PulseCath iVAC 2L®

Types LV16 and LV17

Summary of Safety and Clinical Performance (SSCP)

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 devices.

The SSCP is not intended to replace the Instructions For Use as the main document to ensure the safe use of the device, nor is it intended to provide diagnostic or therapeutic suggestions to intended users or patients.

The following information is intended for users/healthcare professionals.

Reference number of the SSCP: SSCP iVAC 2L_Master_en-6

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1 Device identification and general information

1.1 Device trade name(s)

iVAC 2L

1.2 Manufacturer's name and address

PulseCath B.V.
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Breukelen
The Netherlands

1.3 Manufacturer's single registration number (SRN)

NL-MF-000006626

1.4 Basic UDI-DI

87179530372iVACEG

1.5 Medical device nomenclature

EMDN Code: C019001

Term description in English: AORTIC COUNTERPULSATION CATHETERS

1.6 Class of device

Class III

1.7 Year when the first certificate (CE) was issued covering the device

The LV17 type of the device was first CE marked in 2014 under the Medical Device Directive 93/42/EEC.

1.8 Authorized representative if applicable

Not applicable.

1.9 NB's name (the NB that will validate the SSCP) and the NB's single identification number

Notified Body Name: CE Certiso Orvos- és Kórháztechnikai Ellenőrző és Tanúsító Kft.

Notified body single identification number: 2409.

2 Intended use of the device

2.1 Intended purpose

The iVAC 2L devices, types LV16 and LV17, are intended for use in patients with impaired left ventricular function who require left ventricular mechanical circulatory support for up to 24 hours.

The iVAC 2L Tip should be positioned in the left ventricular cavity through the femoral artery.

Intended users

The iVAC 2L devices are intended to be used by healthcare professionals trained in interventional cardiology procedures.

2.2 Indications and target populations

A cardiologist and or cardiac surgeon will determine if support with the iVAC 2L is the appropriate option. This is based on one or more of the following clinical and/or anatomical criteria.

Clinical criteria:

- Acute coronary syndromes (ACS)
- Chronic kidney disease
- Diabetes mellitus
- Hemodynamic instability
- Left ventricular ejection fraction (LVEF) of <40%
- Previous cardiac surgery

Anatomical criteria:

- Diffuse Coronary Artery Disease (CAD)

- Last patent conduit
- Multivessel disease
- Severe coronary total occlusion
- Severely calcified lesions needing rotational atherectomy
- Unprotected left main coronary disease involving bifurcation

Intended populations and medical conditions to be treated:

The range of patient groups that potentially can benefit from the devices is broad, for example patients suffering from Acute Myocardial Infarction (AMI), cardiogenic shock, candidates for high-risk Percutaneous Coronary Intervention (HR-PCI) including high-risk ablation and mapping.

2.3 Contraindications and limitations

The iVAC 2L devices have the following contraindications:

1. Aortic disease: ascending aortic aneurism, severe aortic wall calcifications
2. Aortic valve disease: aortic valve stenosis, aortic valve insufficiency
3. Aortic valve prosthesis
4. Femoral artery stenosis
5. Aneurism of the aorta
6. Thrombus in left ventricle
7. Ejection fraction lower than 10%
8. “Right ventricular failure”

The iVAC 2L devices have the following limitations:

- The iVAC is safe for use up to 24 hours. There is limited clinical data to support the safe application of the iVAC beyond this time point.
- The iVAC functions are sub-optimal at heart rates lower than 60 bpm or higher than 120 bpm.
- Use of the internal triggering mode of the intra-aortic balloon pump (IABP) driver will decrease the functioning of the iVAC.
- The iVAC is not suitable for mobile use.

3 Device description

3.1 Description of the device

The iVAC 2L devices are percutaneous circulatory support devices, that assist the pump function of the heart in patients with impaired left ventricular function. The iVAC 2L devices consist of four sterile, single use functional parts: a catheter (LV16 Catheter or LV17 Catheter) with insertion set, a single port Membrane Pump, a PTFE Catheter Inner Tube and a Catheter Protector. Refer to Figure 1 for a schematic representation of the device.

The iVAC 2L devices are designed to be used in combination with an IABP driver.

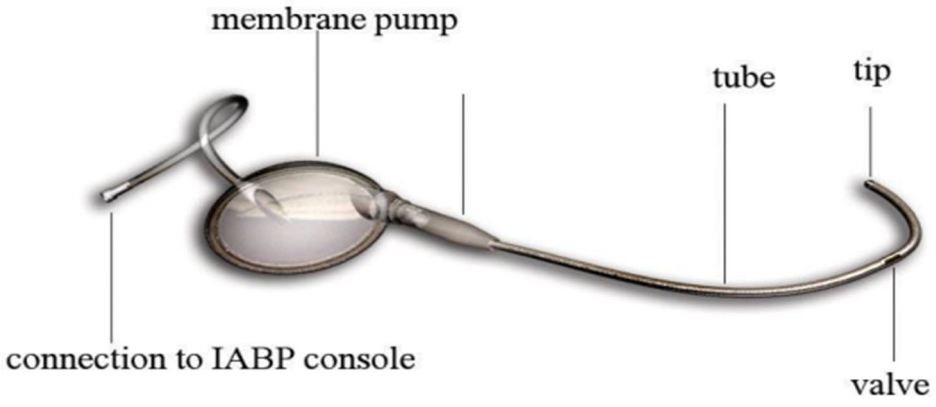

Figure 1. Schematic view of the iVAC 2L devices: it consists of a catheter part, connected to a Membrane Pump. During functioning, the iVAC-tip is positioned in the heart and the iVAC-valve in the descending aorta.

Key functional parts:

The iVAC 2L consists of four sterile packaged, single use functional parts:

1. LV16 or LV17 Catheter with Insertion Set
2. Membrane Pump
3. Catheter Protector
4. Extra PTFE Catheter Inner Tube

LV17 / LV16 Catheter with insertion set

The LV17 / LV16 Catheter is composed of the inlet tip, an integrated two-way iVAC valve and a connector at the distal end (Figure 2). The difference between the LV17 Catheter and LV16 Catheter is the diameter (5.66 mm vs 5.33 mm respectively).

The insertion set is further described below.

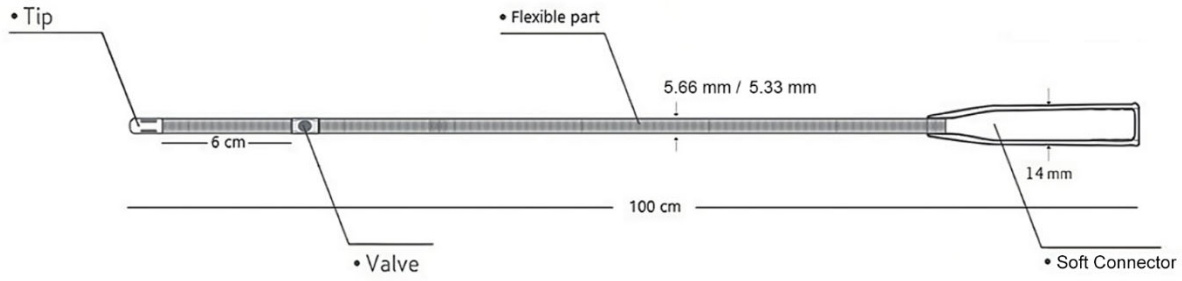

Figure 2. Drawing of a LV17 / LV16 Catheter.

Membrane pump

The membrane pump has a flexible membrane which divides it into a blood chamber and a gas chamber. The blood chamber side is connected to the catheter part, while the gas chamber side is connected to a pneumatic IABP driver.

PTFE Catheter Inner Tube

The insertion set exists of two parts, a plug with side-arm and an inner tube.

The inner tube part of the insertion set that is placed inside the LV16 / LV17 Catheter upon delivery, is replaced by the PTFE Catheter Inner Tube before the insertion procedure. The haemostasias valve at the proximal end of the Inner Tube allows the use of a guide wire.

Catheter protector

The Catheter Protector, is intended to be placed around the LV16 / LV17 Catheter where the sutures are tightened to prevent the catheter from kinking.

Materials of construction

Materials used for production of the iVAC 2L that come into contact with the patient blood or tissue are: Acrylonitrile Butadiene Styrene (ABS), Cyrolite (acrylic-based copolymer compounds), Methacrylate Acrylonitrile Butadiene Styrene (MABS), Polyurethane (PU), Stainless Steel, Polycarbonate (PC) and Polytetrafluoroethylene (PTFE).

Sterilization

The Membrane Pump and PTFE Catheter Inner Tube are sterilized by Ethylene Oxide gas. The Catheter with Insertion Set and Catheter Protector are sterilized by gamma irradiation sterilization.

3.2 A reference to previous generation(s) or variants if such exist, and a description of the differences

The iVAC 2L is the second model that PulseCath has placed on the market. The first iVAC model was the iVAC 3L. The main difference is that the iVAC 3L was intended for surgical introduction into the right subclavian artery or directly into the ascending aorta. The reason for the changing was that introduction of the iVAC 2L through the femoral artery does not require the intervention of a cardiac surgeon.

There are two types of the iVAC 2L, one with a 16Fr catheter (LV16) and one with a 17Fr catheter (LV17).

3.3 Description of any accessories which are intended to be used in combination with the device

Not applicable.

3.4 Description of any other devices and products which are intended to be used in combination with the device

- IABP driver.
- Introducer Sheath, with minimum inside diameter of 16Fr for the LV16 catheter and 18Fr minimum for the LV17 catheter.
- Guide wire: 0.035” or 0.038”, length 260 cm (Super Stiff) and corresponding needle.
- Heparinized saline (2500 IU heparin in 500 mL saline).
- When using an Arrow ACAT1, AutoCat2Wave or AC3 IABP driver: Arrow Pump adapter for 50 cc IABs (Datascope, ref. 0684-00-0501-02).

4 Risks and warnings

4.1 Residual risks and undesirable effects

Invasive procedures should not be attempted by physicians unfamiliar with the possible complications. Complications may occur at any time during the procedure.

Possible complications that have occurred (rate of occurrence) and may occur (not reported) include, but are not limited to the following:

- Acute kidney Injury (<3%)
- Acute Myocardial Infarction (<2%)
- Cardiac arrest requiring CPR (<3%)
- Cerebro-vascular Accident (CVA) (<3%)
- Death (<6%)
- Hemolysis (not reported)
- Induction of mitral valve incompetence (not reported)
- Infection (not reported)
- Injury to the aortic valve (not reported)
- Ischemia of the leg due to obstruction of the femoral artery (<2%)
- Major Bleeding (<2%)
- Mechanical trauma to the heart and inner structures (not reported)
- Perforation of the access site (<2%)
- Repeat revascularization (not reported)
- Severe hypotension (<12%)
- Thrombosis at the insertion site (assuming angiographic finding) (<2%)
- Thrombosis when the device is stopped for a longer period of time (not reported).

4.2 Warnings and precautions

- Read these instructions carefully before use.
- These instructions describe the use of the iVAC in combination with IABP drivers (Datascope 98XT, CS100 and CS300 and Cardiosave Hybrid IABP driver, Arrow Acat 1 and AutoCat2wave and AC3). This manual does not replace the IABP driver’s manual.
- Be sure that all relevant personnel is adequately trained in using the iVAC and the IABP driver. Personnel involved in using the iVAC 2L require specific training on the procedure steps and the use of the IABP driver with the iVAC 2L. In addition, a supervised procedure guided by a PulseCath representative is part of the training.
- Do not reintroduce the insertion set once removed from the catheter.
- Do not leave the device dormant for extended periods of time in order to prevent formation of thrombi.
- In case of problems, please contact the manufacturer.
- The iVAC is for single use only. Do not Reuse or re-sterilize! Reuse or re-sterilization will compromise the mechanical properties of the device which may lead to device failure. As a result, the patient might be injured or die. Reuse or re-sterilization will also create a risk of contamination of the device. Contamination may cause patient infection, illness or death of the patient.
- All components are sterilized by ethylene oxide or gamma radiation.

- After use, dispose of product and packaging in accordance with hospital, administrative and/or local government policy.
- Patients should be kept sedated during use.
- Assure the femoral artery diameter is sufficiently large prior to inserting the iVAC. For femoral arteries with a diameter of ≥ 6.8 mm the LV17 type is recommended, for femoral arteries of ≥ 6.0 mm, the LV16 is recommended.
- Do not use alcohol containing detergents to clean or disinfect the device prior to removal, as these might damage the device which could lead to leakage of parts of the device.
- Do not use tie-wraps to fasten the connection between the catheter and the membrane pump, as tie-wraps can cause leakage of the connection.
- Beware of needle sticks into the catheter: a puncture of the catheter will immediately cause aspiration of air into the device, resulting in the air being ejected in the aorta of the patient. Switch off the IABP driver immediately when a problem is suspected.
- For a Datascope IABP driver, “IAB” in help screens should be read as “iVAC”.
- Assure that the membrane pump driveline remains connected to the IABP driver. Also assure the membrane pump driveline is not kinked or compressed. A loose connection or kink will disturb the pumping action of the iVAC.
- It is recommended to flush both ports of the LV16 / LV17 catheter with insertion set every 5 minutes with heparinized saline after insertion, as long as the insertion set has not been removed. Make sure the insertion set is fully de-aired before flushing.

4.3 Other relevant aspects of safety, including a summary of any field safety corrective action (FSCA)

The device has not been subject to a FSCA.

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

5.1 Summary of clinical data related to equivalent device

The conformity of the LV16 type was assessed and endorsed by the Notified Body on the basis of equivalence. The equivalence was demonstrated to the LV17 type of the iVAC 2L. Both devices have the same device name, Basic UDI-DI and manufacturer. This SSCP applies to both types of the device and will be available in Eudamed. The clinical evidence for the LV16 type was obtained using the LV17 type.

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

The first clinical data with the iVAC 2L was obtained during a clinical investigation. These data were used for CE marking of the device under the Medical Device Directive 93/42/EEC (MDD).

Note: for CE marking of the iVAC 2L under the MDD clinical data obtained with the previous generation of the device, the iVAC 3L, was leveraged.

Identity of the study

Title: Evaluation of the PulseCath® iVAC 2L, a Pulsatile Catheter Pump, PulseCath® in high-risk PCI patients who need cardiac assist

Sponsor: PulseCath B.V.

Publication of study results: Uil, C. A. D. *et al. EuroIntervention* 12, 1689–1696 (2017)[1]

Identity of the device

iVAC 2L, catalogue number (REF) LV17

Intended use of the device in the investigation

The iVAC 2L is intended for use in high-risk PCI patients who require left ventricular assistance.

Objectives of the study

To evaluate the safety and efficacy of the iVAC 2L in HR-PCI patients who require left ventricular assistance in a prospective single-center single-arm feasibility study.

Study design

A prospective single-center single-arm feasibility study.

Study endpoint(s)

Safety endpoints:

1) no CVA's,
2) no thrombo-embolic events,
3) degree of hemolysis remains manageable.

The efficacy endpoints:

1) the insertion, positioning, fixation and removal of the iVAC 2L has been performed without any injury of valvular or vascular structures, and the device has not caused perfusion disorders of the peripheral arteries.
2) Cardiac Index (CI) > 2.5 L/min/$m^{2;}$ Mean Arterial Pressure > 60 mmHg can be maintained during support.

Clinical success is achieved when the patient has successfully been weaned from the device.

Inclusion/exclusion criteria for subject selection

Inclusion Criteria:

- Indicated for HR-PCI , according to hospital standard procedure
- Indicated to have an IABP during the PCI, according to hospital standard procedure
- Expected duration of iVAC 2L support: maximum 24 hours
- Patient older than 18 years
- Patient or legal representative has signed the Informed Consent

Exclusion Criteria:

- Aortic disease: ascending aortic aneurism, severe calcified aorta
- Aortic valvular disease: severe aortic valve stenosis, severe aortic valve insufficiency
- Aortic mechanical valve prosthesis
- Thrombus in left ventricle
- Intra ventricular septum defect
- Severe peripheral vascular disease
- No functioning right ventricle
- History of coagulation disorders
- Participation in another clinical study that may interfere with this study Recent (> 6 m) CVA and/or a residual modified Rankin Score > 2 at baseline

Number of enrolled subjects

Twelve subjects were enrolled in the study. One subject has been excluded from further analysis. From this subject, no Multi-Slice Computer Tomography-scan was performed to assess the conditions of the femoral artery. This was done to safe the subject, that had renal failure, the additional burden of contrast media.

Study population

Total patients (n)	11
Male (n, %)	6 (54.5)
Female (n, %)	5 (45.5)
Average age (year, range)	72 (56 – 83)
Average length (cm)	171 (150 – 184)
Average weight (kg)	83 (60 – 122)
Average body surface area (m^2)	1.99 (1.58 – 2.40)

Summary of study methods

At baseline, patients underwent transthoracic echocardiography and echo of the femoral artery to determine the quality of the access vessel and the minimum required diameter of the femoral artery of (6 mm). iVAC 2L procedure was performed according to the instructions for use. In addition, baseline biochemistry work was performed. Preoperative, perioperative, and postoperative data were collected. Patients were scored using the CI, the Ejection Fraction, the European System for Cardiac Operative Risk Evaluation (EuroSCORE), the congestive heart failure classification (New York Heart Association), and the angina classification (Canadian Cardiovascular Society classification).

Summary of results
The average Mean Arterial Pressure was well above 60 mmHg during support. The Cardiac Index as well as the Cardiac Output indicate clinical success. There were no CVA's or major vascular or access site bleeding complications; the degree of hemolysis was manageable; there were no life-threatening ventricular arrhythmias or valvular complications; no transfusion was necessary. All patients were successfully weaned from the device within 24 hours after insertion.

Limitations of the study
The data obtained through this study is a single-center, uncontrolled observational study with a relatively small sample size. Because the study was carried out in a single center with high expertise, the required access-site management with large bore catheters was available. One should, therefore, be cautious in generalizing the reported absence of access-site and bleeding complications. Without a control group, the changes in the hemodynamic measurements may theoretically be due to factors other than the iVAC 2L support.

Any device deficiency
No device deficiencies occurred during the study.

5.3 Summary of clinical data from other sources

Two other prospective clinical studies with the iVAC 2L have been conducted after the device was CE marked.

The first study was an investigator-initiated study published by Samol et al[2]. The study was a prospective trial to investigate the performance of the pulsatile iVAC 2L system to provide circulatory support in 20 patients undergoing HR-PCI.

The second study (PULSE Trial) is an investigator-initiated study, that prospectively enrolled 29 individuals with heart-team indication for (elective) mechanically assisted HR-PCI using iVAC 2L[3].

The clinical data from these studies is summarized in the next sections.

5.4 An overall summary of the clinical performance and safety

PulseCath maintains a Post-Market Surveillance (PMS) registry with collected clinical data from patients undergoing iVAC 2L supported treatment. The PMS registry includes published reports and collected case report forms filled in by operators after use of the device. Refer to *Table 1* for an overview of the data sources. As a limitation, 30 days clinical endpoints are rarely available as the data collection relies on the willingness of local teams to collaborate with the registry effort. For this reason, the clinical endpoints reported in this document do not include the whole sample of 406 patients that has been gathered up to now.

Table 1. Clinical Data sources

Data source	Year	Number of patients	Reference
Published Study	2017	14	1
Published Study	2019	20	2
Published Study	2022	29	3
Published case report	2015	1	4
Published case report	2017	1	5
Published case report	2018	1	6
Published case report	2018	1	7
Published case report	2020	1	8
Published case report	2020	1	9
Published case report	2020	1	10
Published case report	2021	1	11
Published case report	2022	1	12
Published case report	2022	1	13
Published case report	2023	1	14

Data source	Year	Number of patients	Reference
Published case report	2024	1	[15]
Published retrospective cohort	2024	293	[16]
PMS registry	2024	406	Not applicable

Currently, the PMS registry includes a total of 406 unique cases that originate from 148 different centers across 41 countries worldwide.
After exclusions, two cohorts have been defined, the HR-PCI Cohort (n = 367) and the Emergent Cohort (n = 33).
The emergent cohort was composed by patients whose interventions were qualified as emergent by their operators. That includes patients undergoing primary PCI (a PCI in the context of an acute myocardial infarction), acute decompensated heart failure, cardiogenic shock, and one case of ventricular septal defect.

A summary of the patient demographics included in the iVAC 2L cohorts is exposed in *Table 2*.

Table 2. Demographic characteristics of the whole registry.

Variable	Elective HR-PCI Cohort	Emergent Cohort
Number of observations available	**367**	**33**
Operator	**154**	**25**
Site	**140**	**20**
Country	**40**	**15**
Age (years)	**71 (64 to 77)**	**70 (67 to 77.5)**
SYNTAX I score	**33 (27 to 39)**	**40.43±11.21**
Weight (Kg)	**80 (70 to 89)**	**80.9±16.4**
Height (cm)	**173 (168 to 177)**	**170 (162.5 to 175)**
Left Ventricular Ejection fraction (%)	**30 (25 to 40)**	**25 (20 to 35)**
Gender (Male) (%)	**87**	**78.1**
Ejection Fraction < 40% (%)	**69**	**75.8**
Three-vessel disease (%)	**56**	**80**
Stented left main artery (%)	**58**	**65.5**
Stented left anterior descending artery and branches (%)	**75**	**72.4**
Stented left circumflex artery and branches (%)	**54**	**55.2**
Stented right coronary artery and branches (%)	**32**	**24.1**

Operator, site and country are described as counts. Continuous data is exposed as medians (interquartile range) or mean±SD. Frequencies are exposed as percentages (%) of observations available.

The main clinical outcomes are shown in *Table 3*.

Table 3. Clinical Outcomes

Variable	Elective HR-PCI Cohort	Emergent Cohort
n	367	33
Support time (min)	68 (49 to 102)	60 (37.5 to 92.5)
Maximum flow (L/min)	1.6 (1.5 to 1.8)	1.6 (1.2 to 1.7)
Interruption of support (%)	1.4	6.1
In-hospital death (%)	1.4	3.03 (1/33)

Variable	Elective HR-PCI Cohort	Emergent Cohort
All-cause mortality (30 days) (%)	9.1	37.5 (3/8)
CVA (%)	1.1	0
AMI (%)	0.8	3.12 (1/32)
Repeat revascularization (%)	0	0
Major bleeding (%)	1.7	0 (0/32)
Major vascular complications (%)	0.8	0 (0/32)
Acute kidney Injury (%)	1.1	6.25 (2/32)
Severe hypotension (%)	11.0	39.39 (13/33)
Cardiopulmonary resuscitation	2.8	12.5 (4/32)
Aortic Insufficiency (%)	Not reported	Not reported
Angiographic Failure (%)	0.6	0
MACE (30 days) (%)*	17	37.5 (3/8)
3737MACE (in-hospital) (%)	3.0	3.12 (1/32)

**Major adverse cardiac and cerebrovascular events (MACE): composite endpoint of death, acute myocardial infarction, stroke and repeat revascularization. Continuous data is exposed as median (interquartile range). Frequencies are exposed as percentages (%) of observations available.*

5.4.1 Evaluation of the clinical data

The range of adverse events that can be triggered by iVAC 2L is equivalent to those observed with other transvalvular percutaneous Mechanical Circulatory Support (MCS) devices.

5.4.2 Endpoints in comparison to alternative treatments

The key clinical endpoints available on the iVAC 2L have been compared with available clinical data on the Impella 2.5/CP, which is considered the most appropriate therapeutic alternative (see chapter 6).

Among all individuals who received iVAC 2L with the indication of high-risk PCI, the data shows a 17% MACE rate after 30 days. In contrast, pooled data from two early studies performed in high-risk PCI [17,18] indicate that the expected MACE rates in high-risk PCI without MCS can reach up to 17%. Compared to 4 major studies applying transvalvular devices in high-risk PCI [19–22], iVAC 2L shows one of the lowest rates of MACE, with only two studies reporting lower rates. The Europella registry report, published in 2009[20], shows a 12.4% rate of MACE which also included major bleeding among its components. The authors reported a 6.2% rate of major bleeding and 0.7% rate of hemolysis, while no reports have been published until the present date describing the occurrence of clinically relevant hemolysis with iVAC 2L. The second registry was published three years later by O`Neill et al[22], reporting the outcomes of 175 patients undergoing elective PCI with Impella 2.5. The study reports an 8% rate of MACE but mentions issues with under-reporting. In this manner, it is reasonable to expect that the real rates were actually higher than that.

5.4.3 Safety in comparison to large bore catheters

Safety endpoints have also been compared with published data on large bore catheter studies. Regarding bleeding and vascular complications, the rates found with the iVAC 2L compares favorably with previous data on large-bore catheterizations (> 7Fr). The rates of major vascular complication and major bleeding with the iVAC 2L are lower than previous studies applying similar catheter profiles in the current decade with range of 6-17% and 3-36% respectively[23–31].
If red blood cell transfusion is considered as a proxy for major bleeding, the difference relative to the rate observed with iVAC 2L deepens. Not reported for the iVAC 2L versus 1.6-11% in other studies[24,27,28,30].

5.4.4 Conclusions on clinical performance, safety and benefit-risk

The benefit of the iVAC 2L is that it effectively provides hemodynamic support in patients with impaired left ventricular function.

There is an inherent risk with the use of MCS for undesirable side-effects, but the benefits of providing hemodynamic support with the iVAC 2L favors these risks.

In comparison to other devices on the market that may be used to provide hemodynamic support, the iVAC 2L has demonstrated to be non-inferior in terms of risk-profile. In conclusion, the benefit-risk profile is favorable.

5.5 Ongoing or planned post-market clinical follow-up

PulseCath has several PMCF activities ongoing in accordance with the PMCF plan for the iVAC 2L devices. To date, there are no unanswered questions relating to the use of the device, nor have any emerging risks, complications or unexpected device failures been detected.

PulseCath has set-up a PMS registry of the iVAC 2L. The iVAC 2L registry retrospectively collects clinical data from patients undergoing PulseCath iVAC 2L supported interventions with a variety of indications. The data derives from published studies, medical records and from reports provided by PulseCath personnel who are on-site during the interventions or from the healthcare professional. On-site data is registered after the interventions on a voluntary basis in a specific form “PulseCath iVAC 2L Post Market Surveillance Form”. Additionally, clinical data is gathered through an open prospective multicenter registry according to the iVAC 2L Registry Protocol.

Currently, the available clinical data on support with the iVAC 2L is mostly on patients undergoing elective and semi-elective cases for treatment of Coronary Artery Disease. Gathering more clinical data on the use of the iVAC 2L in patients suffering from cardiogenic shock and acute heart failure is an additional goal of the PMCF plan.

PulseCath monitors the evolution of new and current alternative treatments and continually compares the available data with the available data on the iVAC 2L. PulseCath gathers input from key opinion leaders involved in world leading academic research and investigators in multiple ongoing international trials for new treatments in the field of interventional cardiology.

Expert input is requested from the clinical experts from the Erasmus Medical Center, Rotterdam, The Netherlands.

Also, a formal literature search is performed for the identification of literature relevant to the evaluation of the current state of the art (SOTA) or standard of care treatment options appropriate for use in the same indications and patient populations as the device under evaluation. The search also aims to identify if there is any new clinical data available on similar devices.

By monitoring the evolution of state of the art and alternative treatments, the aim is to ensure the continued acceptability of the benefit-risk ratio.

When PulseCath becomes aware of ongoing investigator initiated studies with the iVAC 2L, PulseCath intends to gather feedback from the investigator to identify possible aspects related to the safety and effectiveness of the device during study. When the data is published, it is appraised and analyzed in the clinical evaluation. The aim of this activity is:

• Confirming the safety of the medical device

• Confirming the performance of the medical device

• Identifying previously unknown side-effects (related to the procedures or to the medical devices).

• Monitoring the identified side-effects and contraindications

• Identifying and analyzing emergent risks

• Ensuring the continued acceptability of the benefit-risk ratio

All PMCF data is analyzed for the continuous evaluation of the benefit-risk ratio of the iVAC 2L.

6 Possible therapeutic alternatives

There are several other therapeutic alternatives for providing circulatory support. This includes:

- Percutaneous Left Ventricular Assist Devices (pLVADs),
- Intra-aortic balloon pump,
- Extra-corporeal Membrane Oxygenation (ECMO) and
- Pharmacological therapy.

The Impella device family (pLVADs), manufactured by ABIOMED, is considered the closest therapeutic alternative [3,32,33]. The Impella devices are catheter-based, continuous axial flow pumps with a propeller at the tip of the catheter, which is positioned in a retrograde way across the aortic valve. The positioning technique is very similar to that of the iVAC 2L. The main difference with the iVAC 2L is that the Impella devices provide

continuous flow, instead of pulsatile flow. Both Impella CP and iVAC 2L are suitable for short-term MCS in catheterization laboratories and in operating rooms. However, besides the use of non-pulsatile flow, Impella also carries a higher risk of hemolysis, while no reports of clinically relevant hemolysis with iVAC 2L have been documented until today. When it is expected that a patient will require longer support than 24 hours, the Impella CP could be considered as it is approved for support up to 5 days [34–36].

The IABP is positioned outside the left ventricle where it applies counter-pulsation to reduce the left ventricular afterload. The effect of counter-pulsation may increase the cardiac output. However, the output flow produced by the IABP is approximately 0.5 L/min. This is lower compared to the iVAC 2L (up to 2.0 L/min). When activated, the IABP does not drain the left ventricle as does the iVAC 2L and other MCS devices. Since the balloon is positioned outside the left ventricle, it results in limited hemodynamic impact and is strongly dependent on the presence of enough residual left ventricular function. The IABP is technically feasible for most Interventional Cardiologists, but the latest guidelines do not recommend its routine use in acute coronary syndromes or in high-risk PCI [22,37–39].

The other two short-term MCS modalities are the Tandem Heart (TH) and ECMO. Each of them has particular features that make them substantially different from iVAC 2L. The differences range from methods of implantation to indications. Both TH and ECMO require an outlet cannula to be positioned in the descending aorta through the femoral artery, but in the case of TH, an inlet cannula has to be positioned in the left atrium via trans-septal puncture. TH can be used in selected cases where there is need for a pLVAD but the trans-aortic pathway is not accessible, as it occurs in the presence of prosthetic aortic valves. The downside is that the TH is more likely to complicate post-procedurally [40–42].

Peripheral ECMO requires an inlet cannula placed in the vena cava or right atrium. The circuit is connected to an oxygenator and blood is ejected in a retrograde way. This outlet configuration, which is similar to TH, causes the pump to eject blood against the native heart. The resulting effect is an acute increase in the afterload that may eventually overload the left ventricle and cause brain hypoxia. Evidence points that this undesirable effect can be countered by the use of a transaortic device such as the iVAC 2L as a venting tool simultaneously with ECMO. ECMO is not equivalent to iVAC 2L. Given their many differences, it should not be regarded as a therapeutic alternative, but rather as an adjunctive tool.

Overall, ECMO is the most drastic means of short-term MCS to be available in catheterization laboratories. It may be life-saving in certain circumstances, but it is also reportedly associated with increased mortality and vascular complications. Both ECMO and TH apply high-speed centrifugal pumps and are linked with higher rates of hemolysis, similarly to the Impella [40–43]. While the TH can be used as a pLVAD in the same way as iVAC 2L, ECMO is in general a last measure that is reserved to severe cases where circulatory collapse is already established and there is hypoxemia. In stable patients undergoing high-risk interventions, iVAC 2L has a better benefit-risk relation.

Besides MCS, pharmacological therapy may be considered as well. Pharmacological alternatives are represented by inotropes. In clinical practice, the inotrope of choice is Dobutamine which has a rapid onset of action and a short half-life. It increases myocardial contractility, while in response to augmentation of stroke volume, leads to a decrease in total peripheral resistance. The expected hemodynamic effects are an increase in cardiac output and a decrease in systemic vascular resistance without significant change in arterial pressure or heart rate. This occurs at the cost of being arrhythmogenic and increasing myocardial oxygen consumption.

Despite the availability of pharmacological treatments for acute heart failure, there are still no drugs that can substitute MCS devices. Current evidence shows that they can actually worsen clinical outcomes [44]. The use of vasoactive drugs has lower benefit-risk relative to MCS and IABP [45].

7 Suggested profile and training for users

The iVAC 2L devices are intended to be used by healthcare professionals trained in interventional cardiology procedures.
Personnel involved in using the iVAC 2L require specific training on the procedure steps and the use of the IABP driver with the iVAC 2L. In addition, a supervised procedure guided by a PulseCath representative is part of the training.

8 Reference to harmonised standards and Common Specification applied

EN 556-1:2024 Sterilization of medical devices — Requirements for medical devices to be designated “STERILE” — Part 1: Requirements for terminally sterilized medical devices

EN ISO 10993-10:2023 Biological evaluation of medical devices – Part 10: Tests for skin sensitization (ISO 10993-10:2021)
EN ISO 10993-12:2021 Biological evaluation of medical devices - Part 12: Sample preparation and reference materials (ISO 10993-12:2021)
EN ISO 10993-23:2021 Biological evaluation of medical devices – Part 23: Tests for irritation (ISO 10993-23:2021)
EN ISO 11135:2014/A1:2019 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)
EN ISO 11137-1:2015/A2:2019 Sterilization of health care products - Radiation - Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices (ISO 11137-1:2006, including Amd 1:2013)
EN ISO 11137-2:2015/A1:2023 Sterilization of health care products – Radiation - Part 2: Establishing the sterilization dose (ISO 11137-2:2013)
EN ISO 11607-1:2020/A1:2023 Packaging for terminally sterilized medical devices - Part 1: Requirements for materials, sterile barrier systems and packaging systems (ISO 11607-1:2019)
EN ISO 11607-2:2020/A1:2023 Packaging for terminally sterilized medical devices - Part 2: Validation requirements for forming, sealing and assembly processes (ISO 11607-2:2019)
EN ISO 11737-1:2018/A1:2021 Sterilization of health care products - Microbiological methods - Part 1: Determination of a population of microorganisms on products (ISO 11737-1:2018)
EN ISO 11737-2:2020 Sterilization of health care products - Microbiological methods - Part 2: Tests of sterility performed in the definition, validation and maintenance of a sterilization process (ISO 11737-2:2019)
EN ISO 13485:2016/A11:2021 Medical devices – Quality management systems – Requirements for regulatory purposes (ISO 13485:2016)
EN ISO 15223-1:2021 Medical devices - Symbols to be used with information to be supplied by the manufacturer - Part 1: General requirements (ISO 15223-1:2021)
EN ISO 14971:2019/A11:2021 Medical devices – Application of risk management to medical devices (ISO 14971:2019)

No applicable common specifications under the European Medical Device Regulation are available at this point.

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9 Revision history

SSCP revision number	Date issued	Change description	Revision validated by the Notified Body
0	2024-02	New document	☒ Yes Validation language: English ☐ No
1	2024-05	Addition of LV16 variant to scope. Change of PulseCath address from Arnhem to Breukelen.	☐ Yes Validation language: English ☒ No
2	2024-10	Removal of LV16 variant from scope.	☒ Yes Validation language: English ☐ No
3	2024-10	Integration of LV16 type to scope as equivalent device.	☒ Yes Validation language: English ☐ No
4	2025-03	Updated with new clinical data. Extended list with residual risks. Added warning on sterilization methods. Updated references to harmonized standards.	☒ Yes Validation language: English ☐ No

SSCP revision number	Date issued	Change description	Revision validated by the Notified Body
5	2025-6	Updated with new clinical data and revision of PMCF Plan. Updated Contraindications: Replaced “No residual function of left ventricle” with “Ejection fraction lower than 10%”. Updated list of complications according revised IFU. Updated references to harmonized standards.	☒ Yes Validation language: English ☐ No
6	2025-10	Removed list of abbreviations. Changed rate for reported severe hypotension from <10% to <12%. Added missing data point table 3.	☒ Yes Validation language: English ☐ No