Results of the combined U.S. multicenter postapproval study of the Nit-Occlud PDA device for percutaneous closure of patent ductus arteriosus

Daisuke Kobayashi MD1 | Morris M. Salem MD2 | Thomas J. Forbes MD1 | Brent M. Gordon MD3 | Brian D. Soriano MD4 | Vivian Dimas MD5 | Bryan H. Goldstein MD6 | Carl Owada MD7 | Alexander Javois MD8 | John Bass MD9 | Thomas K. Jones MD4 | Darren P. Berman MD10 | Matthew J. Gillespie MD11 | John W. Moore MD12 | Daniel S. Levi MD13

1Division of Cardiology, Children's Hospital of Michigan, Carman and Ann Adams Department of Pediatrics, Wayne State University School of Medicine, Detroit, Michigan
2Department of Pediatrics, Division of Cardiology, Kaiser Permanente, Los Angeles, California
3Division of Pediatric Cardiology, Loma Linda University Children's Hospital, Loma Linda, California
4Division of Pediatric Cardiology, Seattle Children's Hospital, Seattle, Washington
5Division of Cardiology, Department of Pediatrics, University of Texas Southwestern Medical Center, Children's Health System of Texas, Dallas, Texas
6The Heart Institute, Cincinnati Children's Hospital Medical Center, University of Cincinnati College of Medicine, Cincinnati, Ohio
7Valley Children's Hospital, Madera, California
8Division of Cardiology, Advocate Children's Hospital, University of Illinois School of Medicine, Oak Lawn, Illinois
9University of Minnesota Masonic Children's Hospital, Minneapolis, Minnesota
10Division of Cardiology, Nationwide Children's Hospital, The Ohio State University, Columbus, Ohio
11Cardiac Center, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania
12Division of Cardiology, Rady Children's Hospital, University of California, San Diego School of Medicine, San Diego, California
13Division of Cardiology, Mattel Children's Hospital at University of California Los Angeles, Los Angeles, California

Abstract

Objectives: To report the results of the Nit-Occlud PDA prospective postapproval study (PAS) along with a comparison to the results of the pivotal and continued access trials.

Background: The Nit-Occlud PDA (PFM Medical, Cologne, Germany), a nitinol coil patent ductus arteriosus (PDA) occluder, was approved by the Food and Drug Administration in 2013.

Methods: The PAS enrolled a total of 184 subjects greater than 6 months of age, weighing at least 5 kg, with PDAs less than 4 mm by angiography at 11 centers. Patients were followed prospectively at 2 months, 12 months, and 24 months postprocedure. These outcomes were compared to the 357 subjects enrolled in the pivotal and continued access protocols. Efficacy and safety data were reported.

Results: Among 184 subjects enrolled for the PAS between 2014 and 2017, 180 (97.8%) had successful device implantation. After 12 months, 98.7% (150/152) had trivial or no residual shunt by echocardiography and two subjects had only small residual shunts. There were three...
INTRODUCTION

Patent ductus arteriosus (PDA) is one of the common congenital heart diseases. Transcatheter closure of PDA is indicated for medium- to large-sized PDA and small audible PDAs.² The Nit-Occlud PDA (PFM Medical, Cologne, Germany) is a nitinol coil designed with two cones of spirals specifically for use as a PDA occluder. Its premarket approval was approved by the Food and Drug Administration in 2013 based on the results of the pivotal trial. The Nit-Occlud is currently approved in the US for closure of PDAs smaller than 4 mm in infants greater than 5 kg and 6 months of age. The result of the combined United States multicenter pivotal and the continuing access study was reported in 2014, showing the excellent efficacy and safety of the Nit-Occlud PDA for closure of small- to medium-sized PDA.²

The Nit-Occlud PDA postapproval study (PAS) was designed to continue to evaluate the safety and efficacy of the Nit-Occlud PDA device in the postapproval phase. The objective of this study was to report the results of the Nit-Occlud PDA prospective PAS along with a comparison to the results of the pivotal and continued access trial.

MATERIALS AND METHODS

Device and procedure

The Nit-Occlud PDA device is a nitinol coil designed for PDA closure. The device specification has been previously described in detail.² The Nit-Occlud PDA device has a reverse-cone shape having proximal and distal coils that is made to fit into the ductal ampulla and anchor to the pulmonary side of the PDA (Figure 1A). There are six sizes available: 4 × 4 mm, 5 × 4 mm, 6 × 5 mm, 7 × 6 mm, 9 × 6 mm, 11 × 6 mm. Each device is named by diameter of distal coil diameter x proximal coil loop diameter. The smaller “Flexible” devices (4 × 4 mm, 5 × 4 mm, 6 × 5 mm) can be delivered through a 4-Fr delivery catheter, whereas the larger “Medium” devices (7 × 6 mm, 9 × 6 mm, 11 × 6 mm) require a 5-Fr delivery catheter. The size of device is selected according to the angiographic measurement of PDA on lateral aortography. The distal coil diameter should be no more than 2 mm larger than the aortic ampulla diameter and at least 3-4 mm larger than the pulmonary end and/or narrowest diameter of PDA. The length of device should not be longer than the ductal length.

The Nit-Occlud PDA device is usually deployed anterograde from the pulmonary side. Distal windings of the device are configured in the descending aorta (DAO) and pulled back to the ductal ampulla. Then, one of the “reverse cone” proximal windings are delivered at the pulmonary side. After confirming a satisfactory position of coil, the device is detached (Figure 1B). If embolized, the device can be retrieved by snaring any part of the coil and retracting it into a 6-Fr sheath.

Study design

The Nit-Occlud PAS study was a prospective, nonrandomized multicenter trial conducted in 11 medical centers (Appendix 1) in the United States. The study evaluated the safety and effectiveness of the Nit-Occlud PDA device in the postapproval phase. The study’s outcomes were defined to determine whether the Nit-Occlud PDA met or exceeded objective performance criteria (OPC) derived from historical results of device and surgical PDA closure.³ Local institutional review board approval was obtained in each participating center for this study. Informed consent was obtained for each study subject.

Inclusion criteria were: age between 6 months and 21 years, weight ≥ 5 kg, and an angiographically confirmed PDA with a minimum diameter of <4 mm. Exclusion criteria included presence of associated cardiac anomalies requiring surgery, bleeding or clotting disorders, pulmonary hypertension (with pulmonary vascular resistance ≥5 Woods unit), contrast or nickel allergy, pregnancy and acute illnesses.

Patients were evaluated before and during cardiac catheterization, at hospital discharge, and 2 months, 12 months, and 24 months after device implant. Subjects with documented residual PDA shunt, any significant left pulmonary artery (LPA) or DAO obstruction and/or on ongoing device-related issue at 12 months were followed yearly postimplant for an additional 4 years (24 months, 48 months, and 60 months). At follow-up, subjects were evaluated on history, physical examination and transthoracic echocardiography. Subject data were maintained in an electronic study database. The consistency of reports with source patient data were confirmed by the periodic site audits.

Outcome measures

The primary outcome of the PAS was effectiveness and safety at 12-month after device implant. The effectiveness measure was
complete closure of PDA, defined as absence of residual PDA flow by color Doppler transthoracic echocardiography. The OPC for the effectiveness measure was 85%. The safety measure was serious device-related adverse event defined as life-threatening events that required surgery to correct, resulted in hospitalization or prolonged hospital stay, caused long-term disability, or resulted in genetic damage or birth defect. Other serious adverse events included cerebral or pulmonary embolism, bacterial endocarditis, device embolization requiring surgery, and persistent cardiac arrhythmia requiring a pacemaker. Total adverse events included serious adverse events and non-life threatening events, which were resolved either by nonsurgical intervention or with no intervention. The OPC for serious device-related adverse events was 1%. Composite success was defined as technical success of device implantation, clinical and echocardiographic closure of the PDA 1 year after device implantation, and absence of device- or procedure related death or serious device-related adverse events after 1 year follow-up. The OPC for the composite success was 80%.

In addition, these outcome measures were evaluated in the combined cohort of the pivotal, continued access and postapproval studies.

2.4 | Statistical analysis

Data were expressed as frequency (percentage) for binary outcomes. Standard errors and exact 95% confidence intervals were calculated. Statistical analysis was performed using the statistical softwares including SAS (SAS Institute Inc., Cary, North Carolina) and STATA (version 10, StataCorp, College Station, Texas) and StatXact software (Cytel Software, Cambridge, Massachusetts). Outcome measures were compared with OPC.

3 | RESULTS

A total of 184 subjects were enrolled from 11 sites in the PAS (Figure 2). The median age of patients was 3.4 years (range 4 months
Female patients constituted 68.5% (126/184) of the subjects. Additional congenital heart diseases were present in 23.9% of the patients (44/184), most commonly interatrial communication. The majority (92.9%) of patients had an audible PDA murmur. Thirteen patients had PDAs without an audible murmur (Table 1).

The median minimum PDA diameter was 1.7 mm (range 0.6 mm–3.6 mm) with median PDA length of 8.0 mm (range 2.5 mm–21.9 mm). PDA was classified angiographically as Krichenko type A (conical) 83.7%, type B (short) 1.1%, type C (tubular) 2.2%, type D (complex) 3.3%, and type E (elongated) 9.8% (Table 1).

Successful implantation was achieved in 180 of 184 patients (97.8%). There were four technical failures (2.2%), which were attributed to a larger ductal size in three and premature release of device in one.

### Table 1: General characteristics of subjects enrolled in the postapproval study

| Characteristics                          | N = 184 |
|------------------------------------------|---------|
| Gender – n (%)                           |         |
| Female                                   | 126 (68.5%) |
| Male                                     | 58 (31.5%) |
| Age (years) at enrollment                |         |
| Median [IQR]                             | 3.4 [1.5, 5.4] |
| Range                                    | 0.3–21.1 |
| Weight (kg) at enrollment                |         |
| Median [IQR]                             | 14.1 [9.9, 20.8] |
| Range                                    | 5.5–86.9 |
| History of congenital heart disease other than PDA – n (%) | 44 (23.9%) |
| Atrial septal defect (ASD)               | 9 (4.9%) |
| ASD/PFO                                 | 1 (0.5%) |
| ASD/ventricular septal defect (VSD)      | 1 (0.5%) |
| ASD/PFO/coarctation of the aorta (CoA)   | 1 (0.5%) |
| ASD/PFO/valve stenosis                   | 1 (0.5%) |
| ASD/VSD/valve stenosis                   | 1 (0.5%) |
| Bicuspid aortic valve                    | 2 (1.1%) |
| Cardiomyopathy                           | 1 (0.5%) |
| Mitral regurgitation                     | 1 (0.5%) |
| Patent foramen Ovale (PFO)               | 10 (5.4%) |
| Perimembranous (PM) vs. supracristal VSD | 1 (0.5%) |
| PFO/aortic arch narrowing                | 1 (0.5%) |
| PFO/valve insufficiency                  | 1 (0.5%) |
| Valve stenosis                           | 2 (1.1%) |
| VSD                                      | 10 (5.4%) |
| VSD/CoA                                  | 1 (0.5%) |
| Previous cardiac intervention operations – n (%) | 2 (1.1%) |

### Table 2: Procedure characteristics for the implant surgery of the postapproval study

| Procedure characteristic                      | N = 184 |
|-----------------------------------------------|---------|
| Successful implant – n (%)                   |         |
| Yes                                           | 180 (97.8%) |
| No                                            | 4 (2.2%) |
| Total fluoroscopy time (min)                  |         |
| Median [IQR]                                 | 11.0 [8, 17] |
| Range                                         | 4–136 |
| Duration of surgery in minutes                |         |
| Median [IQR]                                 | 52.5 [37, 76] |
| Range                                         | 4–190 |
| Sedation or anesthesia type – n (%)           |         |
| General                                       | 120 (65.2%) |
| General with local                            | 47 (25.5%) |
| Conscious sedation                           | 16 (8.7%) |
| None noted                                    | 1 (0.5%) |
| Number of implant attemptsb – n (%)           |         |
| 1                                             | 166 (90.2%) |
| 2                                             | 17 (9.2%) |
| 3                                             | 1 (0.5%) |
| PDA approachc – n (%)                         |         |
| Venous (antegrade)                           | 172 (95.6%) |
| Arterial (retrograde)                        | 8 (4.4%) |
| Device size implanted (mm) – n (%)           |         |
| 4 × 4                                         | 11 (6.2%) |
| 5 × 4                                         | 23 (12.9%) |
| 6 × 5                                         | 39 (21.8%) |
| 7 × 6                                         | 53 (29.4%) |
| 9 × 6                                         | 39 (21.8%) |
| 11 × 6                                        | 15 (8.4%) |

### Notes:
- a Determined prior to device implant with aortogram.
- b Per protocol, it is possible the user may attempt to implant a Nit-Occlud PDA and realize the device is the incorrect size; this is an anticipated occurrence and is not considered a technical failure or a protocol deviation.
- c For subjects with more than one implant attempt, data from the final implant are used for this summary table.

*648 KOBAYASHI ET AL.*
Subjects with failed implants were followed through month 1 and any adverse events (AEs) that occurred were reported. All procedures were performed under general anesthesia (90.7%), or conscious sedation (8.7%). One subject’s anesthesia type was unreported.

The device was delivered by the first attempt in 166/184 (90.2%), and via venous (antegrade) approach in 172/184 (95.6%). The device size implanted were 4 × 4 mm in 11 patients (6.2%), 5 × 4 mm in 23 (12.9%), 6 × 5 mm in 39 (21.8%), 7 × 6 mm in 53 (29.4%), 9 × 6 mm in 39 (21.8%) and 11 × 6 mm in 15 (8.4%) (Table 2).

### 3.1 Efficacy and safety of postapproval study

Effectiveness endpoint was echocardiographic closure of PDA at 12-month postdevice implant (Table 3). This endpoint was also evaluated at hospital discharge, after 2 months, and after 12 months. At the 2-month follow-up, only 2.9% (5/170) of subjects had a small residual PDA shunt by echocardiography. No subjects had medium or severe residual shunt at the 2-month follow-up.

At the 12-month follow-up, 98.7% (150/152) of subjects had trivial or no residual shunt assessed by echocardiography. Eight subjects had trivial shunt at the 12 month evaluation. The clinical closure rate (i.e., lack of a continuous murmur by auscultation) was 100% (152/152). At 24-month follow-up, 98.4% (60/61) had no detectable PDA murmur and all subjects with an echocardiography (n = 30) had no or trivial residual shunt on echocardiography.

The available data include AEs reported through the 12-month follow-up for the subjects with successful implantation. AE data were collected through 1-month postprocedure only for subjects that did not receive the study device. The safety endpoint was serious device-related adverse events at 24-months postdevice implant. However, subjects are continuing in follow-up and only 12-month follow-up data are currently available at this time. Despite having only 12-month data currently, the number of device related AEs by the 24-month may be minimal given there have been no late-reported related events to date across all studies.

There were no deaths and no cases of hemolysis. There were no subjects having significant obstruction in the LPA or DAO on echocardiography at 12-month follow-up, which was defined as a mean gradient >10 mmHg. Thirteen patients had 16 serious adverse events (Table 4). None of the serious adverse events were device-related, but three of the SAEs were probably or definitely procedure-related. There were 6 (4.9%) device-related and 14 (11.5%) procedure-related non-SAEs that occurred within the 12-month follow-up period. Device-related events included three device embolizations all of which occurred immediately following implantation (one embolized to the main pulmonary artery, one to the left femoral artery and a third to the abdominal aorta). In two cases, percutaneous retrieval was performed during the implantation procedure and another Nit-Occlud device was implanted successfully; the third subject was exited and a non-study device was implanted. Additional device-related AEs were device malposition (n = 1), and spontaneous detachment of coil from delivery cable without embolization (n = 3). Three procedure-related SAEs include the following: temporary loss of pulse requiring anticoagulation therapy (n = 2), left vocal cord paralysis (n = 1). Loss of pulse at hospital discharge, after 2 months, and after 12 months. At the 2-month follow-up, only 2.9% (5/170) of subjects had a small residual PDA shunt by echocardiography. No subjects had medium or severe residual shunt at the 2-month follow-up.

At the 12-month follow-up, 98.7% (150/152) of subjects had trivial or no residual shunt assessed by echocardiography. Eight subjects had trivial shunt at the 12 month evaluation. The clinical closure rate (i.e., lack of a continuous murmur by auscultation) was 100% (152/152). At 24-month follow-up, 98.4% (60/61) had no detectable PDA murmur and all subjects with an echocardiography (n = 30) had no or trivial residual shunt on echocardiography.

The available data include AEs reported through the 12-month follow-up for the subjects with successful implantation. AE data were collected through 1-month postprocedure only for subjects that did not receive the study device. The safety endpoint was serious device-related adverse events at 24-months postdevice implant. However, subjects are continuing in follow-up and only 12-month follow-up data are currently available at this time. Despite having only 12-month data currently, the number of device related AEs by the 24-month may be minimal given there have been no late-reported related events to date across all studies.

There were no deaths and no cases of hemolysis. There were no subjects having significant obstruction in the LPA or DAO on echocardiography at 12-month follow-up, which was defined as a mean gradient >10 mmHg. Thirteen patients had 16 serious adverse events (Table 4). None of the serious adverse events were device-related, but three of the SAEs were probably or definitely procedure-related. There were 6 (4.9%) device-related and 14 (11.5%) procedure-related non-SAEs that occurred within the 12-month follow-up period. Device-related events included three device embolizations all of which occurred immediately following implantation (one embolized to the main pulmonary artery, one to the left femoral artery and a third to the abdominal aorta). In two cases, percutaneous retrieval was performed during the implantation procedure and another Nit-Occlud device was implanted successfully; the third subject was exited and a non-study device was implanted. Additional device-related AEs were device malposition (n = 1), and spontaneous detachment of coil from delivery cable without embolization (n = 3). Three procedure-related SAEs include the following: temporary loss of pulse requiring anticoagulation therapy (n = 2), left vocal cord paralysis (n = 1). Loss of pulse

### TABLE 3 Efficacy endpoint: echocardiographic closure of PDA at 12-month postdevice implant and additional timepoints

| Month 2 | N = 170a |
|---------|-----------|
| None    | 153 (90.0%) |
| Trivial | 12 (7.1%)  |
| Small   | 5 (2.9%)   |
| Medium  | 0 (0.0%)   |
| Severe  | 0 (0.0%)   |
| Month 12| N = 152b |
| None    | 142 (93.4%) |
| Trivial | 8 (5.3%)   |
| Small   | 2 (1.3%)   |
| Medium  | 0 (0.0%)   |
| Severe  | 0 (0.0%)   |

### TABLE 4 Safety endpoint: available data for serious device-related adverse events

|                      | Number (%) of AEs | Number (%) of subjects with AE (N = 184)c |
|----------------------|------------------|------------------------------------------|
| All AEs              | 122              | 77 (41.8%), CI =34.3%, 49.3%              |
| Serious              | 16 (13.1%)       | 13 (7.1%)                                |
| Non-serious          | 106 (86.9%)      | 171 (92.9%)                              |
| AEs by relationship to device or procedureb |                |                                           |
| Procedure-related    | 15 (12.3%)       | 14 (7.6%)                                |
| Occurred ≤12-months postprocedure | 14 (11.5%) | 13 (7.1%)                                |
| Device-related       | 6 (4.9%)         | 6 (3.2%)                                 |
| Occurred ≤12-months postprocedure | 6 (4.9%) | 6 (3.2%)                                 |
| Not device or procedure-related | 102 (83.6%) | 165 (97.8%)                              |
| Late onset device or procedure-related | 1 (0.8%) | 1 (0.5%)                                 |

### TABLE 4 Safety endpoint: available data for serious device-related adverse events

|                      | Number (%) of AEs | Number (%) of subjects with AE (N = 184)c |
|----------------------|------------------|------------------------------------------|
| All AEs              | 122              | 77 (41.8%), CI =34.3%, 49.3%              |
| Serious              | 16 (13.1%)       | 13 (7.1%)                                |
| Non-serious          | 106 (86.9%)      | 171 (92.9%)                              |
| AEs by relationship to device or procedureb |                |                                           |
| Procedure-related    | 15 (12.3%)       | 14 (7.6%)                                |
| Occurred ≤12-months postprocedure | 14 (11.5%) | 13 (7.1%)                                |
| Device-related       | 6 (4.9%)         | 6 (3.2%)                                 |
| Occurred ≤12-months postprocedure | 6 (4.9%) | 6 (3.2%)                                 |
| Not device or procedure-related | 102 (83.6%) | 165 (97.8%)                              |
| Late onset device or procedure-related | 1 (0.8%) | 1 (0.5%)                                 |

a Subjects with failed implants were followed through month 1 and any reported AEs are included.

b AEs classified as definitely or probably are considered related; AEs classified as possibly, unlikely or not related are not related.

c Late onset includes AEs that occur after the initial hospitalization for the implant procedure.
resolved at follow-up, whereas left vocal cord paralysis required ongoing speech therapy.

The other non-serious procedure-related AEs reported through 12 months were the following: access site hematoma (n = 8), device malposition (n = 2), inability to re-deploy device (n = 1), transient mitral regurgitation (n = 1), and allergic skin reaction to tape (n = 1). Among 62 subjects completing 24-month follow-up, two subjects had late-onset procedure-related SAEs. These were both residual PDA shunts for which the operators chose to place additional non-study coils at 14 and 19 months post-NitOcclud implant. Composite success accounting for procedure technical success, clinical and echocardiographic closure of PDA, death, and device-related SAE at 1 year follow-up was 92.8% (141/152).

### 3.2 Combined cohort of pivotal, continued access, and postapproval studies

Comparing with the Pivotal and Continuing Access Studies, the PAS had comparable technical success, clinical and echocardiographic closure at 12 months (Table 5). Although there were no device- and procedure-related SAEs in the pivotal and continued access studies, there were three procedure-related SAEs in the PAS. As mentioned above, two of these three SAEs were treated and resolved without clinical consequences.

Combining the subjects from the three clinical trials of pivotal, continued access postapproval studies, technical success at implantation was 97.4% (527 of 541). There were 14 technical failures. At 12-month after device implant, 466 subjects completed clinical evaluation and 436 completed echocardiographic evaluation. Clinical and complete echocardiographic closure (defined as a complete absence of any shunt) at 12 months was 98.5% (460 of 467) and 95.9% (418 of 436). There was no death. Total device-related SAEs at 12 months was 0% (0/467) and procedure-related SAEs at 12 months was 0.6% (3/467). Composite success at 12 months was 94.4% (435/461). There were five device embolizations that were all retrieved by snare without clinical consequence.

### 4 DISCUSSION

The NitOcclud PAS study prospectively enrolled 184 patients at 11 centers. When all three of the FDA mandated clinical trials of Nit-Occlud (pivotal, continuing access, and postmarket) were combined, a total of 541 prospectively enrolled patients were available for analysis. This large cohort with long-term follow-up allows for the performance of a well powered study of the technical success, safety and efficacy of this device. This publication reports both the PAS results as well as an overview of the combined results of all three trials.

The primary safety endpoint of the Nit-Occlud PAS study was assessed primarily by the rate of serious adverse events. In the PAS and in all three studies, there were no deaths, no device-related serious adverse events and no hemolysis in any of the patients. In a total of 461 patients, the rate of device related SAEs was 0.6%. The PAS had five procedure-related SAEs through 24-months postimplant, of which four were treated and resolved without clinical consequence. In the five episodes of Nit-Occlud embolizations, the device was easily snared and retrieved in all cases without the use of a 6–7 Fr sheath. Furthermore, obstruction of flow in the aorta or pulmonary artery was not seen.

The PAS also provided a third test of the Nit-Occlud PDA device’s efficacy for closure of PDA’s < 4 mm in diameter. At the 12-month follow-up, 98.7% (150/152) of subjects had trivial or no residual shunt assessed by echocardiography. When compared with the pivotal and continuing access studies, the PAS showed comparable outcome of technical success and efficacy. In the combined cohort of 541 patients, technical success at implantation was 97.4% with only 10 technical failures. The technical failures were primarily secondary to selection of PDAs too large to accommodate stable Nit-Occlud position. On these occasions, the device was uniformly and easily removed prior to deployment.
In the PAS study at the 12-month follow-up, 98.7% (150/152) of subjects had trivial or no residual shunt assessed by echocardiography. However, in all three studies, 95.9% of patients (n = 436) had no detectable PDA shunting by echocardiography at 12 months with the remaining having trivial or small shunts. Deployment of the Nit-Occlud coil into an ideal conformation is more operator dependent than deployment of self-expanding plug devices. For example, implanting the reversed windings on the aortic side of the narrowest PDA diameter with only one or one and a half loops deployed on the pulmonary side is typically ideal. Small residual shunts are more common when more than two of the reversed windings were on the PA side of the narrowest PDA diameter.

There are several alternative devices and coils for closure of PDA. Amplatzer Duct Occluder (ADO) I and II (St. Jude Medical, St. Paul, MN, USA) are FDA approved devices for the indication of PDA closure. Many other devices including the Amplatz Vascular Plug II (St. Jude Medical) and Flipper coils (Cook Medical, Bloomington, IN) have been used off-label for PDA closure. As such, no FDA pivotal trial data are available for these devices.

In the pivotal trial for the ADO I, there were 393 patients. The 12-month closure rate was 98.6% and there were five (2.7%) serious adverse events including one death.5 While direct comparisons of these devices are not perfect given subtle differences in the trials, clearly the closure rates are very similar. Both the ADO I and Nit-Occlud PDA have excellent overall device characteristics and outcomes for closure of small to moderate sized PDAs.5,6 As it is easily retrievable and repositionable using a low profile delivery catheter, the Nit-Occlud has very high technical success rate with minimal residual shunt at follow-up, and is unlikely to cause obstruction in the LPA and DAO.

4.1 | Study limitations
This study was a prospective observational study lacking a surgical or control group using an approved PDA device. Due to the absence of approved alternative coil-type PDA devices, the study was designed to compare the OPC benchmark designated by the FDA advisory panel. The PAS continues to follow-up the enrolled patients at 24 months postimplant and for 60 months for subjects with residual PDA shunt, any significant LPA or DAO obstruction, and/or an ongoing device-related issue at 12 months follow-up. Nevertheless, authors felt it reasonable to present the interim data of PAS.

5 | CONCLUSIONS
The Nit-Occlud PDA is a safe and effective device for closure of a small to moderate sized PDA in the PAS. At 12 months, echocardiographic closure was 95.9% with device- and procedure-related SAE of 0.6%. This efficacy and safety profile was well above or comparable to the OPC benchmark designated by the FDA advisory panel and contemporary practice data.7 Most importantly, there were no serious adverse events including hemolysis, mortality or need of surgery in a large cohort of three clinical trials and all five device embolizations were percutaneously retrieved with a snare easily.

ACKNOWLEDGMENT
The authors received statistical support from Bright Research Partners (www.brightresearchpartners.com).

CONFLICT OF INTEREST
No conflict of interest.

ORCID
Daisuke Kobayashi https://orcid.org/0000-0002-4682-0309

REFERENCES
1. Feltes TF, Bacha E, Beekman RH 3rd, et al. Indications for cardiac catheterization and intervention in pediatric cardiac disease: A scientific statement from the American Heart Association. Circulation. 2011;123: 2607-2652.
2. Moore JW, Greene J, Palomares S, et al. Results of the combined U.S. multicenter pivotal study and the continuing access study of the Nit-Occlud PDA device for percutaneous closure of patent ductus arteriosus. JACC Cardiovasc Interv. 2014;7:1430-1436.
3. Multiorganization Advisory Panel to FDA for Pediatric Cardiovascular Devices. Proposed standards for clinical evaluation of patent ductus arteriosus occlusion devices. Catheter Cardiovasc Interv. 2000;51: 293-296.
4. Krichenko A, Benson LN, Burrows P, Møes CA, McLaughlin P, Freedom RM. Angiographic classification of the isolated, persistently patent ductus arteriosus and implications for percutaneous catheter occlusion. Am J Cardiol. 1989;63:877-880.
5. St. Jude Medical. Instructions for Use – Amplatzer Duct Occluder and Delivery System. Minnesota, MN; 2014.
6. St. Jude Medical. Instructions for Use – Amplatzer Duct Occluder II. Minnesota, MN; 2013.
7. Moore JW, Vincent RN, Beekman RH 3rd, et al. Procedural results and safety of common interventional procedures in congenital heart disease: Initial report from the National Cardiovascular Data Registry. J Am Coll Cardiol. 2014;64:2439-2451.

SUPPORTING INFORMATION
Additional supporting information may be found online in the Supporting Information section at the end of the article.

How to cite this article: Kobayashi D, Salem MM, Forbes TJ, et al. Results of the combined U.S. multicenter postapproval study of the Nit-Occlud PDA device for percutaneous closure of patent ductus arteriosus. Catheter Cardiovasc Interv. 2019; 93:645–651. https://doi.org/10.1002/ccd.27995