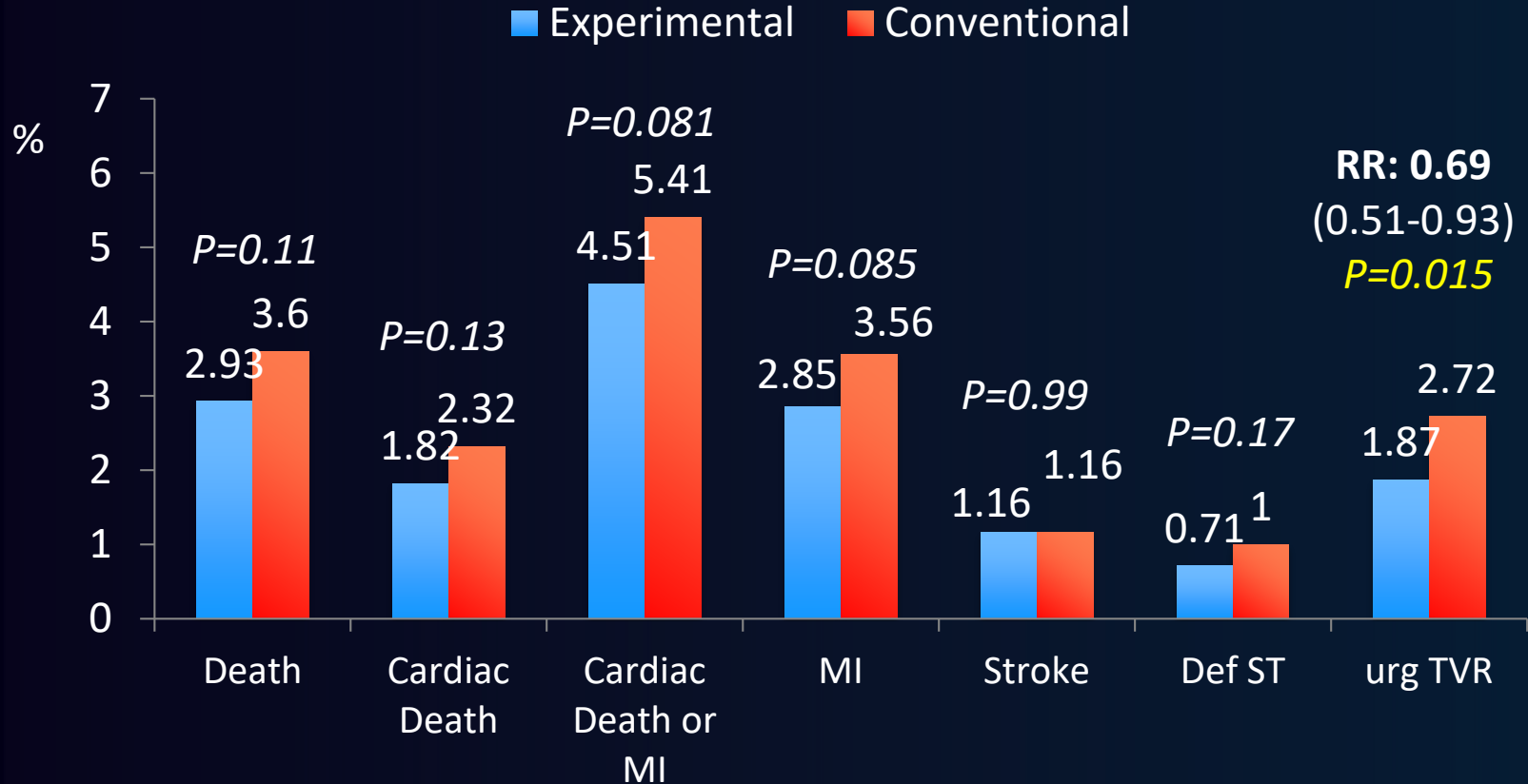
GLASSY – CO-PRIMARY EFFICACY EP



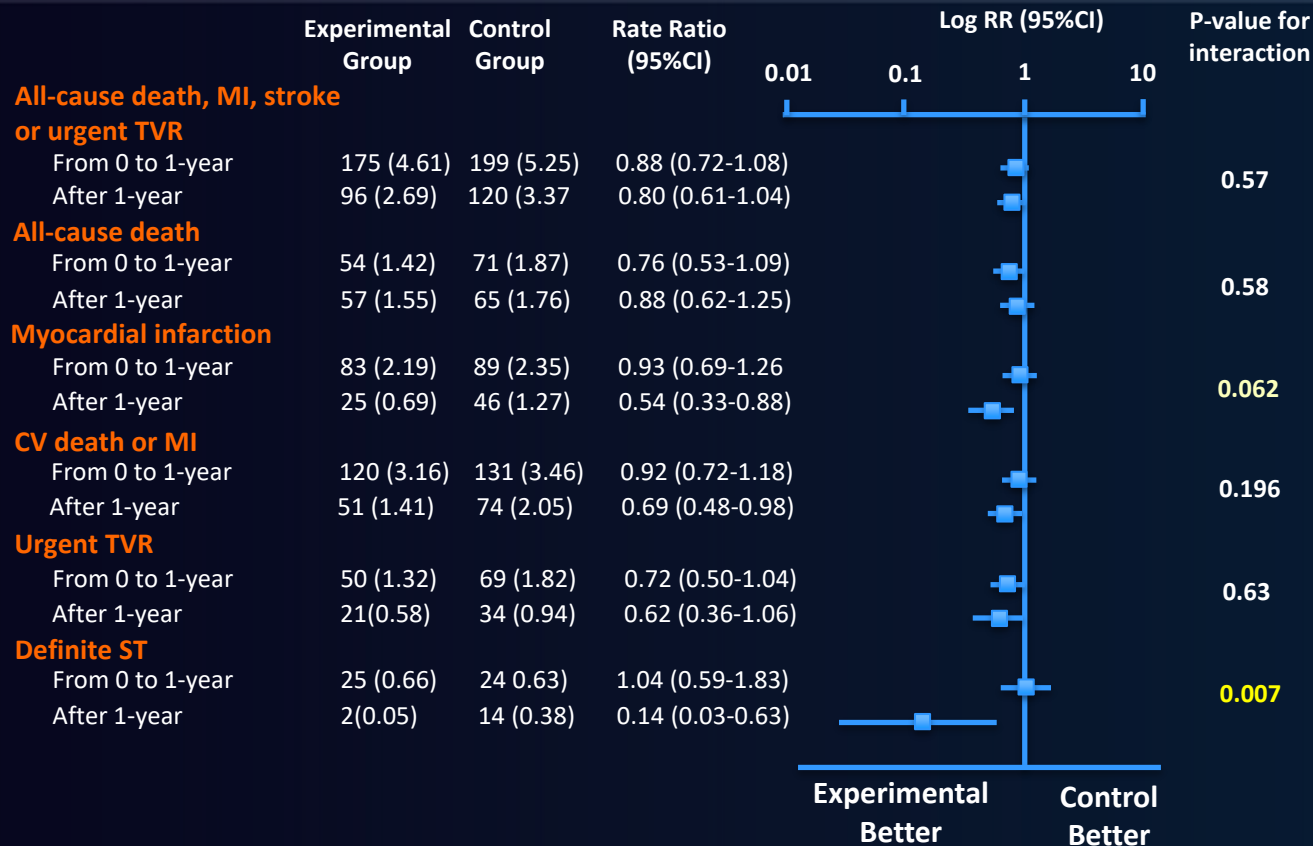
Number at risk

Reference	3791	3671	3644	3626	3603	3591	3565	3547	3526	3503	3483	3465	3420
Experimental	3794	3678	3638	3616	3600	3586	3572	3549	3533	3511	3491	3481	3439

SECONDARY EFFICACY EPS @ 2-YEARS



LANDMARK ANALYSIS @ 1-YEAR

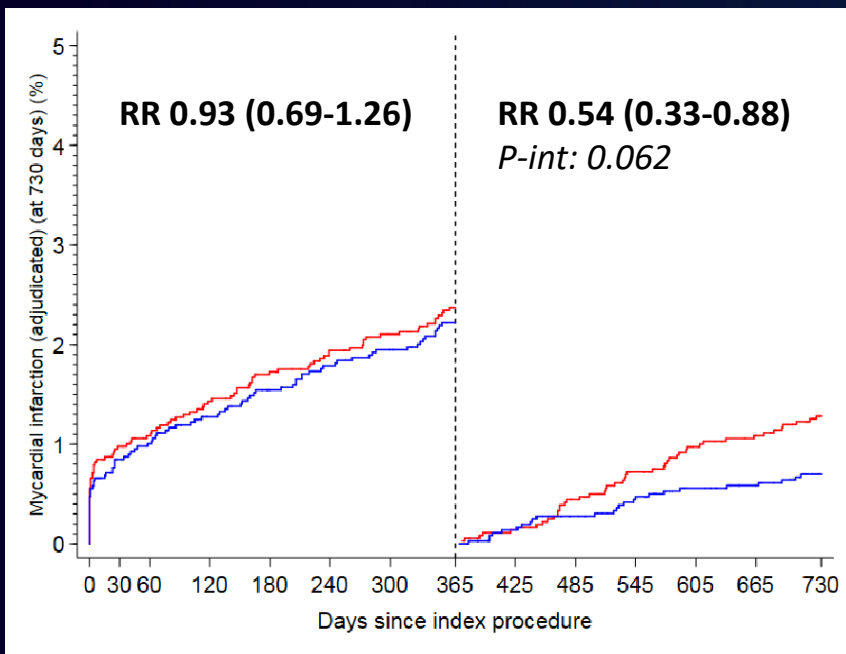


LANDMARK ANALYSIS @ 1-YEAR

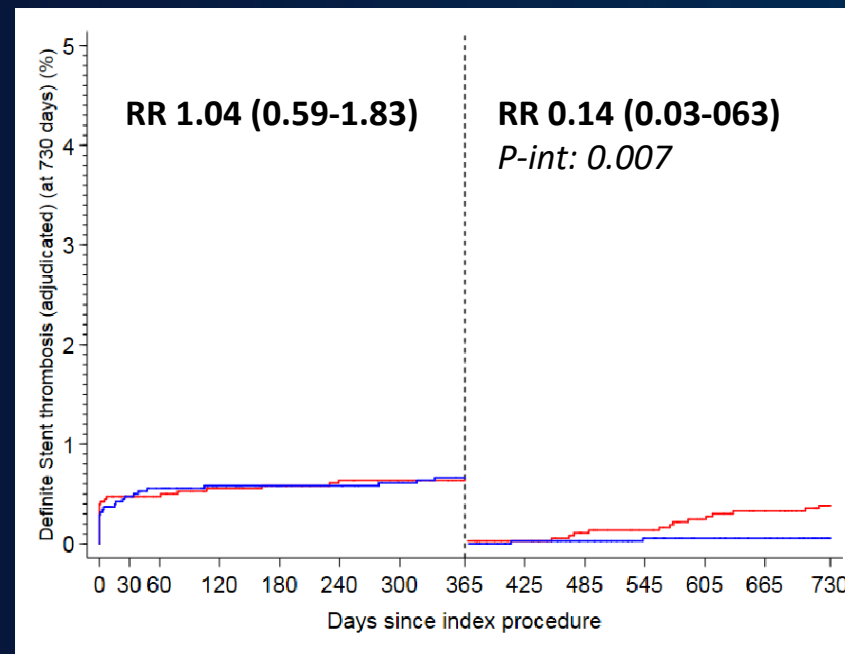
■ Experimental arm

■ Conventional arm

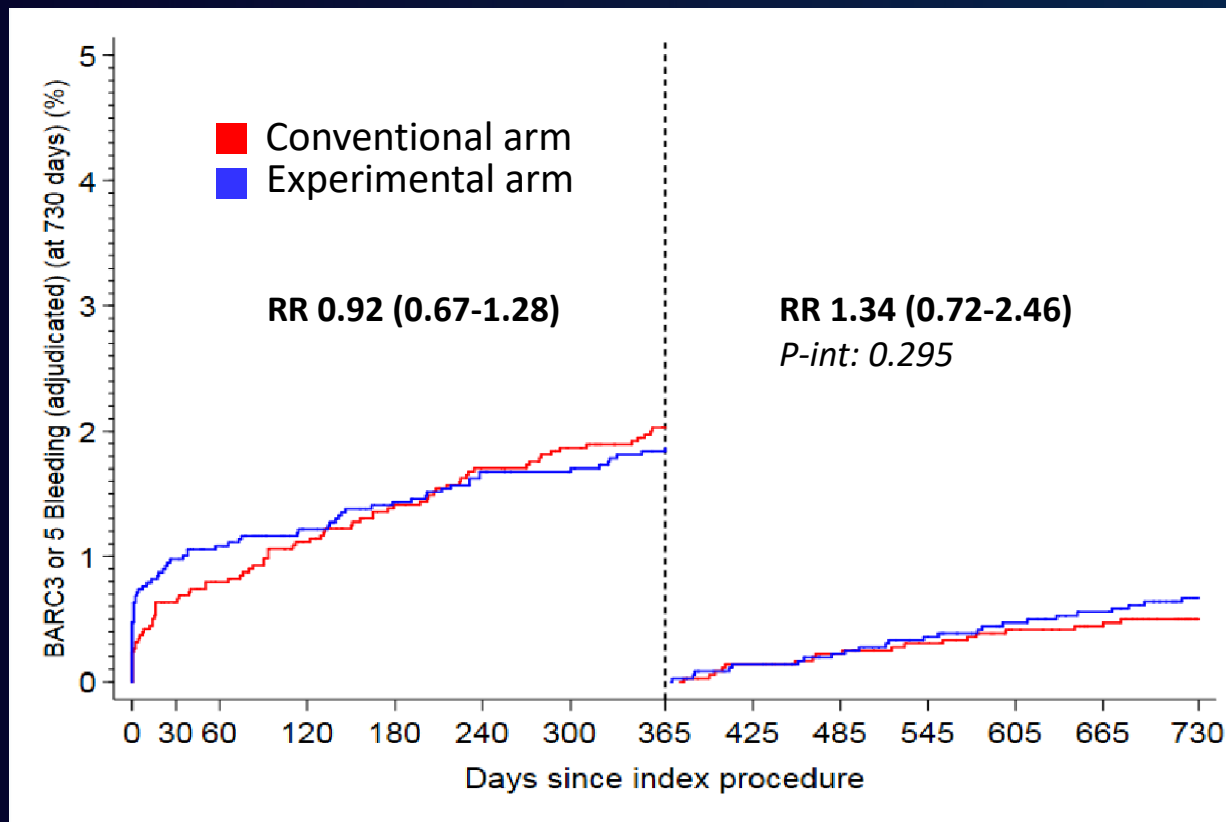
Myocardial Infarction



Definite Stent thrombosis



GLASSY – CO-PRIMARY SAFETY EP



Summary

- Ticagrelor monotherapy after 1-month DAPT was non-inferior to conventional DAPT in the prevention of all-cause death, non-fatal myocardial infarction, non-fatal stroke, or urgent target-vessel revascularization at 2 years.
- Our results provide new evidence that discontinuation of aspirin after 30 days while continuing ticagrelor alone does not expose patients to a higher ischemic risk as compared to a standard DAPT for 1 year and may reduce the rates of MI and stent thrombosis as compared to aspirin alone.
- Furthermore, the experimental treatment did not increase the risk of major bleeding.

1-year landmark: Global leaders vs GLASSY

