ENGINEERING STROKE SOLUTIONS

Summary of Safety and Clinical Performance:

DERIVO® Embolisation Device

DERIVO® mini Embolisation Device

Acandis GmbH

Summary of Safety and Clinical Performance according to Medical Device Regulation (MDR) EU 2017/745

Identifier: 2902

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1 Information for the professional user

This Summary of Safety and Clinical Performance (SSCP) is intended to provide public access to an updated summary of the main aspects of the safety and clinical performance of the DERIVO Embolisation Device and the DERIVO mini Embolisation Device (in the following referred to as “DERIVO” and “DERIVO mini”.

The SSCP is prepared in accordance with the Medical Device Regulation (EU) 2017/745 (MDR) and the document MDCG 2019-9, Rev.1 from March 2022.

The SSCP is not intended to replace the instructions for use (IFU) as the main document to ensure the safe use of the DERIVO and DERIVO mini, nor is it intended to provide diagnostic or therapeutic suggestions to intended users or patients.

The information provided in chapter 1 is intended for users/healthcare professionals.
In addition to this, there is a summary intended for patients provided in chapter 2.

1.1 Device identification and general information

Device trade name(s)	– **DERIVO® Embolisation Device** (Article no. 01-000350 – 01-000375 and 01-000408 – 01-000415) – **DERIVO® mini Embolisation Device** (Article no. 01-000416 – 01-000433)
Manufacturer’s name and address	Acandis GmbH, Theodor-Fahrner-Straße 6, 75177 Pforzheim, Germany
Manufacturer’s single registration number (SRN)	DE-MF-000006259
Basic UDI-DI	DERIVO: 426065033DERIVO4Q DERIVO mini: 426065033DERIVOminiCS
Medical device nomenclature	– EMDN: C010402020380 Embolisation Devices - Accessories – UMDNS: 17-461 Stents, vascular – GMDN: 46352 Bare-metal intracranial vascular stent
Class of device	Class III medical device, as defined in Medical Device Regulation (MDR) EU 2017/745, Annex VIII, rule 8
Year of first CE certificate	DERIVO: on the European market since October 2013 DERIVO mini: on the European market since November 2018
Authorized representative	not applicable
Notified body	DQS Medizinprodukte GmbH (Notified body number: 0297)

1.2 Intended use of the device

Intended purpose	The DERIVO Embolisation Device is intended for the treatment of intracranial aneurysms by diverting the blood flow in the aneurysm-bearing vessel.
Indication(s)	The DERIVO Embolisation Device is intended for the treatment of intracranial aneurysms which cannot be treated with other endovascular techniques or in which other endovascular or neurosurgical techniques present a higher treatment risk.

Targeted population(s)	Intended user: The DERIVO Embolisation Device should only be used by physicians who have the required background knowledge and experience in the field of interventional neuroradiology and the treatment of IAs.
	Patient target group: No specific patient populations have been defined but patients with contraindications are to be excluded.
Contra-indications and/or limitations	Implantation is contraindicated in the following patients: – Patients with the size of the aneurysm and/or the size of the vessel carrying the aneurysm is not within the indicated range – Patients in whom anti-platelet therapy and/or anticoagulant therapy is contraindicated – Patients who present in the angiography with anatomical conditions unsuitable for endovascular treatment due to severe vessel tortuosity or stenosis – Patients in the acute phase after subarachnoid hemorrhage – Patients with an active bacterial infection – Patients with an acutely ruptured aneurysm should not be treated with the DERIVO Embolisation Device alone – Patients who were not pretreated with anti-platelet agents before the procedure. – Patients who are hypersensitive to nickel-titanium. No limitations are mentioned in the IFU.

1.3 Device description

1.3.1 Description of the DERIVO and DERIVO mini

The DERIVO and DERIVO mini are a self-expanding, fully radiopaque devices, with Nitinol wire braiding with a platinum core. The device has three radiopaque platinum/iridium markers each at the distal and proximal ends and is preloaded on a transport wire in an introducer. The DERIVO is designed to be introduced through a microcatheter with an inner diameter of 0.027". The DERIVO mini is designed to be introduced through a 0. 021" microcatheter. The DERIVO and DERIVO mini are implanted for life.

The DERIVO stent family is designed with proximal and distal flared ends for secure vessel wall apposition. The transport is designed with or without tip.

Sizes DERIVO	Ø 3.5 / 4.0 / 4.5 / 5.0 / 5.5 / 6.0, lengths: 15 / 20 / 25 / 30 / 40 / 50 mm
Sizes DERIVO mini	Ø 2.5 / 3.0 / 3.5 mm, lengths: 15 / 20 / 25 mm
Sterility	Yes, for single-use
Generic device group	Intracranial neurovascular stent, self-expandable
MR conditional	up to 3 Tesla acc. ASTM F2052, F2213, F2119, F2182
Foreshortening	≤ 72 %
Stent surface area	< 49.5 %

The implant is transferred into the microcatheter and is guided to the aneurysm/target zone with the corresponding transport wire. The implant will be deployed by pushing the transport

wire in the microcatheter while simultaneously holding the microcatheter in the vessel center. The stent expands by an elastic restoring force. After expansion, the implant covers the complete neck of the aneurysm. The implant is used as a flow diverter.

1.3.2 Previous generations

There have been no previous device generations. The DERIVO has been on the European market since October 2013 and the DERIVO mini since November 2018.

1.3.3 Accessories

Microcatheters with inner diameters of 0.027” (3F) or 0.021” (2.5F).
The NeuroSlider® DLC is the only microcatheter which was tested for compatibility.

1.3.4 Combination with other devices

DERIVO and DERIVO mini are used in combination with microcatheters and medical devices for neurovascular angiography. The physician decides individually whether embolization material is required.

1.4 Risks and warnings

1.4.1 Residual risks and undesirable effects

Possible complications, among others, include the following:

- General complications in connection with endovascular and/or angiographic treatments (e.g. (Pseudo)aneurysm, rupture of or bleeding from aneurysm, (intracerebral) hemorrhage, embolism (air, foreign body, plaque or thrombus), fever, vessel dissection, vessel perforation, vessel rupture, vessel stenosis, (Abrupt) vessel occlusion or thrombosis, Infection, (Cerebral) ischemia/infarction, secondary hemorrhage, reactions due to radiation exposure, subarachnoid hemorrhage, thromboembolic event/stroke, vasospasm, intoxication.
- General complications in connection with thrombocyte aggregation inhibitors/anticoagulants, anesthetics and contrast agents (e.g. renal insufficiency).
- Complications in connection with vessel entry (e.g. hematoma or bleeding at puncture site, pain and/or infection at puncture site)
- Possible problems during device delivery/implantation (e.g. device breakage, device folding, incorrect device placement, device cannot be released, device cannot be drawn back into catheter, device bending, device does not detach from transport wire,

device migration, insufficient opening, delayed treatment, target area inaccessible or cannot be accessed safely, additional stenting required)

- Other complications in connection with the device (e.g. allergic reactions to the device material, device occlusion/thrombosis, in-stent stenosis, perforator infarction, reoperation, incomplete aneurysm occlusion, occlusion of perforators or branching vessels)
- Neurological deficits (e.g. dysphasia, hemiparesis, hemiplegia, impaired vision, oculomotor paresis, speech disorders)
- Death

From the systematic review of the scientific literature and DERIVO post-market clinical follow-up (PMCF) measures, quantitative data on the occurrence of complications with the DERIVO and DERIVO mini could be obtained. For the following complications a statistical analysis in form of a pooled proportion analysis (random effects model) was feasible and yielded the following results concerning the complications' occurrence frequencies:

Technical problems:	7.20 % [95 % CI: 2.28 – 14.07]
Thromboembolic and ischemic events:	6.27 % [95 % CI: 2.82 – 10.73]
Procedure-related morbidity:	2.92 % [95 % CI: 1.81 – 4.22]
Procedure-related mortality:	0.89 % [95 % CI: 0.07 – 2.28]
Aneurysm rupture and bleeding/re-bleeding:	0.01 % [95 % CI: 0.00 – 0.32]
Procedure-related complications:	0.00 % [95 % CI: 0.00 – 0.18]
Angiography-related complications, i.e., arterial spams:	0.00 % [95 % CI: 0.00 – 0.30]

1.4.2 Warnings, precautions and cautions

Warnings

- The DERIVO Embolisation Device should be applied only by physicians who have the necessary background knowledge and experience in the field of interventional neuroradiology and have the required expertise in the treatment of intracranial aneurysms.
- No specific patient populations have been defined but patients with contraindications are to be excluded.
- Before use, the product needs to be carefully checked to ensure there is no transportation damage. Under no circumstances should damaged or kinked components be used.
- On no account whatsoever should you continue advancing the device if you encounter

- resistance without first finding out the cause as otherwise you could damage the device or perforate a vessel.
- The device shortens during deployment.
- The product may only be used for the intended purpose. Any use of the product for other purposes (off-label use) may lead to a deterioration in the patient's state of health or even their death.

Precautions

- The product is provided sterile and for single use only.
- In case of damage to the sterile barrier, the system must not be used. If any damage is visible, please contact your Acandis representative.
- Do not use the product after the expiration date printed on the label.
- Do not reuse, reprocess or re-sterilize. Reuse, reprocessing or re-sterilization may compromise structural integrity of the device and/or lead to device failure that, in turn, may result in complications, patient injury or death. Reuse, reprocessing or re-sterilizing the device also increases the risk of contamination of the device and/or causes patient infection or cross-infection, including, but not limited to, the transmission of infectious disease(s) from one patient to another. Contamination of the device may lead to injury, illness or death of the patient.
- The performance of a responder test is recommended to reduce the risk of complications. For this purpose, the efficacy of the antiplatelet agent is tested prior to application of the product.
- In order to minimize potential complications during and after the intervention, attention should be paid to careful medication treatment in accordance with the current guidelines from the medical societies (antiplatelet agent and anticoagulant therapy prior to treatment and anticoagulants during the intervention). The administration of unsuitable antiplatelet agents and anticoagulants may lead to device thrombosis.
- The medication is an important part of the treatment. Patients must be advised to take medication regularly and informed of potential risks of non-compliance.

Cautions

- Use of the DERIVO Embolisation Device has not been tested in combination with any other medicinal auxiliary products. Special care is required when using auxiliary products and the manufacturer's instructions for use must be observed in each case!
- When using further embolisation materials that are inserted via an additional microcatheter enclosed between the implanted DERIVO Embolisation Device and the vessel wall (jailing procedure), attention must be paid to ensuring that the additional microcatheter is

removed carefully and that the implant is not moved. In such a case, it may be advisable to position the microcatheter with which the DERIVO Embolisation Device was inserted distally to the implant and thus ensure access to the same!

1.4.3 Other relevant aspects of safety

The DERIVO has been on the market since 2013 and the DERIVO mini since November 2018.
DERIVO: According to the periodic safety update report (PSUR), the complaint rate is 1.62 % within the last four years, and the total complaint rate since first market approval is 1.79 %.
The incident rate within the last four years is 0.72 / 0.23 / 0 / 0 %.
DERIVO mini: According to the periodic safety update report (PSUR), the complaint rate is 1.55 % within the last four years, and the total complaint rate since first market approval is 1.19 %. The incident rate within the last four years is 0.40 / 0.25 / 0 / 0.26 %.
The incidents (reportable events) could be reduced by user trainings with advanced simulation technologies. There were no recalls, FSNs or FSCAs for neither device.
There were also no relevant hits on unduly or unknown risks of the DERIVO in the databases of competent authorities.

1.5 Summary of clinical evaluation and post-market clinical follow-up (PMCF)

1.5.1 Summary of clinical data related to equivalent devices

No clinical data of equivalent devices from the same or other manufacturers were used for the clinical evaluation.

Acandis added the DERIVO mini with additional smaller diameters of 2.5 and 3.0 mm to provide adequate treatment for patients with small intracranial vessel diameters.
The DERIVO and DERIVO mini have an identical clinical application, principle of operation and material. Together, technical differences between the devices do not have a clinical impact.
Consequently, clinical data on either of the devices are sufficient to proof clinical safety and performance of both. Hence, clinical data are interchangeable. Thus, the clinical evaluation was conducted by pooling the clinical data of the different variants and evaluating them together.

1.5.2 Summary of clinical data from conducted investigations of the device before CE-marking

No clinical data from proprietary investigations before CE-marking are available.

1.5.3 Summary of clinical data from other sources

1.5.3.1.1 Meta-Analyses and Systematic Reviews

Newer flow diverters are enhanced with anti-thrombogenic surface modifications like the Pipeline Embolization Device with Shield Technology (SPED) and the Derivo Embolisation Device (DED) and are purported to facilitate deployment and reduce ischemic events (Li YL et al., 2021). Li and colleagues reviewed the safety and efficacy of the SPED and the DED in treating patients with cerebral aneurysms. Subgroup analysis was performed for the type of FD (DED versus SPED) for all outcomes. Eight single-arm case series involving 911 patients and 1,060 aneurysms were included. Four of which studied the DED and 4 the SPED. A total of 1,086 flow diverters were placed (1.02 per aneurysm), of which 455 were DED (41.9 %) and 631 were SPED (58.1 %). The overall technical success rate for device placement was 99.6 % (95 % CI: 98.6 % – 99.8 %) with no significant difference between DED and SPED (p = 0.33)., Among cases of technical failure, five cases of improper DED expansion were seen and solved by angioplasty, device substitution, and placement of an additional overlapping stent. The overall median follow-up interval was 8.24 months. Imaging data were available for 825 (90.6 %) and 231 (25.4 %) patients at 6- and 12-month follow-up, respectively. The overall pooled aneurysm occlusion rates at 6 and 12 months were 80.5 % (95 % CI: 74.5 % – 86.0 %) and 85.6 % (95 % CI, 80.6 %–90.0 %), respectively, with no significant difference between DED and SPED (p = 0.42 and p = 0.33). The overall pooled morbidity and mortality rates were 6.0 % (95 % CI: 4.5 %–7.7 %) and 1.0 % (95 % CI: 0.3 – 1.9 %), respectively, with no significant difference between DED and SPED (p = 0.73 and p = 0.41). Among the 10 deaths, 7 were related to early and late rebleeding, one patient died of perforation in DED-assisted coiling, and 1 patient died of stent occlusion from self-discontinuation of anti-platelets shortly after the operation. The cause of death in one case was not specified. The overall pooled ischemic and serious ischemic event rates were 6.7 % (95 % CI: 4.1 %–10.1 %) and 1.8 % (95 % CI, 0.8 %–3.0 %), respectively, with no significant difference between DED and SPED (p = 0.55 and p = 0.24).

Table 1: Overview of meta-analysis results (source: Li YL et al., 2021)

	Overall	DED	SPED	Intergroup Heterogeneity
Efficacy outcomes				
Technical success	99.6% (98.6%–99.8%) $I^2 = 33.0\%$ $P = .165$	100% (99.2%–100%) $I^2 = 0.00\%$ $P = .487$	99.2% (97.2%–100%) $I^2 = 54.4\%$ $P = .087$	$P = .165$
Aneurysm occlusion rate (6 mo)	80.5%[b] (74.5%–86.0%) $I^2 = 70.8\%$ $P = .000$	78.9% (74.3%–83.1%) $I^2 = 0.00\%$ $P = .559$	82.7%[b] (73.4%–90.4%) $I^2 = 75.3\%$ $P = .000$	$P = .420$
Aneurysm occlusion rate (12 mo)	85.6% (80.6%–90.0%) $I^2 = 0.00\%$ $P = .744$	87.8% (80.9%–93.5%) NA	83.2% (75.8%–89.6%) NA	$P = .329$
Safety outcomes				
Mortality rate	1.0% (0.3%–1.9%) $I^2 = 0.00\%$ $P = .608$	1.3% (0.2%–3.1%) $I^2 = 5.47\%$ $P = .366$	0.8% (0.1%–1.9%) $I^2 = 0.00\%$ $P = .675$	$P = .410$
Morbidity rate	6.0% (4.5%–7.7%) $I^2 = 0.00\%$ $P = .857$	6.3% (3.9%–9.1%) $I^2 = 0.00\%$ $P = .618$	5.8% (3.9%–8.1%) $I^2 = 0.00\%$ $P = .710$	$P = .725$
Total ischemia rate	6.7%[b] (4.1%–10.1%) $I^2 = 61.9\%$ $P = .010$	8.3%[b] (2.9%–15.7%) $I^2 = 75.1\%$ $P = .007$	6.3% (3.2%–10.2%) $I^2 = 50.1\%$ $P = .111$	$P = .548$
Serious ischemia rate	1.8% (0.8%–3.0%) $I^2 = 12.1\%$ $P = .335$	2.5% (1.0%–4.6%) $I^2 = 0.00\%$ $P = .685$	1.2% (0.1%–3.2%) $I^2 = 37.0\%$ $P = .190$	$P = .240$

Note:—NA indicates not applicable.

[a] Table shows pooled point estimate, 95% confidence intervals, heterogeneity (I^2 statistic and P value for the Cochrane Q test) and intergroup heterogeneity for all outcomes of the meta-analysis.

[b] Significant heterogeneity.

The authors concluded that surface-modified flow diverters appear as efficacious in closing aneurysms as older FDs and coiling in the early- and midterm outcomes. A uniformly high technical success rate is reported for both SPED and DED. Lower mortality and serious ischemic events are observed compared with previous meta-analyses on older FDs. No significant difference was demonstrated between the SPED and DED. The results may better apply to small, unruptured saccular aneurysms in the anterior circulation. The long-term clinical outcomes of these devices remain to be seen. Larger scale prospective studies with a standardized DAPT regimen; follow-up protocol; and more detailed reporting of patient, aneurysm, and treatment characteristics can permit further analysis to identify the best fit patients for these newer devices and predict treatment failure (Li YL et al., 2021).

Monteiro and colleagues performed a systematic review of pertinent literature, aiming to evaluate the DED's effectiveness and safety (Monteiro A et al., 2021). Five studies comprising 481 aneurysms, of which twenty-six (5.4 %) were ruptured, were included. The studies were conducted in Turkey (Akgul), Brazil, Germany, Poland, and Italy; two were prospective and three were retrospective. The length of angiographic follow-up ranged from 9 to 18 months. Most procedures were uneventful with respect to the technical aspects. Device-related technical issues experienced during the procedures included fish-mouthing, twisting, migration, opening issues, and failure of delivery through the microcatheter. These instances occurred in 37 (7.7 %) of the procedures. Balloon remodeling was performed in 12.7 %. The rate of peri-procedural ischemic and hemorrhagic complications was 4.9 % (95 %: CI: 2.9 % - 7 %). The overall mortality rate was 2.1 % (95 % CI: 0.4 % - 3.9%). The rate of complete occlusion was 81.4 % (95 % CI: 71.3 % - 91.5 %). Of note, adjunctive coiling was used in 25.6 % (95 % CI: 11.4 % - 39.8 %) of aneurysms. Low rates of peri-procedural complications and mortality and a high rate of complete occlusion were identified, which were comparable to rates associated with other available FDs (Monteiro A et al., 2021)

Table 2: Overview of meta-analysis results (source: Li YL et al., 2021)

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Efficacy outcomes				
Technical success	99.6% (98.6%–99.8%) $I^2 = 33.0\%$ $P = .165$	100% (99.2%–100%) $I^2 = 0.00\%$ $P = .487$	99.2% (97.2%–100%) $I^2 = 54.4\%$ $P = .087$	$P = .165$
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1.5.3.1.2 Randomized controlled trials, clinical studies and case series

Table 3: Summary of publications including the use of the DERIVO by Piano M et al., 2021, Mahajan NP et al., 2021; Daglioglu E et al., 2020, Taschner CA et al., 2020 and Trivelato FP et al., 2019. Abbreviations: AEs, adverse events; DED, DERIVO Embolisation Device/System; FD, flow diverter; FDD, flow diverter devices; ICA, internal carotid artery; MAE, mild adverse events with clinical relevance, transient; PTA, percutaneous transluminal angioplasty; SAE: severe adverse events, permanent, SAH: subarachnoid hemorrhage.

Publication [Author, title]	**Piano M et al., 2021** Long-term follow-up of the DERIVO® Embolisation Device (DED®) for intracranial aneurysms [Italian Multicentric Registry]	**Mahajan NP et al., 2021** Retrospective Multicenter Indian Study of DERIVO Embolisation Device (REMIND): Periprocedural Safety	**Daglioglu E et al., 2020** The Experience of the DERIVO® Embolisation Device in Intracranial Aneurysms [Turkish registry]	**Taschner CA et al., 2020** DERIVO embolization device in the treatment of unruptured intracranial aneurysms [German multicenter study]	**Trivelato FP et al., 2019** DERIVO Embolisation Device for the Treatment of Intracranial Aneurysms [Brazilian multicenter study]
Study characteristics					
Study type	observational	retrospective	retrospective	prospective	prospective
Included patient number [female / male / mean age]	108 [88 / 20 / 56 years]	96 [56 / 40 / 60]	146 [96 / 50 / 51.5 years]	96 [71 / 25 / 54 years]	146 [121 / 25 / 55.3 years]
Number of treated aneurysms	109	106	182	96	183
Used device	DERIVO Embolisation Device/System				
Aneurysm characteristics					
Ratio unruptured / ruptured aneurysms	100 (91.7 %) / 9 (8.3 %)	88 (83 %) / 18 (17 %)	100 (55 %) / 46 (45 %)	96 (100 %) / 0 (0 %)	177 (96.7 %) / 6 (3.3 %)
Localization of aneurysms	anterior circulation: 89 (81.7 %) posterior circulation: 20 (18.3 %)	anterior circulation: 98 (92.5 %) posterior circulation: 8 (7.5 %)	anterior circulation: 170 (93.4 %) posterior circulation: 12 (6.6 %)	anterior circulation: 84 (88 %) posterior circulation: 12 (12 %)	anterior circulation: 166 (90.7 %) posterior circulation: 17 (9.3 %)
Aneurysm morphology	saccular: 90 (82.6 %) fusiform/dissecting: 14 (12.8 %) blister-like: 5 (4.6 %)	blister: 6 (5.7 %) dissecting: 6 (5.7 %) fusiform: 10 (9.4 %) saccular: 84 (79.2 %)	saccular: 162 (89 %) other morphologies: 20 (11 %)	saccular: 77 (80 %) fusiform/dissecting:1 9 (20 %)	blister: 1 (0.5 %) dissecting: 11 (6 %) fusiform: 13 (7.1 %) saccular: 158 (86.3 %)
Aneurysm size	< 10 mm: 44 (40.4 %) 10 – 25 mm: 49 (45 %) > 25 mm: 11 (10.1 %)	mean: 9.8 ± 8.2 mm range: 1 – 35 mm average neck size, 6.9±8.5 mm; wide-necked (>4 mm), 63 (59.4%); giant (>25 mm), 8 (7.5%)	8.3 mm (mean, range 2 – 28 mm) < 10 mm: 124 (68.1 %) 10 – 25 mm: 50 (27.5 %) > 25 mm: 8 (4.4 %)	14.2 mm (mean, ± 16.9) < 5 mm: 14 (15 %) 5 – 9.9 mm: 36 (37 %) 10 – 20 mm: 33 (34 %) > 20mm: 13 (14 %)	6.7 mm (mean, ± 5.1 mm) small: 152 (83.1 %) large: 28 (15.3 %) giant: 3 (1.6 %)

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Effectiveness end point/ clinical success					
Complete aneurysm occlusion [final follow-up]	66/88 (75 %) [18 months]	-	115/146 (78.7 %) [7 months in mean]	73/89 (82 %) [12.4 ± 5.84 months]	74/83 (89.2 %) [12 months]
Safety end points					
Mortality (total)	6.5 %	0 %	2.7 %	0 %	1.4 %
Mortality (brief description of the occurrences)	4 in the 30-day peri-procedural period (2 died for clinical complications related to the SAH / 2 died because of respiratory complications) 3 in the postprocedural period (1 with SAH treated acutely died after 2 months despite treatment / 1 with a giant aneurysm of the left PICA causing a huge brainstem edema, died after three months despite treatment / 1 died after 4 months for sepsis after lower limb amputation) **DED-related: 0 %**	-	1 perforation of aneurysm during DED-assisted coiling 1 DED occlusion that led to cerebral infarction	-	1 DED-related thrombosis (after 4 days: self-discontinuation of antiplatelets) 1 giant, ruptured aneurysm (after 5 days)
Morbidity (total)	5.5 %	1 %	3.4 %	3.1 %	4.1 %
Morbidity (SAE + MAE; brief description of the occurrences)	**SAE: 1.8 %** (1 rupture of aneurysm occurred the day after the procedure / 1 accidental vessel perforation by the micro-wire caused a massive SAH). **MAE: 3.7 %** (1 in the 30-day peri-procedural period, represented by a transient loss of visibility due to medium contrast / 3 in the postprocedural period / 1 case of cerebral	1 stent thrombosis followed by MCA territory infarction.	5 thromboembolic events (1 middle cerebral artery aneurysm, 3 ICA aneurysm, 1 basilar artery aneurysm) including perforator infarctions	**Major stroke: 4.2 %** 2 related to prox. Occlusion of DED / 2 in-stent thrombosis **Minor stroke: 2 %** 1 related to temporal hemorrhage 1 caused by multiple embolic infarcts	2 major ischemic strokes / 2 TIA / 1 intracerebral hemorrhage / 1 increase of mass effect **FD-related:** 4 thromboembolic events (2.6 %) Other neurological and systemic peri-operative AEs: 1 asymptomatic intracranial bleeding

Publication [Author, title]	**Piano M et al., 2021** Long-term follow-up of the DERIVO® Embolisation Device (DED®) for intracranial aneurysms [Italian Multicentric Registry]	**Mahajan NP et al., 2021** Retrospective Multicenter Indian Study of DERIVO Embolisation Device (REMIND): Periprocedural Safety	**Daglioglu E et al., 2020** The Experience of the DERIVO® Embolisation Device in Intracranial Aneurysms [Turkish registry]	**Taschner CA et al., 2020** DERIVO embolization device in the treatment of unruptured intracra-nial aneurysms [German multicenter study]	**Trivelato FP et al., 2019** DERIVO Embolisation Device for the Treatment of Intracranial Aneurysms [Brazilian multicenter study]
	edema caused by aneurysm thrombosis / 1 case of TIA / 1 case of worsening of a pre-existing ptosis and diplopia, caused by the increasing volume of a giant PcomA aneurysm (and thus due to ineffectiveness of flow diversion).**DED®-related: 4.6 %** (2 SAE and 3 MAE)				related to vessel perfo-ration during an exchange maneuver / 2 retro-peritoneal hemorrhages **Acute/delayed thromboembolic complications:** 3.4 % **Periprocedural complications:** 7.3 % **Adverse events:** 5.5 % (morbidity + mortality)
Technical notes / periprocedural complications					
Technical notes / periprocedural complications	1.8 % technical failures due to inappropriate deployment of the proximal segment inside the aneurysmal sac (1 aneurysm was occluded with coils in a separate session / 1 FD was pushed inside the sac and the parent artery was occluded with coils)	1 device fish-mouthing occurred in a middle-aged patient who had a ruptured dissecting middle cerebral artery aneurysm with subarachnoid hemorrhage. 1 missed landing zone 1 device migration	2 cases of technical failure: inability to reach target vessel segment, but not FD-related	19 % PTA after FD placement (18/96) 2 % (2/96) FD could not be delivered through MC 3 % (3/96) FD did not open 1 % (1/96) FD twisted 6 % (6/96)FD displaced 11.5 % (11/96) prox. Fish mouthing 1 % ICA dissection	1.3 % (2/183) DED: Twisting that lead to no deployment 2.7 % (5/183) improper DED expansion that needs to be resolved with PTA (1.3 %) 20.5 % (37/183) PTA for better wall apposition was performed 82 % deployment without need for resheathing/ repositioning
Overall conclusion					
Overall conclusion according to the authors of the study	The endovascular treatment with the DERIVO device is a safe and effective option for the treatment of intracranial aneurysm, with a high occlusion rate and safety profile comparable to the other FDDs in use.	The DED Is a newer generation flow diverter stent with low peri-procedural complication rates. Though the construct of the device comes with a promise for better results, larger prospective studies with longer follow-ups, especially with a comparison with other available	The DED device is a new-generation flow diverter with excellent opening behavior and navigational benefits. The results indicated a safe aneurysm occlusion with optimum morbidity and mortality values	DED is a safe and effective treatment for unruptured aneurysms with high rates of satisfactory occlusion and comparably low rates of permanent neurological morbidity and mortality.	The DERIVO Embolization Device is a safe and effective treatment for intracranial aneurysms.

Publication [Author, title]	**Piano M et al., 2021** Long-term follow-up of the DERIVO® Embolisation Device (DED®) for intracranial aneurysms [Italian Multicentric Registry]	**Mahajan NP et al., 2021** Retrospective Multicenter Indian Study of DERIVO Embolisation Device (REMIND): Periprocedural Safety	**Daglioglu E et al., 2020** The Experience of the DERIVO® Embolisation Device in Intracranial Aneurysms [Turkish registry]	**Taschner CA et al., 2020** DERIVO embolization device in the treatment of unruptured intracranial aneurysms [German multicenter study]	**Trivelato FP et al., 2019** DERIVO Embolisation Device for the Treatment of Intracranial Aneurysms [Brazilian multicenter study]
		flow diverter devices may conclusively prove its efficacy and utility in the long run	despite the fact that almost one-third of the patients presented with subarachnoid hemorrhage.		

Table 4: Publications including the use of the DERIVO Embolisation Device by Kaschner MG et al., 2019b; Goertz L et al., 2019a; Goertz L et al., 2019b and Akgul E et al., 2016. Abbreviations: AEs, adverse events; DED, DERIVO Embolisation Device/System; FD, flow diverter; FDD, flow diverter devices; ICA, internal carotid artery, MAE: mild adverse events with clinical relevance, transient; PTA, percutaneous transluminal angioplasty; SAE: severe adverse events, permanent; SAH, subarachnoid hemorrhage; BA, basilar artery; VA, vertebral artery; PCA, posterior cerebral artery.

Publication [Author, title]	**Kaschner MG et al., 2019b** Single-center experience with the new generation DERIVO Embolisation Device in ruptured dissecting and blister aneurysms	**Goertz L et al., 2019a** Safety and efficacy of the DERIVO Embolisation Device for the treatment of ruptured intracranial aneurysms	**Goertz L et al., 2019b** Improved Occlusion Rate of Intracranial Aneurysms Treated with the DERIVO Embolisation Device: One-Year Clinical and Angiographic Follow-Up in a Multicenter Study	**Akgul E et al., 2016** The DERIVO Embolisation Device in the Treatment of Intracranial Aneurysms: Short- and Midterm Results
Study characteristics				
Study type	retrospective	retrospective	retrospective	retrospective
Included patient number [female / male / mean age]	10 [5 / 5 / 48.3 years]	10 [3 / 7 / 54.5 years]	59 [48 / 11 / 52.6 years]	24 [14 / 10 / 50.1 years]
Number of treated aneurysms	11	11	59	34
Used device	DERIVO Embolisation Device/System			
Aneurysm characteristics				
Ratio unruptured / ruptured aneurysms	0 (0 %) / 11 (100 %)	0 (0 %) / 11 (100 %)	49 (83.1 %) / 10 (16.9 %)	33 (97.1 %) / 1 (2.9 %)

Publication [Author, title]	**Kaschner MG et al., 2019b** Single-center experience with the new generation DERIVO Embolisation Device in ruptured dissecting and blister aneurysms	**Goertz L et al., 2019a** Safety and efficacy of the DERIVO Embolisation Device for the treatment of ruptured intracranial aneurysms	**Goertz L et al., 2019b** Improved Occlusion Rate of Intracranial Aneurysms Treated with the DERIVO Embolisation Device: One-Year Clinical and Angiographic Follow-Up in a Multicenter Study	**Akgul E et al., 2016** The DERIVO Embolisation Device in the Treatment of Intracranial Aneurysms: Short- and Midterm Results
Localization of aneurysms	Right ICA paraophthalmic: 4 (33 %) Right V4: 4 (33 %) Basilar artery 1 (8.3 %) Right ICA terminus 1 (8.3 %) Left PI 1 (8.3 %) Right ICA (PCOM) 1 (8.3 %)	anterior circulation: 9 (81.8 %) posterior circulation: 2 (18.1 %)	ICA: 49 (83.1 %) VA: 4 (6.8 %) BA: 3 (5.1 %) PCA: 2 (3.4 %) ACA 1 (1.7 %)	Anterior circulation: 31 (91.2 %) Posterior circulation: 3 (8.8 %)
Aneurysm morphology	Blister: 3 (25 %) Dissecting-fusiform: 6 (50 %) Dissecting-dysplastic: 1 (8.3 %) Saccular: 1 (8.3 %) Saccular dysplastic: 1 (8.3 %)	Saccular: 4 (36.4 %) Blister-like: 3 (27.3 %) Dissecting: 3 (27.3 %) Fusiform: 1 (9.1 %)	n.s.	Saccular (91.2 %) Fusiform: 3 (88.8 %)
Aneurysm size	Size (mm): H/L x W x D; (neck) 1: 1 x 2x 2; (2); 2: 14 x 5.3 x 5.3; 3: 4.8 x 10 x 4.8; 4: 6 x 3.8 x 4; 5: 3.2 x 1.4 x 2.2; (3.2); 6: 1.4 x 3.2 x 2.2; (3); 7: 15 x 4.5 x 4.5; 8: 10 x 4 x 4; 9: 4.6 x 7.2 x 4.5; (7.2); 10: 4 x 4 x 4; (2); 11: 12 x 5 x 5; 12: 10 x 4 x 4	mean 3.6 mm (range 1.1–7.4 mm)	8.1 ± 6.2 mm (range: 1.3 – 25) <10 mm: 46 (78.0 %) ≥10 and ≤20 mm: 8 (13.6 %) >20 mm: 5 (8.5 %) Neck width (mm) 5.2 ± 3.1; range: 1.3 – 19) Dome-to-neck ratio 1.5 ± 0.7	≤ 3 mm: 4 (11.8 %) 4 – 10 mm: 19 (55.8 %) 11 – 24 mm: 7 (20.6 %) ≥ 25 mm 4 (11.8 %):
Effectiveness end point / clinical success				
Complete aneurysm occlusion [final follow-up]	7/7 (100 %) [6 months]	9/10 (90%) [median: 223 days]	24/29 (82.8 %) [12 months]	14/18 (77.8 %) [9 month]
Safety end points				
Mortality (total)	10 %	0 %	0 %	4.3 %
Mortality (brief description of the occurrences)	1 patient died one day after endovascular treatment because of a generalized brain edema.	-	-	1 aneurysm rupture
Morbidity (total)	5.5 %	20 %	10.2 %	8.4 %

Publication [Author, title]	**Kaschner MG et al., 2019b** Single-center experience with the new generation DERIVO Embolisation Device in ruptured dissecting and blister aneurysms	**Goertz L et al., 2019a** Safety and efficacy of the DERIVO Embolisation Device for the treatment of ruptured intracranial aneurysms	**Goertz L et al., 2019b** Improved Occlusion Rate of Intracranial Aneurysms Treated with the DERIVO Embolisation Device: One-Year Clinical and Angiographic Follow-Up in a Multicenter Study	**Akgul E et al., 2016** The DERIVO Embolisation Device in the Treatment of Intracranial Aneurysms: Short- and Midterm Results
Morbidity (SAE + MAE; brief description of the occurrences)	1 Symptomatic EVD-tract hemorrhage 1 EVD revision 1 Hydrocephalus 1 Pneumonia 2 Vasospasm 1 Pulmonal infection, increased ICP 1 Asymptomatic EVD tract hemorrhage after removal	1 acute right-sided hemiparesis and aphasia 4 days after the procedure. A control angiography showed an in-stent thrombosis. 1 chemotoxic reaction to the contrast agent	5 thromboembolic events 1 hemorrhagic event	1 right hemiparesis 1 right-side hemiplegia and aphasia due to stent occlusion 1 severe headache due to severe peri-aneurysmal edema
Technical notes / periprocedural complications				
Technical notes / periprocedural complications	1 Rupture due to coil prolapse of right-sided ICA aneurysm (PCOM) No intraprocedural DERIVO device-related events (aneurysm perforation by intraluminal device prolapse, dissection, vasospasm, incomplete device opening, thrombosis, contrast extravasation) occurred.	Device deployment was successful in all cases. All patients were treated with a single DED. The visibility of the DED during the procedure was rated as ‘excellent’ in nine cases and ‘good’ in one, indicating that the contour and the radiopaque markers at the ends were clearly visible on the DSA images.	Device deployment was technically successful in all cases. Fifty-six aneurysms (94.9 %) were treated with 1 single DED, 2 with 2 DEDs, and 1 with 3 DEDs. One patient had thrombus formation related to the device with distal embolization that was resolved by an immediate intravenous Infusion of tirofiban.	Technical success was 100 % 1 Fish-mouth formation 9 remodeling balloon was applied to provide proper apposition of the DED to the vessel wall in
Technical notes / periprocedural complications continuation	In all 10 patients; DERIVO deployment was technically successful with complete wall apposition of the device. All DERIVOS were clearly visible during the procedure and visibility was rated good in all cases.	Secondary balloon angioplasty was employed for two cases to ensure accurate wall apposition of the DED. In the first case, wall adaptation of the DED was only fair and in the second case balloon angioplasty was performed owing to insufficient proximal opening of the DED		
Overall conclusion				

Publication [Author, title]	**Kaschner MG et al., 2019b** Single-center experience with the new generation DERIVO Embolisation Device in ruptured dissecting and blister aneurysms	**Goertz L et al., 2019a** Safety and efficacy of the DERIVO Embolisation Device for the treatment of ruptured intracranial aneurysms	**Goertz L et al., 2019b** Improved Occlusion Rate of Intracranial Aneurysms Treated with the DERIVO Embolisation Device: One-Year Clinical and Angiographic Follow-Up in a Multicenter Study	**Akgul E et al., 2016** The DERIVO Embolisation Device in the Treatment of Intracranial Aneurysms: Short- and Midterm Results
Overall conclusion according to the authors of the study	Endovascular treatment with the DERIVO in ruptured dissecting and blister aneurysms revealed a sufficient initial division of aneurysms from the circulation without rebleeding. The DERIVO is associated with high procedural and clinical short-term safety.	In this pilot study, endovascular treatment of ruptured intracranial aneurysms with the DED was feasible and not associated with any incidence of rebleeding. Larger series with longer follow-up are warranted to reach a definite conclusion about this device.	The results demonstrate that treatment of intracranial aneurysms with the DED is associated with low rates of ischemic complications and adequate aneurysm occlusion at 1-year follow-up.	The DED seems effective and safe in the treatment of different kinds of intracranial aneurysms.

Table 5: Publications including the use of the DERIVO Embolisation Device by Kraus et al., 2018; Butt W et al., 2021; Bonadio LE, 2021; Simgen A et al., 2021 and Zaeske C et al., 2021. Abbreviations: AEs, adverse events; DED, DERIVO Embolisation Device/System; FD: flow diverter; FDD, flow diverter devices; ICA, internal carotid artery; MAE, mild adverse events with clinical relevance, transient; PTA, percutaneous transluminal angioplasty; SAE, severe adverse events, permanent; SAH, subarachnoid hemorrhage; ICA, internal carotid artery; BA, basilar artery; VA, vertebral artery; PCA, posterior cerebral artery; n.d., not deducible.

Publication [Author, title]	**Kraus B et al., 2018** Safety and efficacy of the DERIVO Embolisation Device for the treatment of unruptured intracranial aneurysms: a multicentric study	**Butt W et al., 2021** Implantation of Large Diameter (5.5 – 6mm) DERIVO Embolisation Devices for the Treatment of Cerebral Aneurysms	**Bonadio LE, 2021** Efficacy and safety in the treatment of paraclininoid brain aneurysms using DERIVO flow diversor stent.	**Simgen A et al., 2021** Retrospective analysis of intracranial aneurysms after flow diverter treatment including color-coded imaging (syngo iFlow) as a predictor of aneurysm occlusion	**Zaeske C et al., 2021** Comparative Analysis of the Pipeline and the DERIVO Flow Diverters for the Treatment of Unruptured Intracranial Aneurysms – A Multicentric Study
Study characteristics					
Study type	retrospective	prospective	retrospective	retrospective	retrospective
Included patient number [female / male / mean age]	42 [37 / 5 / 54.8 years]	18 [37 / 5 / 59.5 years]	126	24 [18 / 6 / 57.4 years]	49 [41 / 8 / 53.1]
Number of treated aneurysms	42	19	159	24	49
Used device	DERIVO Embolisation Device/System				
Aneurysm characteristics					
Ratio unruptured / ruptured aneurysms	0 (0 %) / 11 (100 %)	18 (94.7 %) /1 (5.3 %)	159 (100 %) / 0 (0 %)	24 (100 %) / 0 (0 %)	111 (100 %) / 0 (0 %)

Publication [Author, title]	**Kraus B et al., 2018** Safety and efficacy of the DERIVO Embolisation Device for the treatment of unruptured intracranial aneurysms: a multicentric study	**Butt W et al., 2021** Implantation of Large Diameter (5.5 – 6mm) DERIVO Embolisation Devices for the Treatment of Cerebral Aneurysms	**Bonadio LE, 2021** Efficacy and safety in the treatment of paraclininoid brain aneurysms using DERIVO flow diversor stent.	**Simgen A et al., 2021** Retrospective analysis of intracranial aneurysms after flow diverter treatment including color-coded imaging (syngo iFlow) as a predictor of aneurysm occlusion	**Zaeske C et al., 2021** Comparative Analysis of the Pipeline and the DERIVO Flow Diverters for the Treatment of Unruptured Intracranial Aneurysms – A Multicentric Study
Localization of aneurysms	ICA: 38 (90.5 %) BA: 2 (4.8 %) VA: 1 (2.4 %) PCA: 1 (2.4 %)	ICA: 17 VA: 1 BA: 1	paraclinoid ICA: 159	ICA: 22 VA: 2	ICA: 47 Pcom: 2 Vessel from sac. 12
Aneurysm morphology	Saccular: 34 (81.0 %) Fusiform:6 (14.3 %) Dissecting: 2 (4.8 %)	Saccular: 14 (73.7 %) Dissecting: 3 (15.8 %) Iatrogenic pseudoaneurysm 1 (5.3 %) Fusiform: 1 (5.3 %)	Saccular: 155 (97.4 %) Fusiform or blister-like: 4 2.6 %)	n.d.	Saccular: 42 Fusiform: 6 Blister: 1
Aneurysm size	mean 8.9 ± 6.2 mm; range 2 – 28 mm <10 mm: 31 (73.8 %) ≥10 and ≤20 mm: 8 (19 %) >20 mm: 3 (7.1%) Neck width (mm) 5.3 ± 3.1 Dome-to-neck ratio 1.5 ± 0.8	mean: 9.6 ± 5.2 mm; range: 4 – 10	mean: 5.8 ± 3.53 mm	width: 4.8 ± 2.6 length: 4.1 ± 2.4 depth:4.6 ± 2.9 neck: 3.9 ± 1.9 volume: 199.0 ± 534.7	Size: 11.3 ± 14.9 Neck width: 4.9 ± 2.9
Effectiveness end point / clinical success					
Complete aneurysm occlusion [final follow-up]	24/33 (72.7 %) [6 months]	12/16 (75 %) [6 months]	116/131 (88.5 %) [12 months]	22/24 (91.7 %) [14.9 ± 11.3 months]	32/40 [6 months]
Safety end points					
Mortality (total)	0 %	0 %	0.8 %	0 %	0 %
Mortality (brief description of the occurrences)	-	-	1 Thromboembolic or hemorrhagic	0 %	0 %
Morbidity (total)	2.4 %	0 %	3 %	1.5 %	4.1 %
Morbidity (SAE + MAE; brief description of the occurrences)	2 motor aphasia due to thromboembolism 1 in-stent thrombosis 1 aneurysm perforation	1 pseudoaneurysm at the femoral arterial access site which was repaired surgically.	3.9 % moderate in-stent stenosis (25-50%) occurred 4 thromboembolic/hemorrhagic incidents	1 stroke 1 stent thrombosis/occlusion 1 aneurysm growth	3 Thromboembolic events 1 hemorrhagic event 2 neurologic worsening

Publication [Author, title]	**Kraus B et al., 2018** Safety and efficacy of the DERIVO Embolisation Device for the treatment of unruptured intracranial aneurysms: a multicentric study	**Butt W et al., 2021** Implantation of Large Diameter (5.5 – 6mm) DERIVO Embolisation Devices for the Treatment of Cerebral Aneurysms	**Bonadio LE, 2021** Efficacy and safety in the treatment of paraclininoid brain aneurysms using DERIVO flow diversor stent.	**Simgen A et al., 2021** Retrospective analysis of intracranial aneurysms after flow diverter treatment including color-coded imaging (syngo iFlow) as a predictor of aneurysm occlusion	**Zaeske C et al., 2021** Comparative Analysis of the Pipeline and the DERIVO Flow Diverters for the Treatment of Unruptured Intracranial Aneurysms – A Multicentric Study
Technical notes / periprocedural complications					
Technical notes / periprocedural complications	Secondary balloon angioplasty was necessary in four cases (9.5 %) in order to ensure appropriate wall apposition of the DED. All DEDs were clearly visible during the procedure: visibility was rated 'excellent' in 33 cases (78.6 %), 'good' in 8 cases (19.0 %), and 'fair' in 1 case (2.4 %). The treatment with a 'fair' visibility was for re-currence of a giant (22 mm) Pcom aneurysm that had been treated with stents, coils, and another flow diverter. In this complex case, the implanted stents and the coil package led to restricted visibility of the contour and the radiopaque markers of the DED. Additional balloon angioplasty was neces-sary after deployment in order to achieve full deployment and appropriate wall apposition.	5 (27.8 %) suboptimal opening of the proximal end of the DED and/or "fish mouthing" which was corrected using adjunct stenting.	Success rate for stent placement was 98.7 %.	3 foreshortening Problems during deployment occurred in one case when a DED (4.5 x 30mm) was used in a tortious vessel anatomy to treat an ICA aneurysm. Despite a complete expansion of the distal and proximal ends with adequate vessel wall apposition, the stent showed a high-grade constriction in the central section.	FDD implantation was technically successful in all cases without any significant differences between groups regarding procedural parameters, such as fluoroscopy time, dose, or procedural time
Overall conclusion					
Overall conclusion according to the authors of the study	Endovascular treatment of UIAs with the DED is associated with high procedural safety and adequate occlusion rates. Examinations at 1- and 2-year follow-up will provide data on the long-term safety and	Implantation of large dia-meter (5.5mm and 6mm) DEDs into capacious cere-bral vessels to treat a range of complex aneurysms is safe and technically feasible but may require adjunct stenting to optimize proximal	DERIVO offers an effective and safe treatment option for paraclininoid aneurysms. The aneurysm occlusion rate was 88.5 % in the follow-up, achieved	n.d.	The DED represents a reasonably safe and effective alternative device to the PED. While showing comparable complication rates, morbidity, and angiographic outcome between the groups, anti-

Publication [Author, title]	**Kraus B et al., 2018** Safety and efficacy of the DERIVO Embolisation Device for the treatment of unruptured intracranial aneurysms: a multicentric study	**Butt W et al., 2021** Implantation of Large Diameter (5.5 – 6mm) DERIVO Embolisation Devices for the Treatment of Cerebral Aneurysms	**Bonadio LE, 2021** Efficacy and safety in the treatment of paraclininoid brain aneurysms using DERIVO flow diversor stent.	**Simgen A et al., 2021** Retrospective analysis of intracranial aneurysms after flow diverter treatment including color-coded imaging (syngo iFlow) as a predictor of aneurysm occlusion	**Zaeske C et al., 2021** Comparative Analysis of the Pipeline and the DERIVO Flow Diverters for the Treatment of Unruptured Intracranial Aneurysms – A Multicentric Study
	angiographic outcomes of this device.	wall apposition. Short-term efficacy of this device subset is comparable to previous DED and other flow diverter studies. Long-term follow-up and comparative studies are required for further assessment.	with a single device and a high technical success rate.		thrombogenic surface modi-fication and improved fluoros-copic visibility of the DED did not translate into measurable improvements in regard to thrombo-embolic compl-ications and fluoroscopic time, dose, and procedure time, respectively.

Table 6: Publications including the use of the almost identical DERIVO by Simgen A et al., 2022; Fujimura S et al., 2021, Pinana C et al., 2022 and Yakar F et al., 2023. Abbreviations: AEs: adverse events, DED: DERIVO Embolisation Device/System, FD: flow diverter, FDD: flow diverter device, ICA: internal carotid artery, MAE: mild adverse events with clinical relevance, transient; PTA: percutaneous transluminal angioplasty, SAE: severe adverse events, permanent: SAH: subarachnoid hemorrhage; ICA, internal carotid artery; BA basilar artery; VA vertebral artery; PCA posterior cerebral artery; PICA, posterior inferior cerebellar artery; pt, patient; MCA, middle cerebral artery; ACA; anterior cerebral artery; Acomm, anterior communicating artery; n.d., not deducible.

Publication [Author, title]	**Simgen A et al., 2022** Endovascular treatment of unruptured intracranial aneurysms with flow diverters: A retrospective long-term single center analysis	**Fujimura S et al., 2021** Hemodynamic Characteristics and Clinical Outcome for Intracranial Aneurysms Treated with the Derivo Embolisation Device, a Novel Second-Generation Flow Diverter	**Pinana C et al., 2022** Derivo embolization device for intracranial aneurysms: a Spanish multicenter retrospective study	**Yakar F et al., 2023** Flow diverter stent treatment for unruptured supraclinoid segment internal carotid artery aneurysms: a Turkish multicenter study
Study characteristics				
Study type	retrospective	retrospective	Retrospective	retrospective
Included patient number [female / male / mean age]	35 [31 / 4 / 57.9 years]	23 [19 / 4 / 57.5 years]	209 [162 / 47 / 57.5 years]	54 [44/ 10 / 53.5 years]
Number of treated aneurysms	35	23	250	24
Used device	DERIVO Embolisation Device/System			

Publication [Author, title]	**Simgen A et al., 2022** Endovascular treatment of unruptured intracranial aneurysms with flow diverters: A retrospective long-term single center analysis	**Fujimura S et al., 2021** Hemodynamic Characteristics and Clinical Outcome for Intracranial Aneurysms Treated with the Derivo Embolisation Device, a Novel Second-Generation Flow Diverter	**Pinana C et al., 2022** Derivo embolization device for intracranial aneurysms: a Spanish multicenter retrospective study	**Yakar F et al., 2023** Flow diverter stent treatment for unruptured supraclinoid segment internal carotid artery aneurysms: a Turkish multicenter study
Aneurysm characteristics				
Ratio unruptured / ruptured aneurysms	35 (100 %) / 0 (0 %)	-	247 (100 %) / 3 (1.2 %)	24(100 %) / 0 (0 %)
Localization of aneurysms	Supraophthalmic ICA: 9 Paraophthalmic ICA: 18 Infraophthalmic ICA: 7 VA: 1	ICA: 22/23 (95.7 %) VA 1/23 (4.3 %)	ICA: 217 (86.8 %) PCA (P1): 11 (4.4 %) PICA: 8 (3.2 %) MCA: 6 (2.4 %) ACA: 4 (1.6 %) BA: 3 (1.2 %) Acomm: 1 (0.4 %)	Not assignable to the DED **Note**: Not all aspects can be assigned to the DED as several FDs were used. The most preferred FD stent here was the DED (38.7 %, 24 pts.), followed by the FRED (MicroVention, 33.9 %, 21), the Surpass Evolve (Stryker Neurovascular, 25.8 %, 16 pts.), and the Pipeline Flex (Medtronic, 1.6 %, 1 pt.).
Aneurysm morphology	Saccular: 33 (94.3 %) Fusiform:2 (14.3 %)	-	Saccular: 225 (90.0 %) Fusiform:16 (3.2 %) Dissecting: 8 (3.2 %) Blister: 1 (0.4 %)	Not assignable to the DED
Aneurysm size	width (mm) 5.0 ± 2.8 height (mm) 5.4 ± 3.7 depth (mm) 5.0 ± 3.2 neck (mm) 3.8 ± 1.8 Dome-to-neck ratio 1.3 ± 0.4 volume (mm^3): 165.5 ± 383.0	neck (mm): 3.23 ± 2.98 volume (mm^3): 2.84 ± 3.56	Small (< 10 mm): 173 (69.2%) Large (10 – 20 mm): 43 (17.2%) Very large (>20 mm): 12 (4.8 %) Not reported: 22 (8.8 %) Median aneurysm maximum size (mm): 5.85 (IQR 3.6 – 9.8) Median neck size (mm): 4.00 (IQR 3 – 5) Median aspect ratio: 1.39 (IQR 1.1 – 1.9)	Not assignable to the DED
Effectiveness end point / clinical success				
Complete aneurysm occlusion [final follow-up]	33/35 (94.3 %) [mean 19.7 months]	17/23 (73.9 %) [6 months]	93/108 (83.08 %) [12 months]	18/20 (90.00 %) [12 months]
Safety end points				
Mortality (total)	0 %	0 %	1.9 %	Not assignable to the DED

Publication [Author, title]	**Simgen A et al., 2022** Endovascular treatment of unruptured intracranial aneurysms with flow diverters: A retrospective long-term single center analysis	**Fujimura S et al., 2021** Hemodynamic Characteristics and Clinical Outcome for Intracranial Aneurysms Treated with the Derivo Embolisation Device, a Novel Second-Generation Flow Diverter	**Pinana C et al., 2022** Derivo embolization device for intracranial aneurysms: a Spanish multicenter retrospective study	**Yakar F et al., 2023** Flow diverter stent treatment for unruptured supraclinoid segment internal carotid artery aneurysms: a Turkish multicenter study
Mortality (brief description of the occurrences)	-	-	2 major ischemic stroke 1 major intra-cranial bleeding 1 severe pneumonia	Not assignable to the DED
Morbidity (total)	3.1 %	0 %	8 %	Not assignable to the DED
Morbidity (SAE + MAE; brief description of the occurrences)	3 strokes 2 device occlusions 1 device thrombosis 1 deployment problem 1 side branch occlusion 13 in-stent stenoses	1 stent migration 2 in-stent stenoses 1 pseudoaneurysm at puncture site	5 hemorrhages 21 ischemias 3 other neurological complications 1 non-neurological complication	It is generally stated that no peri-operative complications led to any permanent or transient neurological deficit.
Technical notes / periprocedural complications				
Technical notes / periprocedural complications	In one case, a major stroke was caused by an incomplete proximal opening of a DED during treatment of a supra-ophthalmic aneurysm of the left ICA. An incomplete opening	In total, 24 DEDs were applied in 23 patients with 23 aneurysms. In 1 patient the DED migrated after the procedure, which required retreatment with a second DED. Concomitant coiling was not done; however, 2 patients had preexisting	Concerning the device deployment or technical issues, only two cases of device malfunctioning (1 %) were reported, consisting of inability to obtain optimal opening and safe deployment of the device despite several attempts and maneuvers, as ascertained by the	Not assignable to the DED
Technical notes / periprocedural complications, continuation	of the DED led to an acute stent thrombosis with subsequent occlusion of the parent vessel. Revascularization In one case, a major stroke was caused by an incomplete proximal opening of a DED during treatment of a supra-ophthalmic aneurysm of the left ICA. An incomplete opening of the DED led to an acute stent thrombosis with subsequent occlusion of the parent vessel. Revascularization maneuvers were unsuccessful. The patient suffered territorial infarction of the left middle cerebral artery and the anterior cerebral artery resulting in a Complete media syndrome followed	coiling procedures. All deployment procedures were elective, and none was done in the acute stage after an aneurysmal SAH.	operating interventionalist. In both cases this difficulty prompted substitution of the device, ultimately resulting in successful technical procedures. No other technical difficulties or deficiencies were noted.	

Publication [Author, title]	Simgen A et al., 2022 Endovascular treatment of unruptured intracranial aneurysms with flow diverters: A retrospective long-term single center analysis	Fujimura S et al., 2021 Hemodynamic Characteristics and Clinical Outcome for Intracranial Aneurysms Treated with the Derivo Embolisation Device, a Novel Second-Generation Flow Diverter	Pinana C et al., 2022 Derivo embolization device for intracranial aneurysms: a Spanish multicenter retrospective study	Yakar F et al., 2023 Flow diverter stent treatment for unruptured supraclinoid segment internal carotid artery aneurysms: a Turkish multicenter study
	by a hemicraniectomy. Recovery from mRS 5 at discharge was only possible to mRS 4 at the last follow-up after 19 months.			
Overall conclusion				
Overall conclusion according to the authors of the study	Treatment of unruptured IAs using different FDs is safe and effective with low rates of permanent morbidity and high occlusion rates at long-term follow-up. Direct FD comparisons are difficult due to the high availability of different devices. The study had varying patient numbers for each FD, but it was shown that PED had a lower occlusion rate and a higher retreatment rate than the DED, FRED, and p64. The highest occlusion rates and the lowest complication rates were observed with FRED and p64, but these devices were significantly underrepresented in this study. Complications that influenced the clinical outcome were only observed with PED and DED and were comparable with each other and those reported in the literature. The occurrence of an in-stent stenosis was lowest with DED compared to the other FDs, but the severity of the observed ISS between the FDs did not differ significantly.	The CFD results indicate that the energy loss involved with the blood flow passing through an aneurysm and concentrated inflow into an aneurysm were the most important factors to determine whether an aneurysm will become a complete occlusion or remnant case.	The DED is a surface-modified FD with increasing use in recent years. The results show, in the largest series published to date, high rates of occlusion and comparable safety to other available FD devices. Nonetheless, the risks are not negligible and must always be balanced against the natural history risk of cerebral aneurysms, considering the tendency to widen indications for treatment.	The results of this first multicenter study evaluating FD stent use for unruptured ICA supraclinoid segment aneurysms showed that FD stent treatment is a feasible method for replacing clipping and coil embolization with manageable complications and a high success rate.

1.5.3.1.3 Summary and conclusion out of the scientific literature

Evaluated body of clinical literature

Altogether, 2 meta-analyses, 10 clinical studies and 8 cases series describing the use of the DERIVO in a clinical setting were evaluated with focus on performance and safety information (see Table 3 – Table 6).

Within the scope of the evaluated publications (excluding the meta-analyses), DERIVO devices of various dimensions were applied for the treatment of a total of 1,416 ruptured and unruptured aneurysms of various morphologies in the anterior and posterior circulation of 1,245 patients.

Performance

The device performance assessed by means of technical and clinical success rates achieved by the DERIVO were 99.77 % [95 % CI: 99.11 – 100] and 84.08 % [95 % CI: 80.57 – 87.32], respectively. From this, it can be concluded that the DERIVO and thus the DERIVO mini achieve the performance intended by Acandis.

Safety

Technical and clinical complication rates were low. Complications occurred were within the known and manageable spectrum of device-and procedure-related complications inherent to the application of flow diverter stents for the endovascular treatment of intracranial aneurysms. The evaluated clinical body of literature on the DERIVO does not report risks, complications or contraindications that are currently not covered by the DERIVO's risk analysis or the IFU. Hence, the safety profile of the DERIVO and DERIVO mini seems to be within the expected and known range inherent to the generic device group of self-expandable intracranial stents used as flow diverters.

Conclusion

The evaluated clinical scientific literature on the DERIVO provides sound evidence on the DERIVO's and thus the DERIVO mini's performance and safety according to its intended purpose. No undue performance issues were reported and encountered device-related complications lie within the spectrum of known and manageable complications inherent to the use of this generic device group. In addition, almost all authors evaluated the DERIVO as safe and efficient in the treatment of different kinds of IAs.

1.5.3.2 Clinical data obtained by clinical trials or PMCF-measures

Acandis presented one PMCF study concerning the DERIVO (a prospective multi-center trial) conducted by Taschner and colleagues including 96 patients harboring 96 unruptured IAs. Morbidity was 3.1 % mortality 0 %. Follow-up angiographies were available in 89 (93 %) patients at a median of 12.4 ± 5.84 months with a core laboratory adjudicated satisfactory aneurysm occlusion in 89 % (79/89). It was concluded that DERIVO is a safe and effective treatment for unruptured aneurysms with high rates of satisfactory occlusion and comparably low rates of permanent neurological morbidity and mortality (for more details see also Table 3, Taschner CA et al., 2020).

1.5.3.3 Clinical data from medical device databases

BfArM *(German Federal Institute for Drugs and Medical Devices (Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM) database of Field Corrective Actions).*

The latest search was conducted on October 13, 2023. Searched was for the DERIVO and DERIVO mini, other Acandis DERIVO family devices and a well-established benchmark device from the same generic device group (i.e., SILK (+) Artery Reconstruction Device, BALT Extrusion, Montmorency, France).

Table 7: Clinical data gained from BfArM search conducted on October 13, 2023.

Searched Device	Database entries
DERIVO and DERIVO mini	No entries
Other DERIVO family devices	Two records refer to an urgent safety information concerning the DERIVO 2 and DERIVO 2 heal and issue the same voluntary recall in January 2022: Difficulty in delivery of devices through the catheter in certain sizes. No patient injuries or deaths were reported. (BfArM references: 01491/22 and 01492/22) Meanwhile the device problems have been solved.
Benchmark device (SILK (+) Artery Reconstruction Device, BALT Extrusion, Montmorency, France):	One entry report on faulty application of the 1st generation SILK device resulting in aneurysm rupture and deaths in eight patients in 2010. Four entries report on oversizing and product deficiencies 2018 – 2021. (BfArM references: 00938/10, 12010/18, 03521/19, 03962/21, 07237/21).

MAUDE *("Manufacturer and User Facility Device Experience (MAUDE) Database, maintained by the United States' Food and Drug Administration).*

The latest searches were conducted on October 17, 2022 and October 13, 2023 and the searched time frame comprised November 2021 to October 2023. The DERIVO and DERIVO mini as well as other Acandis DERIVO family devices have not been distributed in the USA. Therefore, it was searched was for a well-established benchmark device from the same

generic device group (i.e., SILK (+) Artery Reconstruction Device, BALT Extrusion, Montmorency, France).

Table 8: Clinical data gained from MAUDE database search conducted on January 12, 2023 and October 13, 2023

Searched Device	Database entries
Benchmark device (SILK (+) Artery Reconstruction Device, BALT Extrusion, Montmorency, France)	The only record refers to a death event due to aneurysm rupture. The patient's injury does not seem to be related to the Silk Vista Baby used but potentially to the angioplasty performed, which could have caused an overpressure in the artery leading to the rupture of the parent artery.

Conclusion:

The data base entries do not indicate high failure or incident rates of the DERIVO and DERIVO mini as well as the generic device group of self-expandable intracranial neurovascular stents, used as flow diverters. Thus, there is no allusion to an unfavorable risk profile of such devices in routine clinical use.

From this point of view, the DERIVO and DERIVO mini as well as devices from the generic device group appear to be effective and safe for their intended use.

1.5.4 An overall summary of the clinical performance and safety

The clinical literature reflecting and summarizing the state-of-the-art in the treatment of intracranial aneurysms in general and by self-expanding intracranial neurovascular stents, used as flow diverter stents, publications stating the use of the DERIVO and the well-established similar/benchmark SILK(+) Artery Reconstruction Device, together with the results from the searches in authority-maintained vigilance databases as well as the data collected from PMS and PMCF measures on the DERIVO prove the clinical performance and safety of the DERIVO and DERIVO mini as well as the device group of self-expandable intracranial neurovascular stents, used as flow diverters in general.

The reviewed clinical data provide sound evidence that by using self-expandable intracranial neurovascular stents, used as flow diverters in general and the DERIVO and thus the DERIVO mini, in particular, a successful and safe treatment of intracranial aneurysms in various locations and of different morphologies by flow diversion is feasible. It could be shown that the DERIVO and thus the DERIVO mini achieve technical and clinical success rates comparable to the well-established similar/benchmark device from the same generic device group and to those achieved by the whole device group reported of in the state-of-the-art literature.

Therefore, the DERIVO and DERIVO mini are suitable for their intended purpose, namely the treatment of intracranial aneurysms by diverting the blood flow in the aneurysm-bearing vessel.

Thus, it can be concluded that the DERIVO and DERIVO mini are state-of-the-art devices that achieve the clinical benefit and the performances intended by Acandis and fulfill the considered relevant GSPRs for performance.

From the evaluation of the clinical literature, we can conclude that the risk profile of flow diverter stents characterized by complications associated with the intervention and the devices themselves is thoroughly characterized and therefore well-known to the professional user.
These complications encompass vessel rupture and bleeding / re-bleeding, thromboembolic and ischemic events, technical issues as well angiography-related complications and the respective clinical consequences for the affected patient as for instance morbidity and death.

No evidence on unduly or, so far, unknown risks emanating from the DERIVO and DERIVO mini was identified from the evaluated clinical data.

Technical and clinical complication rates with the DERIVO and DERIVO mini, as evidenced from the evaluated clinical data, were low, and occurred complications were within the known and manageable spectrum inherent to the use of the generic device group and this kind of intervention.
Hence, the safety profile of the DERIVO and DERIVO mini seems to be within the expected and known range inherent to the generic device group of self-expandable intracranial neurovascular stents, used as flow diverters. It can, thus, be concluded that regarding safety the DERIVO and, hence, the DERIVO mini under evaluation are state-of-the-art devices.

The basic design, as well as the material used for the devices, have been successfully applied for several years. The DERIVO and DERIVO mini were subjected to various pre-clinical and laboratory testing according to (harmonized) standards with successful results. Thus, altogether, the DERIVO and DERIVO mini fulfil the relevant GSPRs for safety.

According to the clinical data presented in the scientific literature, the information gained from PMS and PMCF measures as well as the risk analysis, it can be concluded that risks which may be associated with the intended use of the DERIVO and DERIVO mini constitute acceptable risks when weighed against the benefits conferred to the patient. Further, it can be concluded that for patients carefully selected for this treatment, undesirable side-effects constitute an acceptable risk when weighed against the performance intended by the clinician in charge. The main risks are described and documented in detail in the scientific literature, thus being known to trained professional user. Therefore, by considering all identified data on safety and performance and complying with all warnings and precautions, the DERIVO and

DERIVO mini offer an acceptable benefit-risk profile and meet the relevant GSPRs for the acceptability of side effects and acceptable benefit-risk profile.

Acandis' clinically relevant marketing claims related to safety and performance concerning the DERIVO and DERIVO min are the following:

Table 9: Clinically relevant marketing claims in Acandis' brochure and at website

Device	Marketing claim
DERIVO and DERIVO mini	For vessel diameters from 1.5 mm to 6.0 mm
	Very good visibility due to nitinol composite wires with platinum core
	Perfect adaptability / perfect adaptation to the vessel wall even in tortuous anatomy
	Reliable distal opening behavior due to closed wire ends
	BlueXide® surface finish for optimized hemocompatibility and safe delivery
	Good positioning due to additional platinum markers distally and proximally
	Repositionable up to 95 % of its length (depending on the respective size)
	Case-specific 3D sizing support
DERIVO mini	Up to 3.5 mm device diameter deliverable through 0.021" ID microcatheters

The above-listed marketing claims are acceptable. They are supported by product specification, technical characteristics, comprehensive pre-clinical tests, PMCF study results, and various publications (Li L et al., 2013, Jiang B et al., 2016, Kraus B et al., 2018, Goertz L et al., 2019a, Kraus B et al., 2019) and the 3D Sizing Simulation software ANKYRAS for planning the implantation procedure on request.

In conclusion, the clinical benefit is achieved, the benefit-risk ratio of the DERIVO and DERIVO mini is considered acceptable, the devices could eventually be shown to be in compliance with the considered relevant General Safety and Performance Requirements (GSPRs) and the safety and performance of the DERIVO and DERIVO mini can be confirmed.

1.5.5 Ongoing or planned post-market clinical follow-up

Currently, no PMCF study is ongoing. According to the PMCF plan, further specific PMCF activities are suspended because the current expertise with the DERIVO and the DERIVO mini does not facilitate the need for further PMCF activities.

1.6 Possible diagnostic of therapeutic alternatives

The **conventional surgical approach** consists of performing a craniotomy followed by a clip ligation, also called microsurgical clipping (Armoiry X et al., 2012). In contrast to surgical clipping, endovascular embolization is minimally invasive, thus circumventing the risks

associated with open surgery. Nevertheless, there are several risks and complications, ranging from mild to severe, associated with the procedure and the devices used for flow diversion of IAs.

Alternative endovascular therapies comprise deconstructive methods i.e., parent artery occlusion and reconstructive methods i.e., coil embolization, stent- and balloon-assisted coiling with conventional high porosity stents and coils, trapping and overlapped stent placement (Byrne JV and Szikora I, 2012; Rouchaud A et al., 2015; Li S et al., 2022). Hybrid approaches of surgical and endovascular treatment techniques are also described (Gross BA et al., 2017).

1.7 Suggested profile and training for users

The DERIVO and DERIVO mini should be applied only by physicians who have the necessary background knowledge and experience in the field of interventional neuroradiology and have the required expertise in the treatment of intracranial aneurysms.

1.8 Reference to harmonized standards and common specifications applied

Standard	Title	Revision
EN ISO 10993-1	Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process (ISO 10993-1:2018, including corrected version 2018-10)	2020
ISO 10993-10	Biological evaluation of medical devices- Part 10: Tests for irritation and skin sensitization	2021
EN ISO 10993-11	Biological evaluation of medical devices - Part 11: Tests for systemic toxicity (ISO 10993-11:2017)	2018
EN ISO 10993-12	Biological evaluation of medical devices - Part 12: Sample preparation and reference materials (ISO 10993-12:2021)	2021
EN ISO 10993-15	Biological evaluation of medical devices - Part 15: Identification and quantification of degradation products from metals and alloys (ISO 10993-15:2000)	2009
ISO 10993-15	Biological evaluation of medical devices - Part 15: Identification and quantification of degradation products from metals and alloys	2019
EN ISO 10993-17	Biological evaluation of medical devices - Part 17: Establishment of allowable limits for leachable substances (ISO 10993-17:2002)	2009
EN ISO 10993-18	Biological evaluation of medical devices - Part 18: Chemical characterization of medical device materials within a risk management process (ISO 10993-18:2020)	2020
EN ISO 10993-2	Biological evaluation of medical devices – Part 2: Animal welfare requirements (ISO 10993-2:2022)	2022
EN ISO 10993-23	Biological evaluation of medical devices - Part 23: Tests for irritation (ISO 10993-23:2021)	2021
EN ISO 10993-3	Biological evaluation of medical devices - Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity (ISO 10993-3:2014)	2014
EN ISO 10993-4	Biological evaluation of medical devices - Part 4: Selection of tests for interactions with blood (ISO 10993-4:2017)	2017
EN ISO 10993-5	Biological evaluation of medical devices- Part 5: Tests for in vitro cytotoxicity (ISO 10993-5:2009)	2009
EN ISO 10993-6	Biological evaluation of medical devices- Part 6: Tests for local effects after implantation (ISO 10993-6:2016)	2016

EN ISO 10993-7	Biological evaluation of medical devices - Part 7: Ethylene oxide sterilization residuals (ISO 10993-7:2008)	2008/ AC:2009
ISO 10993-7	Biological evaluation of medical devices - Part 7: Ethylene oxide sterilization residuals – Amendment 1: Applicability of allowable limits for neonates and infants	2008/ Amd1:2019
EN ISO 11135	Sterilization of health care products – Ethylene oxide - Requirements for the development, validation and routine control of a sterilization process for medical devices (ISO 11135:2014+Amd.1:2018)	2014 +A1:2019
EN ISO 11138-1	Sterilization of health care products - Biological indicators - Part 1: General requirements (ISO 11138-1:2017)	2017
EN ISO 11138-2	Sterilization of health care products - Biological indicators - Part 2: Biological indicators for ethylene oxide sterilization processes (ISO 11138-2:2017)	2017
EN ISO 11139	Sterilization of health care products – Vocabulary of terms used in sterilization and related equipment and process standards (ISO 11139:2018)	2018
EN ISO 11607-1	Packaging for terminally sterilized medical devices - Part 1: Requirements for materials, sterile barrier systems and packaging systems (ISO 11607-1:2019)	2020
EN ISO 1 1607-2	Packaging for terminally sterilized medical devices - Part 2: Validation requirements for forming, sealing and assembly processes (ISO 11607- 2:2019)	2020
EN ISO 11737-1	Sterilization of health care products - Microbiological methods - Part 1: Determination of a population of microorganisms on products (ISO 11737-1:2018 + Amd 1:2021)	2018 + A1:2021
EN ISO 13485	Medical devices - Quality management systems - Requirements for regulatory purposes (ISO 13485:2016)	2016 +AC:2018 +A11:2021
EN ISO 14630	Non-active surgical implants - General requirements (ISO 14630:2012)	2012
EN ISO 14644-1	Cleanrooms and associated controlled environments - Part 1: Classification of air cleanliness by particle concentration (ISO 14644-1:2015)	2015
EN ISO 14644-2	Cleanrooms and associated controlled environments - Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration (ISO 14644-2:2015)	2015
EN ISO 14644-3	Cleanrooms and associated controlled environments - Part 3: Test methods (ISO 14644-3:2019)	2019
EN ISO 14644-4	Cleanroom and associated controlled environments - Part 4: Design, construction and start-up (ISO 14644-4:2001)	2001
EN ISO 14644-5	Cleanroom and associated controlled environments - Part 5: Operations (ISO 14644-5:2004)	2004
EN ISO 14698-1	Cleanroom and associated controlled environments – Biocontamination control - Part 1: General principles and methods (ISO 14698-1:2003)	2003
EN ISO 14698-2	Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data TECHNICAL CORRIGENDUM 1	2003/ Cor. 1:2004
EN ISO 14971	Medical devices. Application of risk management to medical devices (ISO 14971:2019)	2019
EN ISO 15223-1	Medical devices - Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements (ISO 15223-1:2021)	2021
EN 17141	Cleanrooms and associated controlled environments - Biocontamination control	2020
ISO/TR 20416	Medical Devices - Post-Market Surveillance for Manufacturers	2021
EN ISO 20417	Medical devices - Information to be supplied by the manufacturer (ISO 20417:2021)	2021
EN ISO 25539-1	Cardiovascular implants – Endovascular devices – Part 1: Endovascular prostheses (ISO 25539-1:2017)	2017
EN ISO 25539-2	Cardiovascular implants - Endovascular devices – Part 2: Vascular stents (ISO 25539-2:2020)	2020
EN 556-1	Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices	2001 +AC:2006

EN 62366-1	Medical devices - Part 1: Application of usability engineering to medical devices (IEC 62366-1:2015 + COR1:2016 + A1:2020)	2015 + COR1:2016 + A1:2020
EN 868-2	Packaging for terminally sterilized medical devices - Part 2: Sterilization wrap – Requirements and test methods	2017

2 Information for the patient

Document revision: 03

Date issued: October 25, 2023

This Summary of Safety and Clinical Performance (SSCP) is intended to provide public access to an updated summary of the main aspects of the safety and clinical performance of the device. The information presented below is intended for patients or lay persons. An extensive summary of its safety and clinical performance prepared for healthcare professionals is found in the first part of this document (chapter 1).

The SSCP is not intended to give general advice on the treatment of a medical condition. Please contact your healthcare professional in case you have questions about your medical condition or about the use of the device in your situation. This SSCP is not intended to replace an implant card or the instructions for use to provide information on the safe use of the device.

2.1 Device identification and general information

Device trade name(s)	– **DERIVO® Embolisation Device** (Article no. 01-000350 – 01-000375 and 01-000408 – 01-000415) – **DERIVO® mini Embolisation Device** (Article no. 01-000416 – 01-000433)
Manufacturer's name and address	Acandis GmbH, Theodor-Fahrner-Straße 6, 75177 Pforzheim, Germany
Basic UDI-DI	The Unique Device Identification System is a system for the unambiguous identification of medical devices. The basic UDI for the DERIVO is 426065033DERIVO4Q The basic UDI for the DERIVO mini is 426065033DERIVOminiCS
Year of first CE certificate	DERIVO: October 2013 DERIVO mini: November 2018

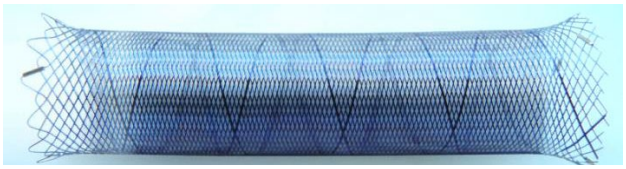
2.2 Intended use of the device

Intended purpose	The DERIVO devices are used for the treatment of vessel bulges in the brain (intracranial aneurysms (IA)). The blood flow is redirected in the vessel. Blood flow into the aneurysm is prevented (diverting the blood flow in the aneurysm-bearing vessel).

Indication(s)	The DERIVO devices are used for the treatment of vessel bulges in the brain (intracranial aneurysms (IA)) The DERIVO devices are used for patients which cannot be treated inside the blood vessel with other procedures. The DERIVO devices are also used for patients in which other brain surgery (neurosurgical) techniques pose a higher risk.
Intended patient groups	No specific patient populations have been defined but patients with contraindications are to be excluded.
Contraindications	- Patients in whom the size of the aneurysm and/or the diameter of the brain vessel in which the aneurysm is located do not match the size of the stent - Patient for whom anti-blood clotting therapy (anti-platelet and/ or anti-coagulation therapy) is contraindicated - Patients with conditions seen in X-rays (angiography) unsuitable for endovascular treatment due to severe vessel curvatures and/or abnormal vessel narrowing - Patients shortly after bleeding in the brain. - Patients with a bacterial infection - Patients who were not pretreated with anti-blood clotting drugs - Patients who are hypersensitive to nickel-titanium.

2.3 Device description

2.3.1 Description of the devices



DERIVO

DERIVO mini

The DERIVO (left) and DERIVO mini (right) are self-expanding stents. They are braided of Nitinol wires. Due the dense meshes, they are called flow diverter stents. The devices are sterile and biocompatible. They are free of latex and salts or ester of phthalic acid (phthalate). The devices can be seen under X-rays. The devices are implanted for a lifetime.

2.3.2 Mode of action

The devices are inserted through a small, flexible hollow tube (microcatheter). The insertion point is usually in the groin. The folded devices are advanced with a transport wire up to the place of the vessel wall bulge.

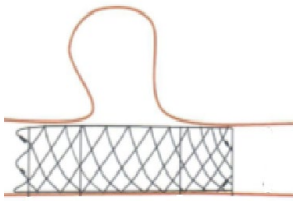


Figure 1: DERIVO/DERIVO mini (black grid) when placed under the vessel wall bulge (aneurysm).

When correctly placed, the folded device expands itself. Then, it is fixed firmly (implanted). Eventually, the transport wire and the microcatheter are removed.

2.3.3 Accessories

Small, flexible hollow tubes (microcatheters) for insertion.

2.4 Risks and warnings

Contact your healthcare professional, if you believe that you are experiencing side effects related to the device, its use or if you are concerned about risks. This document is not intended to replace a consultation with your healthcare professional, if needed.

2.4.1 Residual risks and undesirable effects

Acandis employed a risk management system according to the ISO (International Organization for Standardization): ISO 14971:2019. This is the industry standard. The risk management of the DERIVO and DERIVO mini does not reveal unacceptable residual risks.

In the risk analysis Acandis states:
“The residual risks are reduced as far as possible. Based on this result, the product is safe for treatment. The clinical experiences, market surveillance data, literatures of the DERIVO (mini) Embolisation Device and similar products on the market show that the considerable benefits provided to the patient outweigh the overall residual risk.”

Possible complications are known that even may arise when the DERIVO and DERIVO mini are used according to common knowledge. The physicians are aware of these unwanted effects. They can manage them.

The most commonly reported complications are technical problems during the placement procedure of the device in the brain, blood clotting with vessel blockage and restriction in blood supply.

In the following, the complete list of possible complications is described:

- General complications in connection with treatments inside the vessel wall (endovascular treatment) or treatments with X-rays and contrast agent (angiographic treatments: (e.g. false aneurysm (pseudoaneurysm), rupture of or bleeding from aneurysm, bleeding, bleeding in the brain (intracerebral hemorrhage, subarachnoid hemorrhage), blood clotting

(embolism), fever, tears or holes in the wall of a blood vessel (vessel dissection, vessel perforation), vessel rupture, narrowing of the vessel (vessel stenosis), (abrupt) vessel closure (occlusion or thrombosis), infection, limited blood supply, limited blood supply in the brain (cerebral ischemia/infarction), bleeding after the intervention (secondary hemorrhage), reactions due to radiation exposure, stroke (thromboembolic event/stroke), contraction of the blood vessel (vasospasm), poisoning)

- General complications in connection with anti-blood clotting drugs (antiplatelet agents/anticoagulants), anesthetics and contrast agents (e.g. renal failing (insufficiency))
- Complications in connection with the insertion point (vascular access) (e.g. bruise (hematoma), bleeding, paint or infections at the insertion point of the catheter (puncture site)
- Possible problems when introducing/implanting the device (e.g. device breakage, device folding, incorrect device placement, device cannot be deployed, device cannot be pulled back into catheter, device kinking, device does not detach from transport wire, device movement (migration), insufficient opening, delayed treatment, area of the aneurysm (target area) inaccessible or cannot be accessed safely, additional stenting required)
- Further complications in connection with the device (e.g. allergic reactions to the device material, closure of the device, blood clotting within the blood vessel (thrombosis), narrowing of the device (in-stent stenosis, reoperation, incomplete closure (occlusion) of the aneurysm, closure of a branch of a blood vessel)
- Deficits of the brain (neurological deficits), e.g. speech impediment (dysphasia), speech disorders, impaired vision, weakening of the eye muscles (oculomotor paresis), weakening or paralysis of one side of the body (hemiparesis or hemiplegia).
- Death

Only few quantitative data on the frequency of complications that occurred with the use of the DERIVO could be collected from the evaluated clinical data:

Technical problems:	7.2 %
Thromboembolic and ischemic events:	6.3 %
Procedure-related morbidity:	2.9 %
Procedure-related mortality:	0.9 %
Aneurysm rupture and bleeding/re-bleeding:	0.0 %
Procedure-related complications:	0.0 %
Angiography-related complications, i.e., arterial spams:	0.0 %

2.4.2 Warnings and precautions

Acandis gives comprehensive information on warnings, cautions and precautions for the user to ensure a safe and successful implantation of the DERIVO and DERIVO mini.
In the following, only the patient-related warnings and precautions are listed:

- The DERIVO and DERIVO mini should be applied only by physicians who have the necessary background knowledge and experience in the field of X-rays and treatment methods in the brain (interventional neuroradiology) and have the required expertise in the treatment of intracranial aneurysms.
- The effect of the pretreatment with anti-blood clotting drugs should be checked before the intervention to minimize potential complications.
- Anti-blood clotting drugs (antiplatelet agent and anticoagulant therapy prior to treatment and anticoagulants during the surgery). should be given accordance with the current guidelines from the medical societies.
- Drugs (the medication) are an important part of the treatment to avoid potential complications. For this reason, patients should regularly take the prescribed medication.
- Further embolization materials (appropriate drugs or small metal spirals) may be inserted via an additional small, flexible hollow tube (microcatheter).

2.4.3 Other relevant aspects of safety

Since market launch, there have been no relevant aspects of safety.

2.5 Summary of clinical evaluation and post-market clinical follow-up (PMCF)

For many types of vessel wall bulges in the brain (intracranial aneurysms; abbreviation: IAs), flow diversion with stents has rapidly become the treatment of choice because healing rates are high and rates of undesired effects are reasonably low (Dmytriw AA et al., 2019). Consequently, flow diverter stents have become important tools, replacing established treatment methods for many IA types (Maragkos GA et al., 2020). Flow diversion redirects the blood flow away from the aneurysm without the need for additional treatment techniques (Armoiry X et al., 2012; Walcott BP et al., 2016). Scientific literature reports that treatment with a flow diverter stent is effective, regardless of the aneurysmal rupture status (Walcott BP et al., 2017). Thus, complex, unruptured aneurysms (thought to be untreatable by established methods) may be treated with flow diverter stents (Lv X et al., 2016).
Flow diverter stents consist of a large number of braided wires with very small diameters (30 to 35 µm). Due to the braiding technique, the devices are porous. Therefore, small branches of a blood vessel receive sufficient blood flow (Zhu D et al., 2018).

However, incomplete vessel wall fitting may occur. Vessel wall fitting is important for the healing inside the blood vessel and the complete occlusion of the aneurysm (Maragkos GA et al., 2020). The use of flow diverter stents limits the re-treatment options (Raper DM et al., 2017).
The DERIVO and DERIVO mini belong to the Acandis DERIVO device family of flow diverter stents. The design and the material of these devices have been successfully applied for several years. The clinical performance and safety of the Acandis DERIVO and DERIVO mini and other flow diverter stents that are used for the treatment of IAs and other aneurysms has been well-proven in every day clinical practice. This is reported in general clinical literature, proven by records in governmental surveillance databases and data collected after market release.

Acandis presented one post-market clinical follow-up (PMCF) study in form of a prospective multi-center trial (Taschner CA et al., 2020). It was concluded that the DERIVO is a safe and effective treatment for unruptured aneurysms with high rates of satisfactory occlusion and comparably low rates of permanent neurological morbidity and mortality. Further PMCF activities are suspended because the current expertise with the DERIVO and the DERIVO mini does not facilitate the need for further PMCF activities.

The main risks related to the use of flow diverter stents and hence the DERIVO and DERIVO mini are described and documented in detail in the scientific literature. Therefore, medical specialists know how to prevent and manage these risks. The range and frequency of adverse events occurred with the DERIVO was comparable to other flow diverter devices on the market. To date, no unduly or, so far, unknown risks have been found in connection with the use of the DERIVO and DERIVO mini. Overall, the clinical literature rates the use of the product group of flow diverter stents - including the DERIVO and DERIVO mini - as safe and effective.
It can be concluded that the risk profile of flow diverter stents and hence the DERIVO and DERIVO mini is throughout known by medical professionals. The complications that may occur when the DERIVO and DERIVO mini are used constitute acceptable risks when weighed against the clinical benefit to the patient. The benefit-risk ratio of the devices is therefore acceptable. The devices achieve technical and clinical success rates which are comparable to a similar benchmark, well-established flow diverter stent and the whole device group of flow diverter stents for the treatment of IAs.

Considering the above, it can be stated that concerning safety and performance the DERIVO and DERIVO mini are state-of-the-art devices.

In conclusion, the DERIVO and DERIVO mini are state-of-the-art devices providing a clinical benefit to the patients and exhibiting an acceptable benefit-risk ratio. The DERIVO and DERIVO mini are in accordance with the provisions made by recent law and the safety and performance of the devices can be confirmed.

2.6 Possible diagnostic or therapeutic alternatives

Alternative treatment is open surgical operation; that means that a bone flap is temporarily removed from the skull to access the brain (craniotomy) followed by cutting off the aneurysm from blood flow (microsurgical clipping) (Armoiry X et al., 2012) and therapies performed from inside the vessel (endovascular) bearing the aneurysm (Byrne JV and Szikora I, 2012; Rouchaud A et al., 2015; Zhao J et al., 2017; Li S et al., 2022):

- Surgical closure of the vessel in which the aneurysm resides (parent artery occlusion)
- The medical doctor inserts one or more very small wires into the aneurysm until there is no more blood flow (coil embolization).
- Combination of coil embolization with a standard stent or balloon, which is placed under the aneurysm to prevent the coils from protruding into the vessel (stent- and balloon-assisted coiling).
- Placement of several overlapping stents.
- If possible: placing of clips next to the aneurysm to relieve the pressure in the aneurysm (aneurysm trapping).
- Wrapping: The lesion side of a ruptured aneurysm is wrapped with patient-own (autogenous) tissue or absorbable material to reconstruct the vessels.

In contrast to open surgical operation, therapies performed from inside the vessel is minimally invasive, circumventing the risks associated with open surgery. Nevertheless, there are several risks and complications, ranging from mild to severe, associated with therapies performed from inside the vessel such as flow diversion. Also, combinations of surgical and endovascular treatment techniques (hybrid techniques) were described (Gross BA et al., 2017).

2.7 Suggested profile and training for users

The DERIVO and DERIVO mini should be applied only by physicians who have the necessary background knowledge and experience in the field of X-rays and treatment methods in the brain (interventional neuroradiology) and have the required expertise in the treatment of intracranial aneurysms.

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