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# 1-month safety results in a randomized controlled trial (COATING) evaluating a surface-modification flow diverter (p64-MW-HPC) under single antiplatelet treatment

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## ABSTRACT

**Background** Flow diversion is an effective technique for treating intracranial aneurysms (IAs), with a high rate of complete aneurysm occlusion at 1 year. As dual antiplatelet treatment (DAPT) is required, it is restricted to unruptured IA. Surface-modification (SM) flow diverters (FDs), introduced to reduce thrombogenicity, have been poorly evaluated. COATING (Coating to Optimize Aneurysm Treatment In the New Flow Diverter Generation) is the first randomized controlled trial (RCT) evaluating an SM FD (p64-MW-HPC (hydrophilic polymer coating), phenox GmbH) under single antiplatelet treatment (SAPT).

**Methods** We compared the treatment arm, SM p64-MW-HPC under SAPT (ticagrelor or prasugrel), to the control arm, bare p64-MW under DAPT (ticagrelor or prasugrel+aspirin), for unruptured IA management. The primary endpoint (number of diffusion-weighted imaging (DWI) lesions on MRI 48 hours (±24 hours) after the index procedure) and safety data up to 1 month post-procedure were analyzed.

**Results** From September 2021 to November 2024, 171 patients (female 84.8%, mean age 55±11 years) were included in 15 centers in Europe and Israel with 83 patients in the treatment arm and 88 in the control arm. The mean (±SD) number of DWI lesions within 48 hours (±24 hours) of the index procedure in the treated aneurysm territory was 6.0 (±13.28) in the HPC and 5.3 (±11.75) in the bare group ($P_{\text{non-inferiority testing}}<0.0001$). 1-month safety data showed no statistically significant difference in thromboembolic events between study arms.

**Conclusion** COATING is the first RCT to evaluate an SM FD (p64-MW-HPC) under SAPT and shows favorable safety at 1 month.

### WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Flow diversion is the most effective treatment for intracranial aneurysms (IAs), but its use is restricted to unruptured IAs since it requires dual antiplatelet treatment (DAPT).

### WHAT THIS STUDY ADDS

⇒ COATING is the first randomized controlled trial evaluating a surface-modified (SM) flow diverter (FD) (p64-MW-HPC (hydrophilic polymer coating)) under single antiplatelet treatment (SAPT), showing non-inferiority in terms of diffusion-weighted imaging (DWI) lesions as a marker for thromboembolic events (TE) at 48 hours post-procedure compared with bare FD (p64-MW) under DAPT. No statistically significant difference between the study arms in terms of intra-procedural and post-procedural (up to 1 month) TE was observed.

### HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE, OR POLICY

⇒ These results confirm a similar level of safety in terms of TE in patients treated with SM p64-MW-HPC under SAPT and those treated with bare p64-MW under DAPT, permitting a change in the perioperative antiplatelet treatment and leading to a potential expansion of FD indications when using p64-MW with HPC surface modification.

## INTRODUCTION

Flow diversion involves the placement of a low porosity stent in front of the aneurysm neck to reduce intra-aneurysmal blood flow and induce thrombosis.[1 2] This technique was initially used to treat large and giant unruptured intracranial aneurysms (IAs) located at the internal carotid artery (ICA) and basilar artery (BA), and has shown good efficacy with a high rate of complete aneurysm occlusion mid and long term.[3] The range for flow diverter (FD) use has been expanded progressively to small and distal aneurysms.[4 5] One important limitation when using FDs is that patients require dual antiplatelet treatment (DAPT) to avoid procedural and post-procedural complications (primarily

thromboembolic), at the cost of an increased risk of cerebral and peripheral hemorrhagic complications.[3 4 6] Therefore, when treating ruptured IA, flow diversion is currently limited to those aneurysms that are not treatable by other endovascular (and surgical) techniques like blister aneurysms.[7] To overcome these limitations, one option is to apply a surface modification (SM) to the FD. SM can have several effects, including a decrease in FD thrombogenicity and more rapid device surface endothelialization.[8]

There are several SMs currently available, including Shield (Medtronic), X (Terumo NV), HEAL (Acandis), and hydrophilic polymer coating (HPC) (phenox GmbH).[9–12] Until now, SMs have not been evaluated in a comparative way, so their efficacy remains uncertain. Additionally, the recommendation to use SM FDs under the protection of DAPT remains in place; only SM p64-MW-HPC and p48-MW-HPC, if justified by individual circumstances, can be used under single antiplatelet treatment (SAPT) as noted in its instructions for use.

COATING (Coating to Optimize Aneurysm Treatment In the New Flow Diverter Generation) is the first randomized controlled trial (RCT) evaluating an SM FD. We compared the use of SM p64-MW-HPC under SAPT to the use of the bare p64-MW device under DAPT, which is the current clinical practice, in patients with unruptured IAs. This intermediate analysis presents the safety data at 1 month (1M).

## METHODS

### Study design, enrollment, and patient selection

COATING (ClinicalTrials.gov: NCT04870047) is an international, multicenter, prospective, RCT. It compares the safety and efficacy of SM p64-MW-HPC under SAPT (prasugrel or ticagrelor) with bare p64-MW under DAPT (aspirin plus prasugrel or ticagrelor). This study was approved by an Ethics Committee (CPP Sud Est III, France; Number: 2021–025 B).[13] The study protocol (online supplemental file 1), as well as data generated or analyzed during the study, is available from the corresponding author on request. The study was sponsored and financially supported by phenox GmbH.

The eligibility criteria are listed in online supplemental file 2. Subjects with an unruptured or recanalized aneurysm for which endovascular treatment (EVT) with an FD was indicated were enrolled in this trial once written informed consent had been obtained and eligibility confirmed. A total of 170 subjects were to be randomized in the trial, with the possibility to extend to 200 subjects after the interim power analysis.[13] The subjects were randomized (1:1 ratio) according to stratification by aneurysm location (proximal/distal). Proximal locations are internal carotid artery (ICA) extra-dural, ICA intra-dural (including ICA tip), and vertebro-basilar. Distal locations are anterior communicating artery (Acom)/anterior cerebral artery (ACA), pericallosal artery, middle cerebral artery (MCA), posterior inferior cerebellar artery, and posterior cerebral artery.

All participating investigators were required to have experience with FD and p64-MW (HPC) and were required to undergo training by performing three ‘lead-in cases’ supervised by an experienced proctor before participating in the study.

The trial is ongoing, collecting 1-year follow-up; this publication reports only on the primary trial endpoint and safety data up to 1M post-procedure.

### Study devices

The FDs bare p64-MW and SM p64-MW-HPC, collectively p64-MW (HPC), received the Conformité Européenne (Medical Device Directive; MDD CE mark) on 22 December 2019. The p64 MW (HPC) consists of 64 interwoven platinum-filled nitinol (nickel-titanium alloy) wires that facilitate the implant’s complete X-ray visibility. The device has an independent movable wire (MW) to support FD deployment. The HPC coating is designed to initially reduce the FD’s thrombogenicity.[14 15]

### Medication: antiplatelet regimen

Heparin use was recommended and administered according to the local procedure.

All patients received a P2Y12 inhibitor (prasugrel or ticagrelor, chosen according to the site’s standard of care) at least 12 hours pre-procedure and for an additional 6 months post-procedure. Patients randomized to the HPC/SAPT arm received a P2Y12 inhibitor only, and patients randomized to the bare/DAPT arm received a P2Y12 inhibitor and aspirin (online supplemental file 3).

Antiplatelet activity of prasugrel or ticagrelor was systematically tested in participants, and investigators had the ability to change the medication/dosage according to test results.

### Procedure

Pre-procedure, baseline neurological status was assessed using the modified Rankin Scale (mRS) and the National Institutes of Health Stroke Scale (NIHSS). During the procedure, the study device was advanced up to the cerebral circulation via standard access techniques (radial or femoral access) and implanted under general anesthesia. Coils, stents, or intrasaccular flow disruptors were permitted as adjunctive devices. FDs from other companies were not allowed. Angioplasty with a balloon or a stent was performed at the discretion of the investigator in case of poor wall apposition or incomplete opening of the FD.

### Follow-up assessments

A post-procedural diffusion-weighted imaging (DWI) 3T-MRI was performed after 48 hours (±24 hours) to evaluate the primary safety endpoint (online supplemental file 4).

At 1M (30 days (±7 days)), a neurological evaluation (including mRS and NIHSS) was performed via phone or in-person visit.

### Committees and safety monitoring

The blinded Core Lab consisting of three physicians (two readers and one adjudicator) independently assessed the primary endpoint based on pseudonymized (reduces the linkability of the imaging dataset to the identity of the patient) imaging.

Investigators reported all serious adverse events and adverse events of special interest (AESI) via a web-based electronic case report form. The following events were classified as AESI in the protocol: transient ischemic attack; stroke; thromboembolic events (TE); side branch occlusion; hemorrhagic events (HE); intrastent stenosis; and peripheral events (including groin hematoma requiring surgical or EVT and/or antiplatelet treatment (APT) modification, bleeding from the gastrointestinal tract, or other peripheral bleeding).

The Clinical Event Committee (CEC), which included three independent physicians with >10 years’ experience in the field of neuroradiology and neurology, adjudicated all investigator-reported events.

The Data Monitoring Committee (DMC) ensured study safety during an interim assessment after 85 patients were enrolled, followed by a safety review after 140 patients were enrolled. During the interim assessment, the total required sample size

was determined as 170. The DMC consisted of three physicians with expertise in the neuroradiology field and one statistician.

### Study endpoints

The primary endpoint was the absolute number of DWI lesions within 48 hours (±24 hours) of the index procedure visualized with 3T-MRI, assessed by the Core Lab in the treated aneurysm territory. In addition to DWI lesions, an ischemic stroke (irrespective of lesion size) was counted as one lesion.

Secondary safety endpoints reported in this analysis were the morbimortality rate 1M post-procedure. Cerebral TE and cerebral and peripheral HE are also analyzed. Other secondaruy endpoints are presented in

### Statistical analysis

The primary analyses were conducted in the intent-to-treat (ITT) population. ITT includes all randomized patients (excluding screening failures and randomized patients who withdrew their consent before procedure and for whom no data beyond the screening data could have been collected) assessed according to randomization assignment regardless of the treatment received. A secondary analysis was conducted on the per-protocol population (PPP), including randomized patients who met eligibility criteria with no major deviations and who had the primary endpoint assessments according to the protocol (ie, underwent treatment and received a DWI-MRI assessment with no major deviation to the 48 hours imaging timelines).

This study's primary hypothesis asserts the non-inferiority of the SM p64-MW-HPC FD under SAPT to the bare p64-MW FD under DAPT regarding the number of DWI lesions visualized by MRI 48 hours (±24 hours) after the index procedure.

All statistical analyses were performed using SAS Version 9.4 and SPSS (version 28.0).

For the primary endpoint analysis, non-inferiority was tested by using a Mann-Whitney U test after all DWI lesions 48 hours post-procedure were assessed by the Core Lab. The pre-specified non-inferiority margin was three lesions.

The secondary endpoints analysis, morbimortality rate at 1M, which was assessed by hierarchical approach in case the primary null hypothesis was rejected, used an exact two-sided binomial test to test for significant differences between the groups, not for non-inferiority or equality since the study was powered only for the primary endpoint. Additionally, the proportion of patients with TE and HE in both groups was compared using an exact two-sided binomial test.

Missing primary and secondary endpoints were imputed using multiple imputations with the fully conditional specification method with age and lesion location as covariates.

## RESULTS

Both ITT and PPP study populations showed similar results; therefore, this paper presents the ITT population only.

### Study population and aneurysm characteristics

From September 2021 to November 2024, 171 patients including 145 females (84.8%) were included in the COATING study in 15 centers in Europe and Israel, with 83 patients in the treatment arm (SM p64-MW-HPC under SAPT) and 88 patients in the control arm (bare p64-MW under DAPT) (figure 1).[16] Mean age was 55±11 years (range 27–83 years).

Most aneurysms were small (<10 mm; 139/171, 81.3%), had a wide neck (161/171, 94.2%), and were located at the ICA (133/171, 77.8%). Recanalized aneurysms were initially treated with coils (31/33, 93.9%), WEB (Woven EndoBridge) device (1/33, 3.0%), and both coils and WEB (1/33, 3.0%).

Baseline patient and aneurysm characteristics are described in table 1.

### Flow diversion procedure

Antiplatelet medications used before, during, and after the procedure (at hospital discharge), as well as the number of patients tested for antiplatelet activity and the results of testing, are shown in table 2. Ticagrelor and prasugrel were used preoperatively in 107/171 patients (62.6%) and 64/171 patients (37.4%), respectively. Tirofiban was used as a rescue treatment in seven patients (4.1%) with distal clot or slow flow in a covered branch.

There were five procedural failures (2.9%, 5/171): one in the HPC group (1.2%, 1/83) and four in the bare group (4.5%, 4/88). In three patients, failure was related to the complex vascular anatomy of the patient including one patient in the HPC group and two in the bare group. Two additional patients in the bare group were treated with non-investigational devices due to difficulty (twisting) during the deployment.

A total of 14 patients (8.2%) had two investigational devices implanted, with a higher proportion observed in the bare group (11.4%, 10/88) compared with the HPC group (4.8%, 4/83). Additional devices were used for target aneurysm treatment (12.0%, 10/83 HPC group; 19.3%, 17/88 bare group) and included coils (10.8%, 9/83 HPC group; 14.8%, 13/88 bare group) and an intrasaccular device in one patient (1.2%, 1/83 HPC group).

Angioplasty of the FD was performed in 19.3% (16/83) and 21.6% (19/88) of patients in the HPC and bare groups, respectively, with balloon in 15/83 (18.1%) and 18/88 (20.5%) in the HPC and bare groups, respectively, and with a stent in one patient in each group.

Additional procedural data are presented in .

### Number of DWI lesions (primary study endpoint) and patients with DWI lesions

All but one patient in the bare group had 48 hours MRI.

The mean (±SD) number of DWI lesions within 48 hours (±24 hours) of the index procedure visualized via MRI in the treated aneurysm territory was 6.0 (±13.28) in the HPC group and 5.3 (±11.75) in the bare group, with a median of 0 and 1 DWI lesion and the maximum number of 69 and 68 DWI lesions, respectively. Results of the Mann-Whitney U test showed that the number of DWI lesions in the HPC group was non-inferior to the bare group (P<0.0001).

The number of patients with DWI lesions in the treated aneurysm territory was similar in both groups (41/83 (49.4%) in the HPC group and 49/87 (56.3%) in the bare group).

### Morbimortality at 1 month

There was no mortality in either study arm.

Morbidity (defined as mRS 3–5) was not significantly (P=0.209) higher in the HPC group (4.8%) compared with the bare group (1.4%). In all patients, morbidity was related to TE complications.

### Thromboembolic events at 1 month

The rate of TE complications at 1M is shown in table 3. The rate of intra-procedural and post-procedural TE complications is similar in both HPC and bare groups.

Among the 19 TE complications occurring in 17/171 patients, six patients experienced seven TEs that were classified as major

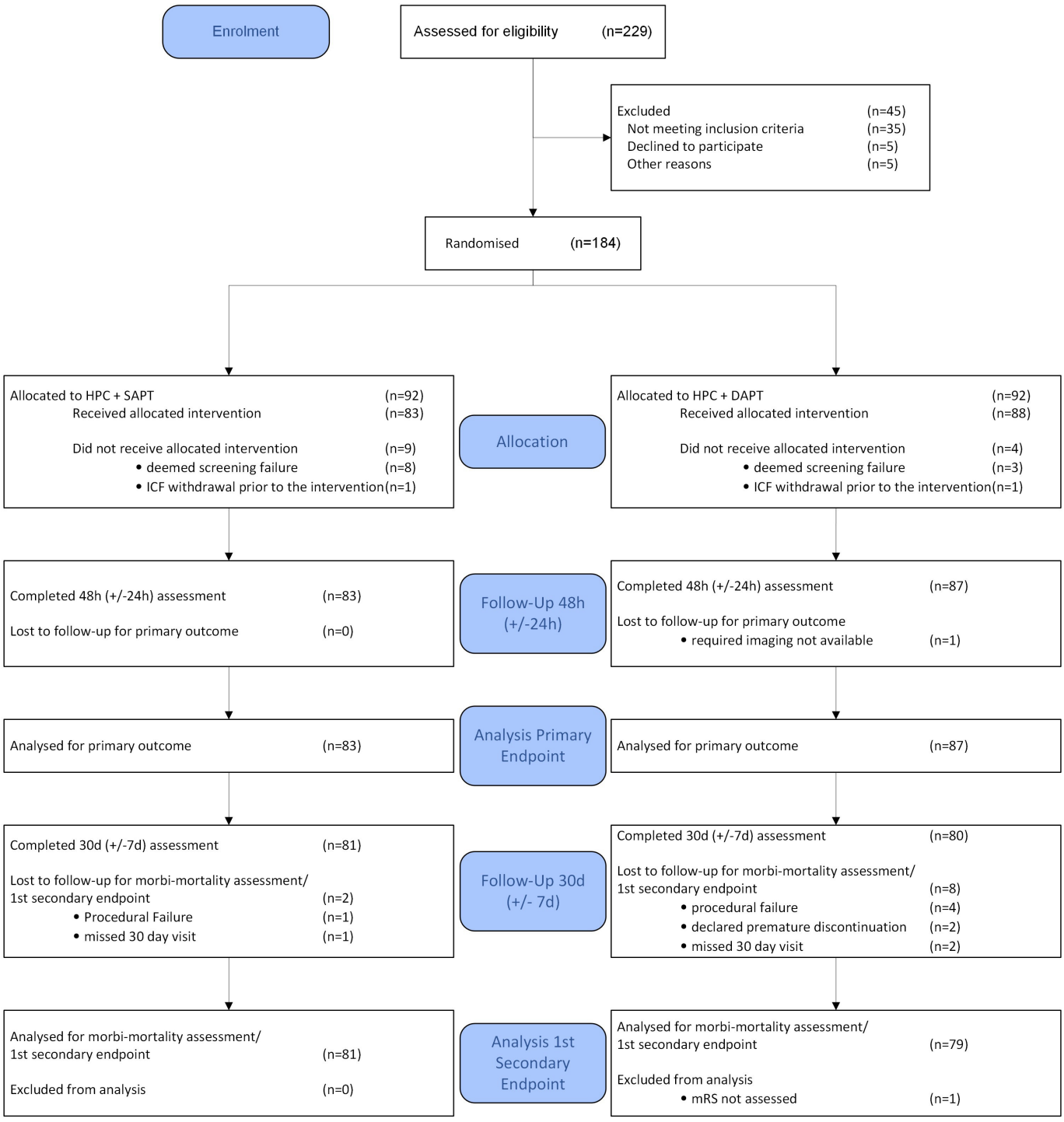


**Figure 1** Flow chart of the study. DAPT, dual antiplatelet treatment; HPC, hydrophilic polymer coating; ICF, informed consent form; mRS, modified Rankin Scale; SAPT, single antiplatelet treatment.

ischemic stroke (change in NIHSS of 4 points or more) by the CEC. Six TE complications occurred in five HPC group patients (6.0%). One patient had a distal clot in another arterial territory than where the investigational device was implanted during a control angiography with mRS 3 at 1M. One patient had an ischemic stroke with intra-stent thrombosis the day after not taking one dose of ticagrelor (14 days after the index procedure) with mRS 4 at 1M. One patient had an ischemic stroke related to the presence of a proximal fish mouthing of the FD associated with its partial clotting, which was treated with recombinant tissue plasminogen activator (r-tPA), intravenous aspirin, and low-molecular-weight heparin and subsequently had a hemorrhagic transformation (see below) with mRS 3 at 1M. This patient was left under aspirin only after the hemorrhagic complication. One patient treated under ticagrelor with an FD placed in the ICA had an intra-stent thrombosis 11 days after the index procedure leading to an mRS 5 at 1M. Finally, one patient suffered from an intra-procedural TE event (occlusion of a branch covered by the FD) without clinical worsening and a second TE event post-procedurally and had an mRS 1 at 1M. One patient in the bare group had a TE complication following the disconnection and migration of the platinum tip of the wire

**Table 1** Patient and aneurysm characteristics

| | p64-MW-HPC | p64-MW | Total |
|---|---|---|---|
| | SAPT | DAPT | n=171 |
| | n=83 | n=88 | |
| Patient characteristics | | | |
| Sex, n (%) | | | |
| Female | 68 (81.9) | 77 (87.5) | 145 (84.8) |
| Male | 15 (18.1) | 11 (12.5) | 26 (15.2) |
| Age (years) | | | |
| Global mean (SD) | 55 (12) | 56 (10) | 55 (11) |
| Range | 27–83 | 32–76 | 27–83 |
| Female mean (SD) | 56 (12) | 56 (10) | 56 (11) |
| Range | 27–83 | 32–76 | 27–83 |
| Male mean (SD) | 50 (11) | 55 (9) | 52 (10) |
| Range | 31–72 | 41–70 | 31–72 |
| Elevated blood pressure | 6 (7.2%) | 14 (15.9%) | 20 (11.7%) |
| n (%) | | | |
| Current smoking, n (%) | 27 (32.5%) | 32 (36.4%) | 59 (34.5%) |
| mRS score at baseline*, n (%) | | | |
| Grade 0 | 69 (83.1) | 65 (73.9) | 134 (78.4%) |
| Grade 1 | 10 (12.0) | 22 (25.0) | 32 (18.7) |
| Grade 2 | 1 (1.1) | 1 (1.2) | 2 (1.1) |
| Aneurysm characteristics | | | |
| Aneurysm size, n (%) | | | |
| <10 mm | 70 (84.3) | 69 (78.4) | 139 (81.3) |
| 10 mm to 25 mm | 12 (14.5) | 17 (19.3) | 29 (17.0) |
| >25 mm | 1 (1.2) | 2 (2.3%) | 3 (1.8) |
| Wide neck, n (%) | | | |
| n≥4 mm or D/N ratio <2 | 77 (82.8) | 84 (95.5) | 161 (94.2) |
| Aneurysm location†, n (%) | | | |
| ICA intradural/extradural | 63 (75.9) | 70 (79.5) | 133 (77.8) |
| ACA/Acom/pericallosal | 5 (6.0) | 9 (10.2) | 14 (8.2) |
| MCA | 6 (7.2) | 7 (8.0) | 13 (7.6) |
| VB | 9 (11.9) | 2 (2.3) | 11 (6.4) |
| Recanalized, n (%) | 19 (22.9) | 14 (15.0) | 33 (19.3) |

*1 missing data
†ICA
ACA, anterior cerebral artery; Acom, anterior communicating artery; DAPT, dual antiplatelet treatment; D/N, Dome-to-Neck; HPC, hydrophilic polymer coating; ICA, internal carotid artery; MCA, middle cerebral artery; mRS, modified Rankin Scale; MW, movable wire; SAPT, single antiplatelet treatment; VB, vertebrobasilar system (including basilar artery, posteroinferior cerebellar artery, and posterior cerebral artery).

of the FD in a lenticulostriate branch leading to a lacunar stroke with mRS 4 at 1M.

In addition to the patients who had in-stent thrombosis associated with major stroke (see above), one patient (in the HPC group) had an in-stent thrombosis occurring 2 days after the procedure (without symptoms and mRS 0 at 1M). Another patient had a partial FD clotting leading to a minor stroke 9 days after the index procedure (mRS 1 at 1M).

### Cerebral and peripheral hemorrhagic complications

Cerebral and peripheral hemorrhagic complication rates are shown in table 3.

**Table 2** Preoperative, procedural, and post-procedural antiplatelet treatment)

| | p64-MW-HPC | p64-MW | Total |
|---|---|---|---|
| | SAPT | DAPT | n=171 |
| | n=83 | n=88 | |
| Preoperative APT | | | |
| Aspirin | | | |
| Patients, n (%) | 0/83 (0.0) | 86/88 (97.7) | 87/171 (50.9) |
| Testing*, n (%) | 0/83 (0.0) | 68/86 (77.3) | 68/87 (78.2) |
| Responders, n (%) | 0/83 (0.0) | 64/68 (94.1) | 65/68 (95.6) |
| Duration (days), mean (SD) | – | 3 (5) | 3 (5) |
| Prasugrel | | | |
| Patients, n (%) | 35/83 (42.2) | 29/88 (33.0) | 64/171 (37.4%) |
| Testing†, n (%) | 35/35 (100.0) | 29/29 (100.0) | 64/64 (100.0%) |
| Responders, n (%) | 34/35 (97.1)‡ | 29/29 (100.0) | 63/64 (98.4%) |
| Duration (days), mean (SD) | 6 (3) | 5 (3) | 5 (3) |
| Ticagrelor | | | |
| Patients, n (%) | 49/83 (59.0)† | 58/88 (65.9) | 107/171 (62.6) |
| Testing§, n (%) | 44/49 (89.8) | 53/58 (91.4) | 97/107 (90.7) |
| Responders, n (%) | 44/44 (100.0) | 52/53 (98.1)¶ | 96/97 (99.0) |
| Duration (days), mean (SD) | 2 (4) | 2 (2) | 2 (3) |
| Intraoperative APT | | | |
| Aspirin, patients, n (%) | 3/83 (3.6)** | 88/88 (100.0) | 91/171 (53.2) |
| Prasugrel, patients, n (%) | 34/83 (41.0) | 29/88 (33.0) | 63/171 (36.8) |
| Ticagrelor, patients, n (%) | 49/83 (59.0) | 58/88 (65.9) | 107/171 (62.6) |
| APT at discharge | | | |
| Aspirin, patients, n (%) | 3/83 (3.6)†† | 88/88 (100.0) | 91/171 (53.2) |
| Prasugrel, patients, n (%) | 34/83 (41.0) | 29/88 (33.0) | 63/171 (36.8) |
| Ticagrelor, patients, n (%) | 48/83 (57.8) | 57/88 (64.8) | 105/171 (61.4) |

For 1 patient considered a procedural failure, the aneurysm was left untreated due to complex patient vessel anatomy: the P2Y12 inhibitor was replaced with ASA only.
*Aspirin testing was performed with VerifiNow in 54/68 patients, Multiplate in 21/68 patients, PFA (Platelet Function Assay) in 1 patient, and other in 3 patients (11 patients were tested with two tests).
†Prasugrel testing was performed with VerifiNow in 56/64 patients, Multiplate in 15/64 patients, and other in 2 patients (9 patients were tested with two tests).
‡1 patient was a non-responder to prasugrel, and medication was changed to ticagrelor.
§Ticagrelor testing was performed with VerifiNow in 70/97 patients, Multiplate in 31/97 patients, PFA in 5/97, and other in 1 patient (10 patients were tested with two tests).
¶1 patient was very close to the responder zone and APT was unchanged.
**3 patients received aspirin bolus on the day of procedure by mistake: a major deviation to APT regimen was registered for these patients.
††1 patient received aspirin for an ischemic stroke and 1 patient for a contrast media encephalopathy.
APT, antiplatelet treatment; DAPT, dual antiplatelet treatment; HPC, hydrophilic polymer coating; MW, movable wire; PFA, Platelet Function Analizer; SAPT, single antiplatelet treatment.

No hemorrhagic stroke (intraoperative rupture) occurred in either arm. One post-procedural hemorrhagic event occurred in an HPC group patient, who was treated with r-tPA, aspirin, and low-molecular-weight heparin for an ischemic stroke (see above). Two patients in the bare group had post-procedural HEs: subarachnoid hemorrhage in one and occurrence of microbleeds in another. APT was unchanged, and both patients had a good clinical outcome (mRS 0).

Table 3 Rate of patients with intra- and post-procedural thromboembolic and hemorrhagic complications (at 1 month)

| | p64-MW-HPC SAPT n=83 | p64-MW DAPT n=88 | Total n=171 | P value |
|---|---|---|---|---|
| Thromboembolic complications | | | | |
| Intra-procedural, n (%) | 3*/83 (3.6) | 3/88 (3.4) | 6/171 (3.5) | >0.9999 |
| Post-procedural, n (%) | 6*†/83 (7.2) | 6/88 (6.8) | 12/171 (7.0) | >0.9999 |
| Intracranial hemorrhagic complications | | | | |
| Intra-procedural, n (%) | 0/83 (0.0) | 0/88 (0.0) | 0/171 (0.0) | >0.9999 |
| Post-procedural, n (%) | 1/83 (1.2) | 2/88 (2.3) | 3/171 (1.8) | >0.9999 |
| Peripheral hemorrhagic complications | | | | |
| Post-procedural, n (%) | 0/83 (0.0) | 3/88 (3.4) | 3/171 (1.8) | 0.2462 |

*1 patient experienced one intra- and one post-procedural thromboembolic complication and is therefore captured twice in the table.
†1 patient experienced two minor thromboembolic complications in the post-procedural phase.
DAPT, dual antiplatelet treatment; HPC, hydrophilic polymer coating; MW, movable wire; SAPT, single antiplatelet treatment.

Three peripheral hemorrhagic complications occurred in the bare group (metrorrhagia, hematemesis, and epistaxis), while none was observed in the HPC group. No peripheral hemorrhagic complications were associated with clinical worsening.

## DISCUSSION

COATING is the first study to evaluate an SM FD in a randomized way. We compared surface-modified p64-MW-HPC under SAPT (prasugrel or ticagrelor) with bare p64-MW under DAPT (aspirin plus prasugrel or ticagrelor).[13] In this intermediate analysis dealing with the primary and secondary safety endpoints, the rate of DWI lesions on 48 hours MRI is similar in both groups: 6.0 in the HPC group and 5.3 in the bare group. Additionally, the percentage of patients presenting DWI lesions is similar in both groups (49.4% in the HPC group and 56.3% in the bare group) as are the rate of intra-procedural and post-procedural TE complications (HPC: 3.6% and 7.2%, respectively, and bare: 3.4% and 6.8%, respectively). No intra-procedural hemorrhagic complications were encountered in either group, and the rate of post-procedural cerebral hemorrhagic complications was similar (HPC 1.2% and bare 2.3%). No 1M mortality was encountered in either arm, and morbidity at 1M was slightly higher in the HPC group (4.8%) than in the bare group (1.4%), but not significantly (P=0.2087).

Even though the great efficacy of FDs has resulted in a high rate of complete aneurysm occlusion at 1 year and use has progressively expanded to distal and bifurcation aneurysms, FD use remains globally restricted to unruptured and recanalized aneurysms.[4] The restriction regarding FD use in ruptured aneurysms is primarily because patients must be treated under DAPT, which carries a high risk in the context of a recent bleeding. These observations have led to a search for options that will enable decreasing DAPT to SAPT, when treating an aneurysm with an FD. One option is to modify the FD surface to decrease the FD's thrombogenicity, which may also act in different ways by accelerating the formation of neointima and decreasing inflammatory reaction in the aneurysm and arterial wall.[6] Several SMs (Shield, X, Heal, HPC) are currently available, but their efficacy has been minimally evaluated primarily in retrospective single-center and multicenter studies.[9–12] HPC is an SM that has demonstrated good antithrombotic activity in vitro and in vivo, which is evaluated in COATING.[14 15] The optimal way to evaluate the effectiveness of an SM is to compare randomly the treatment with a bare FD. There are several possible designs for such studies. COATING aimed to demonstrate that patients did not experience more TE complications when using an SM FD under SAPT than a bare FD under DAPT.

A preliminary study using SM p48-MW-HPC in distal IAs under aspirin SAPT showed a high rate of TE complications.[17] Accordingly, antiplatelet medications used in COATING were P2Y12 antagonists, but as clopidogrel is associated in the cardiology literature with a high resistance rate (around 30%), two drugs were authorized in COATING: prasugrel and ticagrelor.[18]

Since the study's primary goal was to evaluate the rate of TE complications in both arms, the method selected to evaluate TE complications was crucial. In the literature, TE complications are usually defined as those occurring during the procedure or those revealed postoperatively by the occurrence of a neurological deficit and confirmed by CT or MRI. However, this methodology does not permit detection of all TE events because some distal clots occurring during the procedure and some silent TE events occurring after the procedure can be missed. To avoid this heterogeneity of reporting, one option is to use DWI-MRI. This highly sensitive sequence depicts ischemic stroke, whatever its mechanism, size, and location, and offers a more objective way to analyze and quantify the thromboembolic phenomenon.[19 20] Depicted lesions correspond to all TE that may occur during any procedure step: cervical artery(ies) catheterization; intermediate catheter placement, if any; aneurysm territory super selective catheterization; FD deployment; or FD angioplasty, if any. Furthermore, if the SM in combination with the reduced APT induces TE events, DWI-MRI will depict these events. Interestingly, the relatively high incidence of DWI lesions after FD implantation allows a smaller sample size, which is not the case if only symptomatic TE events occurring during or after the procedure are analyzed.[19 20]

The different parameters evaluated in COATING (DWI-MRI or event occurring during the procedure or in the following month) show that the placement of an HPC FD under SAPT with prasugrel or ticagrelor is not associated with a higher rate of TE complications at 1M. From a clinical point of view, no deaths occurred in either arm until 1M after the index procedure. Morbidity (exclusively related to TE complications) was also similar in the HPC group and in the bare group. In fact, in some patients, the TE complication was not directly related to the use of SM under SAPT, but to other causes such as a lack of APT compliance. This was previously reported in a large series of patients treated with HPC FDs under prasugrel SAPT, in which the TE complications in three patients were related to a problem with APT compliance.[12]

Following this study, the next step will be the comparative analysis of safety and anatomical results at 12 months, which will determine if the rate of late (post 1M) thromboembolic and hemorrhagic complications differs between arms. The 12-month results will also reveal whether SM impacts the rate of complete aneurysm occlusion at 12 months. Finally, this follow-up study will also verify if SM has some impact on the occurrence of in-stent stenosis. These data will be important to confirm HPC SM effectiveness.

### Limitations

The main study limitation is that the primary endpoint is not a clinical outcome, but relies on brain imaging (DWI-MRI). As previously discussed, DWI-MRI provides a more objective and quantitative evaluation of TE. And, as the number of DWI lesions is higher compared with the number of clinical events, the use of this endpoint facilitates a more feasible study population sample. This limitation is counterbalanced by the fact that several secondary clinical endpoints were analyzed and reported.

## CONCLUSION

HPC is the first SM evaluated by directly comparing TE events under different antiplatelet regimens (SAPT for SM p64-MW-HPC and DAPT for bare p64-MW). The 1M safety results of COATING show non-inferiority in the number of DWI lesions in patients treated with SM p64-MW-HPC under SAPT and those treated with bare p64-MW under DAPT. Similarly, the rate of morbimortality and cerebral TE and HE were similar in both groups.

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