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One-Year Outcomes After Amulet or Watchman Device for Percutaneous Left Atrial Appendage Closure: a Pre-Specified Analysis of the SWISS-APERO Randomized Clinical Trial

Running title: *Galea et al. One-Year Outcomes of SWISS-APERO Trial*

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Non-standard Abbreviations and Acronyms

AF	Atrial Fibrillation
DRT	Device Related Thrombus
CCTA	Cardiac Computed Tomography Angiography
IDL	IntraDevice Leak
LAA	Left Atrial Appendage
LAAC	Left Atrial Appendage Closure
MIL	Mixed Leak
PA	Patent Appendage
PANVL	Patent Appendage with Non Visible Leak
PDL	PeriDevice Leak
TEE	Trans-Esophageal Echocardiography

Percutaneous left atrial appendage (LAA) closure (LAAC) prevent thromboembolisms in atrial fibrillation (AF) patients. However, residual LAA patency post-LAAC has been associated with higher thromboembolic risk, especially when detected remotely after the procedure (1). Residual leaks are typically assessed by means of transesophageal echocardiography (TEE) or cardiac computed tomography angiography (CCTA), and the latter imaging modality provides a comprehensive operator-independent assessment and higher sensitivity compared with TEE (2). The SWISSAPERO (https://www.clinicaltrials.gov.-Unique identifier:NCT03399851) trial is the first randomized comparison between Watchman FLX (Boston Scientific, USA) and Amplatzer Amulet (Abbott, USA), which are the two most frequently used devices for LAAC worldwide (3,4). Patients with non-valvular AF and clinically indicated LAAC were eligible if provided written informed consent, had CHA2DS2-VASc score ≥ 2 and either HAS-BLED score ≥3 or presence of high bleeding risk features (3). The key exclusion criteria included the presence of LAA thrombus or LAA morphology not suitable for both study devices at TEE. All patients randomized to Watchman before October 2019 received Watchman 2.5, whereas Watchman FLX was exclusively used thereafter. Post-implantation treatment was left at discretion of the treating physician. At 13 months (395 ±30 days), patients underwent an on-site clinical visit and CCTA. The CCTA images and the clinical events were centrally and blindly assessed. LAA was defined as patent (PA) if LAA density ≥ 100 Hounsfield unit (HU) or ≥ 25% of that of the LA (3,4). In patients with PA, the presence of visible leaks was adjudicated as intradevice leak [IDL], peridevice leak [PDL] or mixed leak [MIL] if contrast medium was visible along the entire or part of the length of device respectively; or as PAs with no visible leak (PANVL) if none of the above was detected. DRT was defined as homogenous hypoattenuated thickening (HAT) on the atrial surface of the device and centrally adjudicated as definitive or possible DRT (3). The trial was an investigator initiated

trial, partially supported by a research grant from Abbott (St. Jude Medical/Abbott, Nathan Lane North Plymouth, MN, USA). The trial protocol was approved by the institutional review boards and all patients provided informed consent before enrolment.

The imaging endpoints were analysed by using chi-squared test and the risk ratios (RR) with 95% confidence intervals (CI) are reported. The clinical endpoints were analysed by using Cox proportional hazards model and the hazard ratios (HR) with 95% CI are reported. Data were analysed according to the intention-to-treat principle. A value of $P<0.05$ was considered statistically significant.

The data that support the findings of this study are available from the corresponding author upon reasonable request.

A total of 221 patients were assigned to Amulet (111[50.2%]) or Watchman (110[49.8%]; 85 received Watchman FLX and 25 Watchman 2.5). At 13 months (393[378-419] days), 24 patients died, 24 refused CCTA, 2 were lost-to-follow-up and 7 did not undergo CCTA for medical reasons. A total of 164 [74.2%; 84(75.7%) with Amulet and 80 (72.2%) with Watchman 2.5/FLX] patients underwent 13-month CCTA. PAs were observed in 45 (53.6%) patients with Amulet and 39 (48.8%) patients with Watchman 2.5/FLX (RR:1.10; 95%Confidence Interval [CI]:0.81-1.48; p=0.537) (Figure 1). The LAA patency subtypes were similarly distributed between groups. IDL occurred in 20 (23.8%) patients with Amulet and 14 (17.5%) patients with Watchman 2.5/FLX (RR: 1.36; 95%CI: 0.74-2.51; p=0.319). Side gap-leaks (the composite of PDL and MIL) occurred in 24 (28.6%) patients with Amulet and 22 (27.5%) patients with Watchman 2.5/FLX (RR: 1.04; 95%CI: 0.64-1.70; p=0.879). PANVL was detected in a minority of patients in both device groups (7.1% vs. 12.5%; RR: 0.57; 95%CI: 0.22-1.50; p=0.248). Definite or possible DRT at 13-month CCTA did not differ with Amulet or Watchman 2.5/FLX (2.4% vs. 3.8%; RR: 0.63; 95%CI: 0.11-3.70; p=0.610). The composite of cardiovascular death, ischemic stroke and systemic

embolism (9.5% vs. 10.2%; HR:0.91; 95%CI: 0.39-2.14; p=0.829), cerebrovascular events (2.7% vs. 3.7%; HR: 0.75; 95%CI: 0.17-3.35; p= 0.706) or bleeding (40.8% vs. 31.4%; HR:1.46; 95%CI: 0.93-2.28; p= 0.098) were comparable between groups. Results remained entirely consistent when only patients with Watchman FLX were compared with Amulet.

In the Amulet IDE trial, LAA complete occlusion rate at 12-month TEE was higher with Amulet compared with Watchman 2.5 (63.2% vs. 53.1%; p<0.01)(5). It is unclear if the inconsistent findings between our and Amulet IDE trials are explained by the predominant use of Watchman FLX in the Watchman group in our trial, by the different primary imaging modality used to assess PA, or a combination of both factors. Roughly, a quarter of patients did not undergo 13-month CCTA, which may have impacted study power to assess differences between the two groups. Our trial was not powered to show differences with regard to clinical endpoints. On the other hand, we confirmed in a smaller cohort involving the new iteration Watchman FLX, the similar long-term clinical outcomes after Watchman or Amulet device, which was similarly observed in the 3-year Amulet IDE follow-up(5).

Among patients undergoing clinically indicated LAAC and in whom LAA anatomy was deemed suitable for both Amulet and Watchman 2.5/FLX devices, rates of PA and DRT at 13-month CCTA, as well as clinical outcomes, did not differ between the two groups.

Article Information

Registration: URL: https://www.clinicaltrials.gov; Unique identifier: NCT03399851.

Acknowledgments

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Figure 1. One-Year Outcomes of SWISS-APERO Trial

AF, Atrial Fibrillation; CCTA, Cardiac Computed Tomography Angiography; CI, Confidence Interval; CVD, Cardiovascular Death; DRT, Device Related Thrombus; HR, Hazard Ration; LAA, Left Atrial Appendage; LAAC, Left Atrial Appendage Closure; RR, Relative Risk; SE, Systemic Embolism.

In a European Multicenter Cohort of 221 High Risk AF Patients with Clinical Indication to LAAC

RANDOMIZATION

From June 2018 to May 2021

(n=221)

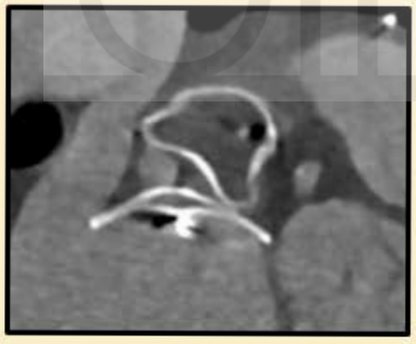
AMULET
(n=111)

WATCHMAN 2.5 (n=25)
From June 2018 to October 2019

WATCHMAN FLX (n=85)
From November 2019 to May 2021

Pre-Specified Secondary Analyses

13-month CCTA (n=164):



Residual LAA Patency

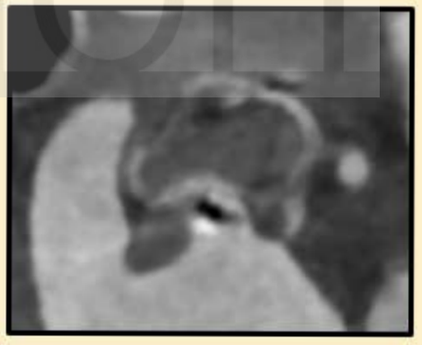
53.6%	=	48.8%

RR: 1.10; 95%CI: 0.81-1.48; p=0.537

Definite or Possible DRT

2.4%	=	3.8%

RR: 0.63; 95%CI: 0.11-3.70; p=0.610



13-month clinical follow-up (n=221):

9.5%	=	**Composite of CVD/Stroke/SE**	=	10.2%

HR: 0.91; 95% CI: 0.39-2.14; p=0.829

2.7%	=	**Composite of Ischemic Stroke/SE**	=	3.8%

HR: 0.75; 95%CI: 0.17-3.33; p=0.701