Amulet or Watchman FLX Device for Percutaneous LAAC: Primary Results of the SWISS-APERO Randomized Clinical Trial

Roberto Galea, MD

Department of Cardiology, Bern University Hospital, Bern, Switzerland

on behalf of the SWISSAPERO Investigators

@robertogalea7

roberto.galea@insel.ch

Disclosure Statement of Financial Interest

I, Roberto Galea, DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

Acknowledgements

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Background and objectives

- **Residual LAA patency after LAAC is routinely assessed after intervention, by means of TEE or CCTA, as it might undermine LAAC therapeutic principle (i.e. complete LAA sealing)**

- ***Watchman and Amulet are the two most frequently used LAAC devices worldwide and were recently compared in the Amulet IDE trial***
  - **The new Watchman FLX was not included**
  - **CCTA (with greater ability to detect LAA patency) was not routinely performed during follow-up**
  - **Post-implantation drug regimen was different between the 2 arms reflecting the US but not the EU IFUs**

- ***To assess whether Amulet is superior to Watchman FLX in terms of crossover to the other device or complete LAA sealing, as assessed by means of CCTA 45 days after implantation***

Study Organization

Sponsor: **University Hospital of Bern**

Coordinating Investigators: **M. Valgimigli**

Study Project Leader: **R. Galea**

Grant Supplier: **Abbott**

CROs: **Advice Pharma**

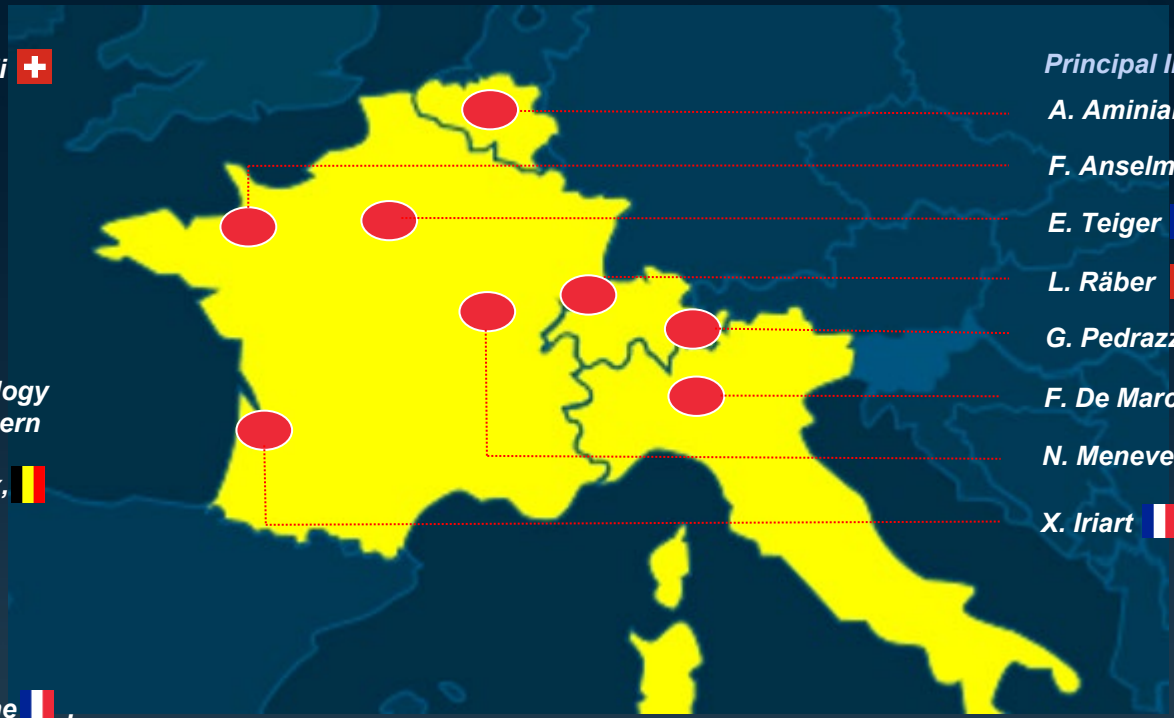
Sites: **8** *Countries:* **4 countries**

Imaging Core Lab: **Department of Radiology and Cardiology, University Hospital of Bern**

CEC: **A. Franzone (Chair), P. Vranckx, U. Fischer**

DMC: **Enrica Paschetto, E. Frigoli**
Stats: **F. Babongo, D. Heg**

Executive Committee:
M. Valgimigli, L. Räber, F. Anselme, A. Aminian, F. De Marco



Principal Investigators:

A. Aminian

F. Anselme

E. Teiger

L. Räber

G. Pedrazzini

F. De Marco

N. Meneveau

X. Iriart

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SWISS APERO

SWISS-APERO Trial Design

Screening phase

LAAC clinically indicated

Eligibility
- High bleeding risk
- LAA morhology suitable for both devices
- No LAA thrombus

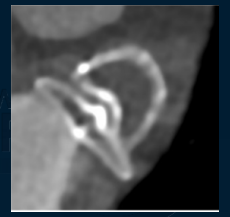
LAAC

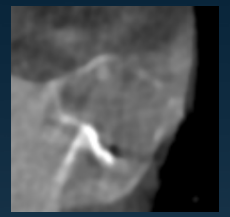
DEVICE RANDOMIZATION

Amulet

CROSSOVER

Watchman FLX





45-DAY fu

Mid-term LAA PATENCY

ASA
Clopidogrel or (N)OAC

Days after LAAC **45 ± 7**

- Medical and drug history assessment
- Laboratory tests
- TEE (optional if intraprocedural TEE)
- CCTA

- Intraprocedural TEE/ICE
- Randomization

- Medical and drug history assessment
- TEE
- CCTA

Study Endpoints

Primary Endpoint

The Composite of **justified crossover** to the non-randomly allocated device and
LAA **patency at 45-day CCTA**

DEFINITIONS

→ implantation of the non-randomized device **after at least an attempt to implant the assigned device**

→ LAA density **≥ 100 HU** or **≥ 25%** of that of the LA

Both components **centrally evaluated**

Secondary Endpoints

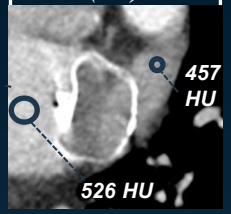
- PDL at 45-day TEE
- DRT at 45-day TEE and CCTA
- Procedural complications
- Clinical outcomes at 45 days:
  - Composite of CV death, stroke or systemic embolism
  - All bleedings (BARC 1-5)

LAA Patency subtypes

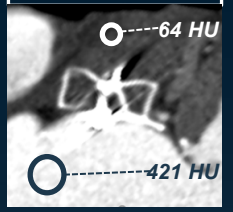
LAA PATENCY DEFINITION:

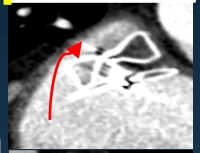
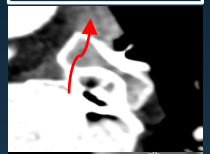
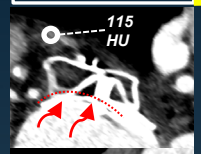
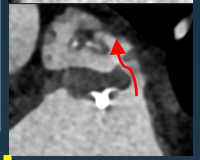
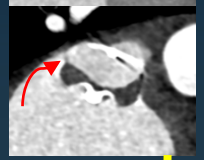
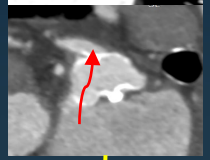
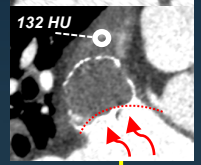
LAA density ≥ 100 HU and/or LAA density ≥ 25% of that of the LA

PATENT LAA (PA)



NON PATENT LAA (NPA)



	PERIDEVICE	MIXED	INTRADEVICE	PANVL
AMULET				
WATCHMAN				

Underlying Leak Mechanisms → **INCOMPLETE SIDE SEALING (GAP LEAKS)** | **DEVICE PERMEABILITY** | **UNCLEAR**

SWISS APERO

Flow Chart

LAA Closure performed (n = 423)

Excluded (n=202)
- Enrolled in other cardiovascular device or an investigational drug trial (n=47)
- Patient did not provide consent (n=44)
- Severe chronic kidney insufficiency (n=40)
- Incomplete screening (n=25)
- First operator with limited experience with one of the two LAAC devices (n=18)
- Intra-cardiac thrombus (n=10)
- LAA morphology not suitable for one of the two devices (n=9)
- Other eligibility criteria not met (n=9)

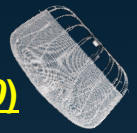
Randomized (n = 221)

Allocated to Amulet (n=111)

- Death (n = 2)
- CCTA not performed (n=1)
- LAA patency not assessable (n=2)
- Withdrew consent (n=1)

Considered for primary endpoint analysis (n=105)

Allocated to Watchman/FLX (n=110)



Until October 2019 only Watchman 2.5 available (n = 25)

- Death (n = 4)
- CCTA not performed (n=5)
- LAA patency not assessable (n=1)

Considered for primary endpoint analysis (n=100)

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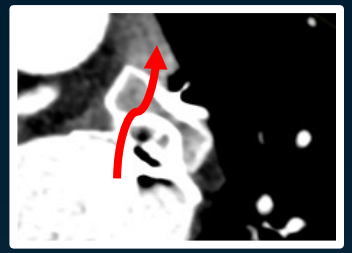
Baseline Characteristics

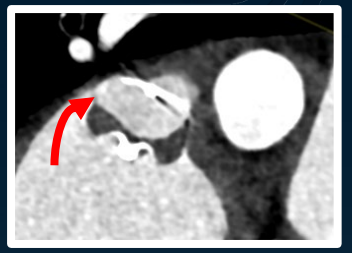
	Amulet *(N=111)*	Watchman/FLX *(N=110)*
Age (years), mean ±SD	76.5 ± 7.1	77.3 ± 8.4
Male sex, no. (%)	79 (71.2%)	77 (70.0%)
Diabetes mellitus, no. (%)	24 (21.6%)	34 (30.9%)
History of coronary heart disease, no. (%)	39 (35.1%)	41 (37.3%)
Prior cerebrovascular event, no. (%)	45 (40.5%)	42 (38.2%)
Paroxysmal atrial fibrillation, no. (%)	43 (38.7%)	44 (40.0%)
CHA2DS2Vasc score, mean ± SD	4.2 ± 1.4	4.4 ± 1.4
HASBLED score, mean ± SD	3.1 ± 0.8	3.2 ± 1.0
History of relevant bleeding, no. (%)	98 (88.3%)	96 (87.3%)
Documented anaemia, no. (%)	34 (30.6%)	31 (28.2%)
Bowel angiodysplasia, no. (%)	17 (15.3%)	25 (22.7%)
Blood cell dyscrasia associated with increased bleeding risk, no. (%)	9 (8.1%)	6 (5.5%)
Patients under anticoagulation at the randomization, no. (%)	51 (45.9%)	57 (51.8%)

Procedural Outcomes and Discharge Medication

		Amulet *(N=111)*	Watchman/FLX *(N=110)*	*P value*
Sinus rhythm at the begin of procedure, no. (%)		57 (51.4%)	51 (46.4%)	0.683
Conscious sedation, no. (%)		65 (58.6%)	67 (60.9%)	0.784
Transesophageal echocardiography, no. (%)		108 (97.3%)	108 (98.2%)	1.000
Procedure time (min), mean ± SD		45.9 ± 25.1	43.0 ± 23.1	0.371
Fluoroscopy time (min), mean ± SD		12.3 ± 8.1	12.8 ± 9.2	0.628
Contrast medium (ml), mean ± SD		60.1 ± 42.7	62.9 ± 45.3	0.643
Concomitant procedure, no. (%)		21 (18.9%)	16 (14.5%)	0.472
First device used successfully implanted, no. (%)		105 (94.6%)	107 (97.3%)	0.499
Justified crossover, no. (%)		1 (0.9%)	0 (0%)	0.318
Aborted procedure, no. (%)		1 (0.9%)	0 (0%)	1.000
Any PDL detected by TEE or Angiography, no. (%)		5 (4.5%)	13 (11.8%)	0.053
Drug regimen at discharge	Any SAPT, no. (%)	22 (20.2%)	23 (21.1%)	1.000
	Any DAPT, no. (%)	78 (71.6%)	77 (70.6%)	1.000

Primary Endpoint ≈ PA at 45-day CCTA



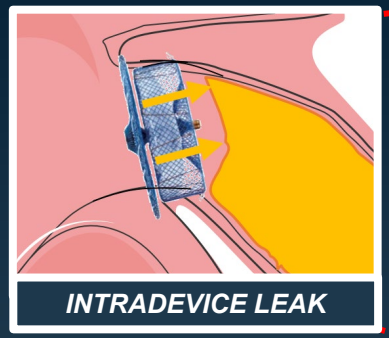


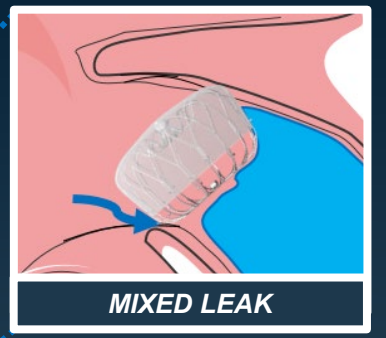
AMULET
67.6%
(n=71/105)

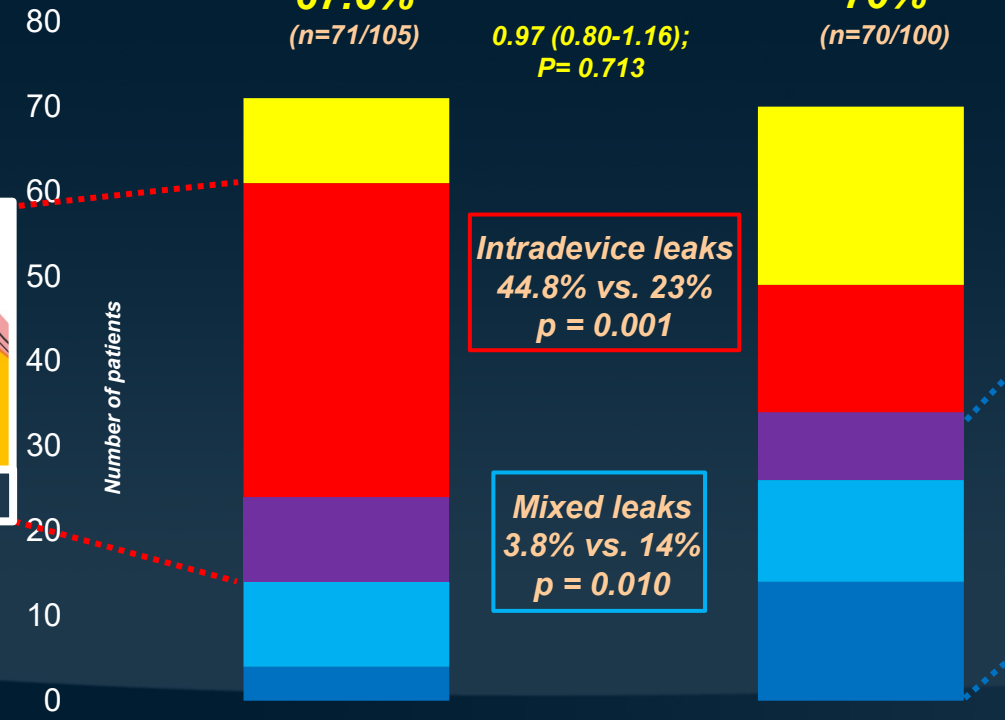
VS.

0.97 (0.80-1.16);
P= 0.713

WATCHMAN/FLX
70%
(n=70/100)







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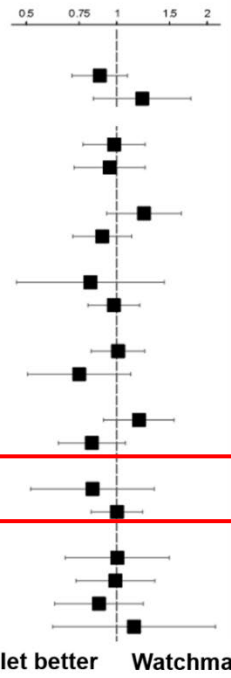
Primary Endpoint ≈ PA at 45-day CCTA

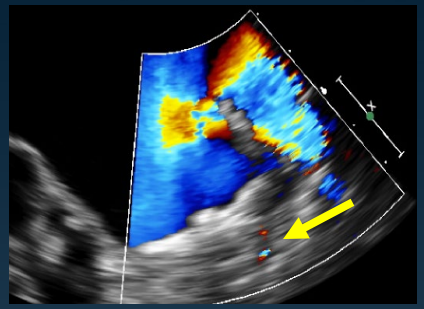
	AMULET N = 105 number of primary endpoint/ number of patients	WATCHMAN N = 100 number of primary endpoint/ number of patients	Risk ratio (95% CI)	Risk ratio (95% CI)	p-value	interaction p-value
Age						0.134
≥75	45/67 (67.2%)	52/68 (76.5%)	0.88 (0.71; 1.09)		0.229	
<75	26/38 (68.4%)	18/32 (56.3%)	1.22 (0.84; 1.77)		0.294	
Gender						0.850
Male	49/76 (64.5%)	46/70 (65.7%)	0.98 (0.77; 1.24)		0.875	
Female	22/29 (75.9%)	24/30 (80.0%)	0.95 (0.72; 1.25)		0.701	
Diabetes mellitus						0.079
yes	19/22 (86.4%)	21/30 (70.0%)	1.23 (0.93; 1.64)		0.166	
no	52/83 (62.7%)	49/70 (70.0%)	0.90 (0.71; 1.12)		0.339	
LVEF						0.560
<40	7/11 (63.6%)	7/9 (77.8%)	0.82 (0.46; 1.44)		0.492	
≥40	62/92 (67.4%)	62/90 (68.9%)	0.98 (0.80; 1.19)		0.828	
History of relevant bleeding						0.183
yes	62/92 (67.4%)	58/87 (66.7%)	1.01 (0.82; 1.24)		0.918	
no	9/13 (69.2%)	12/13 (92.3%)	0.75 (0.51; 1.11)		0.135	
History of cerebrovascular event						0.057
yes	34/43 (79.1%)	26/39 (66.7%)	1.19 (0.91; 1.55)		0.206	
no	37/62 (59.7%)	44/61 (72.1%)	0.83 (0.64; 1.07)		0.145	
LAAC device *						0.468
Watchman 2.5 period	13/24 (54.2%)	15/23 (65.2%)	0.83 (0.52; 1.33)		0.440	
Watchman FLX period	58/81 (71.6%)	55/77 (71.4%)	1.00 (0.82; 1.22)		0.980	
Preprocedural antithrombotic regimen						0.406
none	19/29 (65.5%)	15/23 (65.2%)	1.00 (0.67; 1.50)		0.982	
SAPT or DAPT	29/42 (69.0%)	23/33 (69.7%)	0.99 (0.73; 1.34)		0.952	
Any single-anticoagulant therapy	15/22 (68.2%)	25/32 (78.1%)	0.87 (0.62; 1.23)		0.413	
SAPT or DAPT with anticoagulant therapy	8/12 (66.7%)	7/12 (58.3%)	1.14 (0.61; 2.13)		0.673	



Watchman 2.5 and Watchman FLX periods (before and after 22.10.2019, respectively) are the two time periods when Watchman 2.5 or Watchman FLX was the only Watchman device available in the study centers, respectively

LAA patency at 45-day TEE

AMULET
13.7%
(n=13/95)



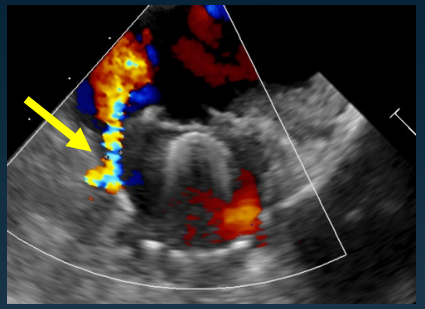
NO PDL >5mm

NO MULTIPLE PDLs

VS.

0.50 (0.27-0.91);
P= 0.020

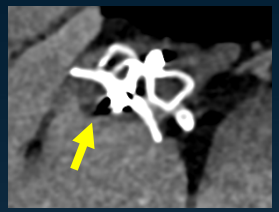
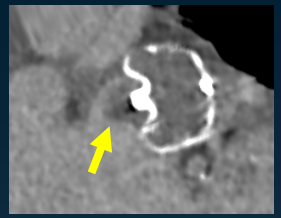
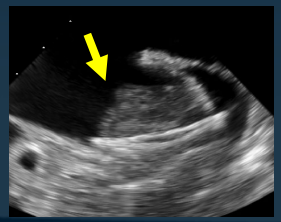
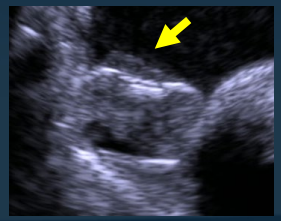
WATCHMAN/FLX
27.5%
(n=25/91)



NO PDL >5mm

2.2% MULTIPLE PDLs
(all in Watchman 2.5)

Device Related Thrombus at 45 days

	AMULET			WATCHMAN/FLX		
CCTA						
Definite DRT	0.9% (n=1/107)		VS.		3.0% (n=3/101)	0.31 (0.03-2.98); P= 0.285
Definite or possible DRT	3.7% (n=4/107)		VS.		9.9% (n=10/101)	0.38 (0.12-1.17); P= 0.076
TEE						
	2.1% (n=2/95)		VS.		5.5% (n=5/91)	0.38 (0.08-1.93); P= 0.225
	1.1% (n=1/92)		VS.		6.4% (n=6/94)	0.17 (0.02-1.39); P= 0.058

«as treated population»

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Procedure related complications

	Amulet *(N=111)*	Watchman/FLX *(N=110)*	*Amulet vs Watchman Risk ratio (95% CI)*	*P value*
Major procedure related complication, no. (%) *	**10 (9.0%)**	**3 (2.7%)**	**3.30 (0.93 - 11.68)**	**0.047**
Death, no. (%)	2 (1.8%)	0 (0.0%)		0.498
Cerebrovascular event, no. (%)	2 (1.8%)	0 (0.0%)		0.498
Systemic embolism, no. (%)	0 (0.0%)	0 (0.0%)		1
Major bleeding (BARC 3-5), no. (%) ¶	8 (7.2%)	2 (1.8%)	3.96 (0.86 - 18.25)	0.054
Clinically relevant pericardial effusion, no. (%)	4 (3.6%)	0 (0.0%)		0.122
Device embolization, no. (%)	1 (0.9%)	1 (0.9%)	0.99 (0.06 - 16.04)	0.995
Acute kidney injury, no. (%)	0 (0.0%)	0 (0.0%)		

*** Composite of death, CVE, systemic embolism, major bleeding, cardiac tamponade, device embolization, or acute kidney injury occurring within 7 days or thereafter if deemed procedure-related.**

¶ All 4 cardiac tamponades observed within 45 days after LAAC occurred in the Amulet group

Clinical outcomes at 45 days

	Amulet *(N=111)*	Watchman/FLX *(N=110)*	*Amulet vs Watchman Risk ratio (95% CI)*	*P value*
Composite of CV death, stroke or systemic embolism, no. (%)	3 (2.7%)	5 (4.5%)	0.59 (0.15 - 2.43)	0.463
Death, no. (%)	2 (1.8%)	4 (3.6%)	0.50 (0.09 - 2.72)	0.409
Cardiovascular death, no. (%)	2 (1.8%)	4 (3.6%)	0.50 (0.09 - 2.72)	0.409
Cerebrovascular event, no. (%)	2 (1.8%)	2 (1.8%)	1.00 (0.14 - 7.16)	0.998
Systemic embolism, no. (%)	0 (0.0%)	1 (0.9%)		0.498
Any bleeding, no. (%)	36 (32.4%)	25 (22.7%)	1.43 (0.92 - 2.21)	0.107
-Minor bleeding (BARC 1-2), no. (%)	29 (26.1%)	19 (17.3%)	1.51 (0.90 - 2.53)	0.11
-Major bleeding (BARC 3-5), no. (%)	9 (8.1%)	7 (6.4%)	1.27 (0.49 - 3.30)	0.617
Any pericardial effusion (new onset), no. (%)	22 (19.8%)	8 (7.3%)	3.09 (1.32 - 7.27)	0.006
-non clinically relevant, no. (%)	18 (16.2%)	8 (7.3%)	2.23 (1.01 - 4.91)	0.039
-clinically relevant, no. (%)	4 (3.6%)	0 (0.0%)		0.122

Study Limitations

- ***Open label study**: the two devices can be easily distinguished during CCTA and TEE assessment*
- *Trial **not powered** to show differences with regard to **clinical endpoints***
- *Minority yet sizable proportion of Watchman/FLX patients received **Watchman 2.5***
- *Rates of **procedural complications** observed were higher compared to those reported by previous studies (0.5-5%)*

Conclusions

In patients with high bleeding risk undergoing clinically indicated LAA Closure

Amulet compared with Watchman/FLX was associated with:

- **similar** residual LAA **patency** at 45-day CCTA
- **lower PDL** rates at 45-day **TEE**
- **higher procedural complications**
- **similar clinical outcomes at 45 days**

Circulation

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AMULET OR WATCHMAN DEVICE FOR PERCUTANEOUS LEFT ATRIAL APPENDAGE CLOSURE: PRIMARY RESULTS OF THE SWISS-APERO RANDOMIZED CLINICAL TRIAL

ROBERTO GALEA, MD; FEDERICO DE MARCO, MD; NICOLAS MENEVEAU, MD; ADEL AMINIAN, MD; FRÉDÉRIC ANSELME, MD,PHD; CHRISTOPH GRÄNI,MD,PHD; ADRIAN T. HUBER MD,PHD; EMMANUEL TEIGER MD,PHD; XAVIER IRIART, MD; FLORA BABONGO BOSOMBO, PHD; DIK HEG, PHD; ANNA FRANZONE, MD,PHD; PASCAL VRANCKX, MD,PHD; URS FISCHER, MD; GIOVANNI PEDRAZZINI, MD; FRANCESCO BEDOGNI, MD; LORENZ RÄBER, MD,PHD, MARCO VALGIMIGLI MD,PHD

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