Berlin Heart®

EXCOR® Pediatric

The Gold Standard in Pediatric VAD Therapy

A Compilation of Publications Demonstrating the Clinical Excellence of EXCOR® Pediatric

EXCOR® Pediatric – The Gold Standard in Pediatric VAD Therapy

EXCOR® Pediatric is the only VAD system approved to provide circulatory support for pediatric patients in the US, Canada, the European Union and several other countries worldwide. The excellent clinical performance has been proven in clinics around the world and has been documented in various clinical studies including a prospective multicenter controlled clinical trial conducted in the US.
EXCOR® Pediatric offers solutions for univentricular or biventricular support. The EXCOR® Pediatric system can support pediatric patients of all ages, from newborns to adolescents. The wide portfolio of pumps and cannulae allows Berlin Heart to meet the individual needs of each patient.

Since 1990, the EXCOR® Pediatric VAD has been successfully used in increasing numbers at 166 pediatric heart centers in 37 countries. More than 1,700 EXCOR® Pediatric patients have been implanted with the EXCOR® Pediatric VAD system and benefited from Berlin Heart's life saving technology.

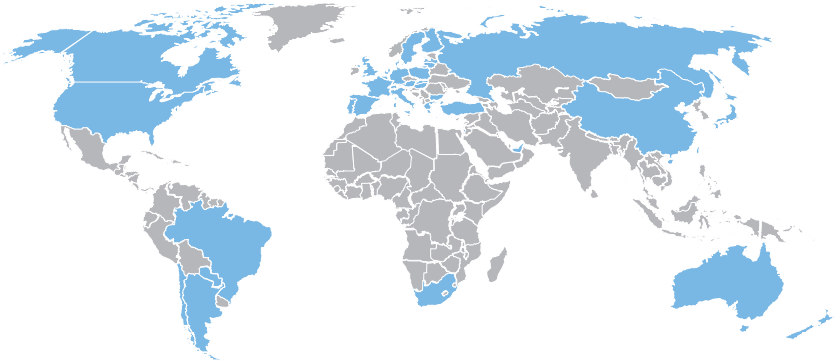


FIGURE 1 **Illustration of countries in which EXCOR® Pediatric is used worldwide (labeled in blue)**

"The EXCOR® Pediatric has become an important option for our pediatric patients with severe cardiac failure, providing successful outcomes for even our smallest patients ."

Dr. M. Bleiweis, University of Florida, Shand's Children's Hospital

Worldwide EXCOR® Pediatric Experience

Source: Berlin Heart Registry

Clinical data of patients implanted between February 1990 and August 2015 has been captured and analyzed.

Worldwide VAD therapy with EXCOR® Pediatric demonstrates excellent outcome (1-year survival 74%, n=1,609).

Patient characteristics

Variable	EXCOR® Pediatric patients
Age, Median (range)	2.0 years (1 day-17 years)
Mean cardiac index	2.1 l/min/m²
Mean LVEF	19%
Preoperative MCS (short-term)	33%
Ratio male/female sex	52%/48%

Primary diagnosis

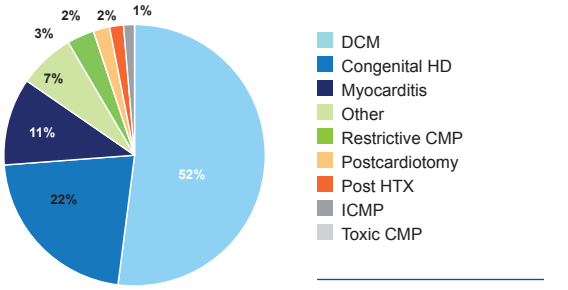


FIGURE 2 Primary diagnosis

Type of support

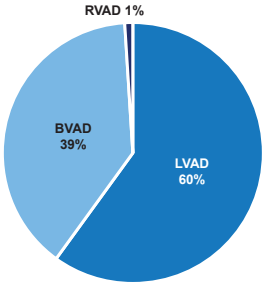


FIGURE 3 Type of support

Outcome

The mean duration of support was 85 days. The longest duration of support for toddlers and adolescents was 2.5 years and 3.5 years, respectively. 1-year survival for all patients was 74%.

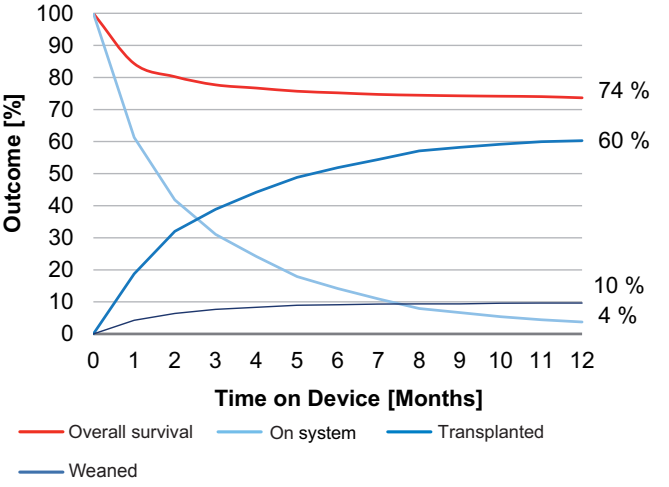


FIGURE 4 **Competing outcome with overall survival of EXCOR® Pediatric patients worldwide**
At 1-year, 60% of the patients (n=1,609) have been transplanted, 10% have been weaned and 4% are still on support.

Review of the IDE Trial Results

Fraser CD Jr, Jaquiss RD, Rosenthal DN, Humpl T, Canter CE, Blackstone EH, Naftel DC, Ichord RN, Bomgaars L, Tweddell JS, Massicotte MP, Turrentine MW, Cohen GA, Devaney EJ, Pearce FB, Carberry KE, Kroslowitz R, Almond CS, N Engl J Med. 2012;367(6):532-41

Background

Options for mechanical circulatory support as a bridge to heart transplantation or recovery in children with severe heart failure are limited.

Methods

Study design: Prospective, multicenter, single-arm study

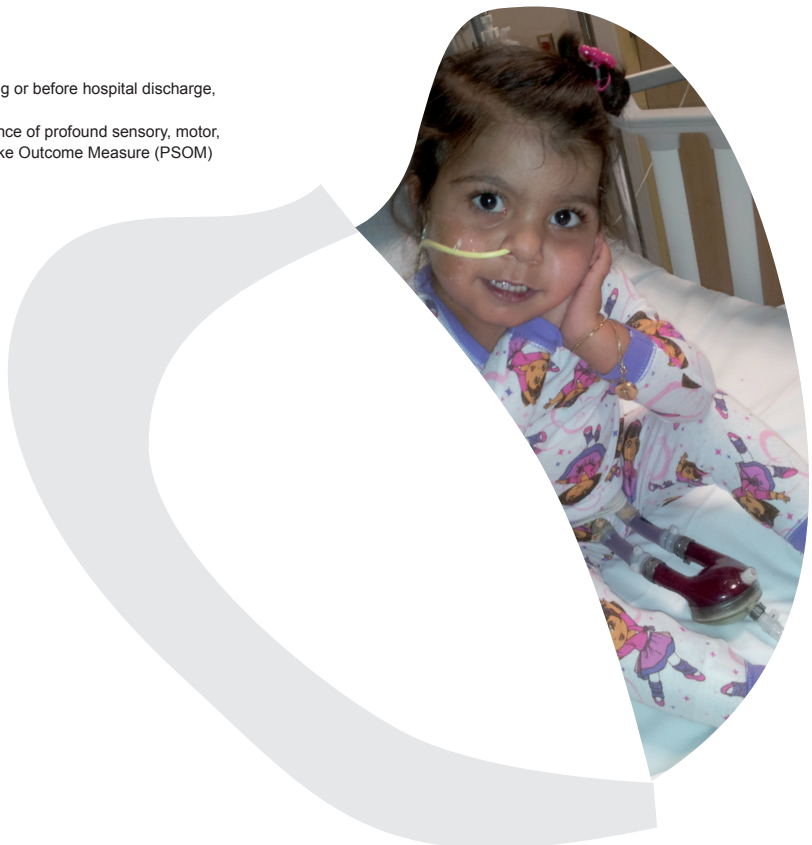
Patients (n=48) 16 years of age or younger were divided into two cohorts according to body-surface area:

- Cohort 1: n=24, BSA <0.7 m^2
- Cohort 2: n=24, BSA ≥0.7 to <1.5 m^2

The primary efficacy endpoint for the EXCOR® Pediatric VAD was time to cardiac transplantation, death[1] or weaning with an unacceptable neurologic outcome.[2]

1 Definition *death*: death while on support or within 30 days after weaning or before hospital discharge, whichever was longer

2 Definition *unacceptable neurologic outcome*: either coma or the presence of profound sensory, motor, language, or cognitive impairment as assessed with the Pediatric Stroke Outcome Measure (PSOM)



Patient characteristics

Variable	EXCOR® Cohort 1	EXCOR® Cohort 2
Age in months, Median (range)	11.7 (2.6 - 45.6)	111.2 (50.8 - 191.8)
Weight in kg, Median (range)	9.2 (3.6 - 13.6)	30.7 (16.0 - 58.1)
BSA in m^2, Median (range)	0.44 (0.23 - 0.62)	1.08 (0.71 - 1.66)
Male/female sex (%)	50/50	54/46
INTERMACS profile status (%) 1 2	 46 54	 54 46
Preoperative ECMO for 10 d or less (%)	25	33
Preoperative centrifugal VAD (%)	8	0
Preoperative mechanical ventilation (%)	83	46
Preoperative inotrope infusion (%)	92	88
Preoperative cardiac arrest (%)	29	21
Closure of intracardiac shunt at implantation (%)	29	12
Valve repair or replacement at implantation (%)	8	17
Time (minutes) required for cardiopulmonary bypass [Average ± h]	185 ± 49	176 ± 52

Primary diagnosis

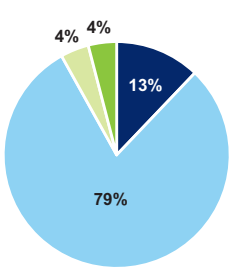


FIGURE 5 Primary diagnosis EXCOR® Pediatric – cohort 1

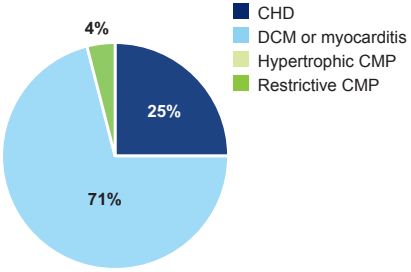


FIGURE 6 Primary diagnosis EXCOR® Pediatric – cohort 2

Type of support

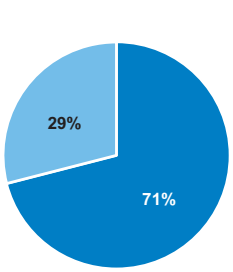


FIGURE 7 Type of EXCOR® Pediatric support – cohort 1

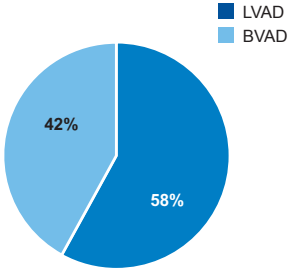


FIGURE 8 Type of EXCOR® Pediatric support – cohort 2

For children in cohort 1 and 2, the median duration of support with EXCOR® Pediatric VAD was 28 days and 43 days, respectively. The longest duration of support with EXCOR® Pediatric VAD in cohort 1 and 2 was 174 days and 192 days, respectively.

Competing outcome with overall survival of EXCOR® Pediatric VAD cohort 1 and cohort 2

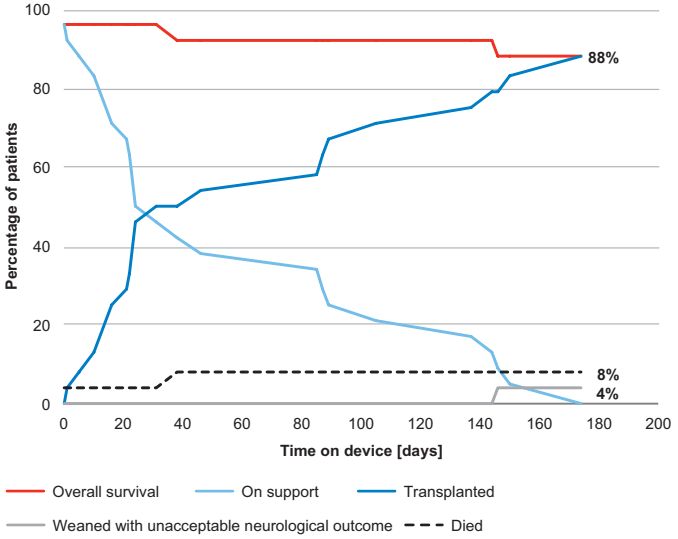


FIGURE 9 Competing outcome with overall survival of EXCOR® Pediatric VAD cohort 1
At 174 days, 88% of the patients had undergone a successful transplantation, 4% had an unacceptable neurologic outcome after weaning from the device and 8% had died. Figure adapted from Fraser et al. N Engl J Med. 2012.

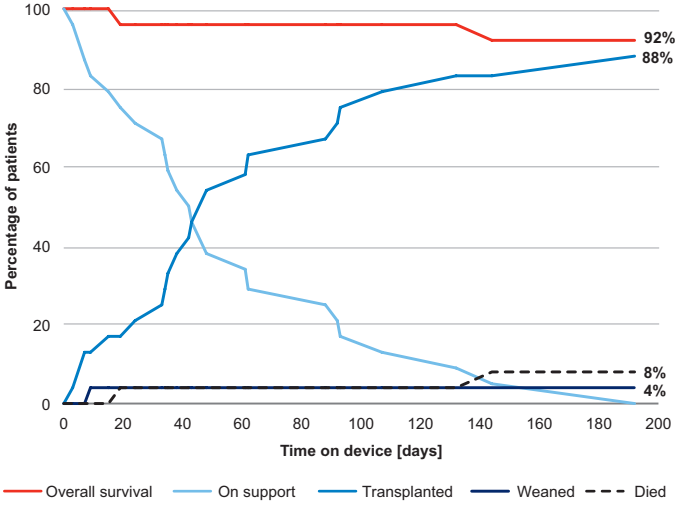


FIGURE 10 Competing outcome with overall survival of EXCOR® Pediatric VAD cohort 2
At 192 days, 92% of the patients had been transplanted or weaned. 88% of the patients had undergone a successful transplantation and 4% had been weaned successfully from the device. Figure adapted from Fraser et al. N Engl J Med. 2012.

Overall, for patients supported with EXCOR® Pediatric VAD, 88% in cohort 1 and 92% in cohort 2 were bridged to transplant or recovery with acceptable neurological outcome.

The results of the EXCOR® Pediatric IDE trial demonstrated high survival rates with acceptable complications rates.

Serious Adverse Events

Serious adverse events include bleeding, infection and neurological dysfunction. In total, neurological dysfunctions occurred in 29% of the patients (n=48). Thereof, 14% with no reported deficits (PSOM 0), 29% with mild deficits (PSOM 0.5 - 1.0), 29% with moderate deficits (PSOM 1.5 - 2.0) and 14% with severe deficits (PSOM >2.5)*. 2 patients were not assessed. Of the patients with neurological dysfunction, 50% were on ECMO or other VAD support prior to implantation of EXCOR® Pediatric VAD. The neurological dysfunction rate of 29% in cohort 2 is similar to that reported in patients (BSA >1.2 m^2) who were supported with adult-sized VAD[1]. The sequelae of neurological dysfunction did not preclude eligibility for transplantation in the majority of patients.

46 pump exchanges occurred in cohorts 1 and 2 combined.
43 pumps were changed due to blood clots.

Serious Adverse Events	Patients with event cohort 1	Patients with event cohort 2
Major bleeding[a,b] [a] ≥Units PRBC within 24 h during 1st 7 d post-implant (≥20 cc/kg PRBC for patients <50 kg) [b] Any transfusion or PRBC after 7 d post-implant	42%	50%
Infection Localized non-device related Percutaneous site Internal pump component Sepsis	 50% 17% 0% 21%	 42% 0% 0% 25%
Neurological dysfunction[c,d,e] Ischemic Hemorrhagic [c] TIA [d] Ischemic/Hemorrhagic CVA [e] Patients <6 months: new abnormality head ultrasound/EEG positive for seizure activity	29%* 29% 0%	29%* 21% 8%
Non-CNS thromboembolism Arterial Venous	 4% 4%	 0% 0%
Device malfunction	0%	0%
Hemolysis Early (<72 h post-implant) Late (>72 h post-implant)	 0% 4%	 0% 4%

* The severity of neurological complication was assessed according to a standardized neurological exam, that included imaging and a clinical examination using the Pediatric Stroke Outcome Measure (PSOM)

[1] Reinhartz et al., Multicenter experience with the Thoratec Ventricular Assist Device in children and adolescents. J. Heart Lung Transplantation, 2001

EXCOR® Pediatric – Prospective Post-Approval Trial

Preview of Post-Approval Trial Results

Jaquiss et al., Berlin Heart Post Approval Outcomes in North America, Oral Communication ISHLT 2015

Background
Assessment of clinical efficacy and safety in prospective study

Methods
The clinical efficacy and safety of the EXCOR® Pediatric in the commercial setting was assessed in an FDA mandated, prospective, multicenter post-approval study.
Within the post-approval study 39 non-selected patients were enrolled, while the post-approval study phase (2011 - 2015) included 247 "all comer" patients.
This study compared the clinical efficacy and safety to the IDE study (n= 48) and the IDE compassionate use cohort (2007 - 2011).

Patient characteristics

	Post-approval phase (n=247)	Post-approval study (n=39)	IDE compassio-nate use (n=204)	IDE (n = 48)
Age in months, Median (range)	19.5 (0-389.3)	23.1 (0-196.1)	18.6 (0.2-191.8)	48.2 (2.6-191.8)
Weight in kg, Median (range)	10.7 (2.9-112.0)	10.6 (3.4-70.0)	10.0 (2.8-60.0)	14.8 (3.6-58.1)
BSA in m^2, Median (range)	0.49 (0.20-2.30)	0.49 (0.23-1.76)	0.48 (0.19-1.67)	0.67 (0.23-1.66)
Diagnosis CHD (%) Single-ventricle physiology (%) Two-ventricle physiology (%)	24.3 11.3 13.0	12.8 7.7 5.1	28.9 8.8 20.1	18.8 0 18.8
Preoperative ECMO (%)	n.s.	25.6	n.s.	29.2
Preoperative mechanical ventilation (%)	n.s.	59.0	n.s.	66.7
Device type LVAD or RVAD (%) BVAD (%)	 72.5 27.5	 64.1 35.9	 62.8 37.3	 64.6 35.4
Time on support in days, Median (range)	55 (0-457)	55 (0-457)	40 (1-435)	38 (0-192)

The post-approval phase patient population was at higher risk compared to the IDE cohort (smaller, younger, longer on support, higher CHD and especially single ventricle physiologiy population).

Adjudicated adverse events IDE vs. Post-approval cohort (in events per 100 patient-months):

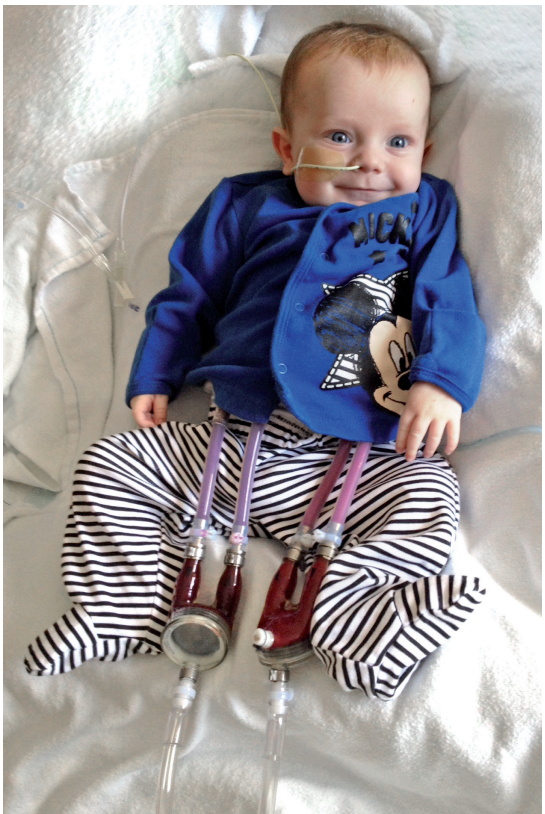
Event	IDE (n=48)	Post-Approval Study (n=39)	p-value
Major Bleeding	40.4	16.6	0.001
Major Infection	63.4	14.4	<0.001
Stroke (any stroke)	18.6	12.3	0.299
Ischemic stroke	16.4	8.7	0.143
Hemorrhagic stroke	2.2	3.6	0.848
Pump changes	47.0	22.4	0.002

An improved safety profile in the post-approval study cohort compared to the IDE cohort was observed despite longer time on support. The improved safety reflects the growing expertise in EXCOR® Pediatric therapy.

Efficacy Outcomes: IDE vs. Post-Approval Phase Cohort

Outcome	IDE (n = 48)	Post-Approval Phase (n = 247)
Transplanted	42 (87.5%)	172 (69.9%)
Successfully Weaned	1 (2.1%)	8 (3.2%)
Died or Unsuccessfully Weaned	5 (10.4%)	54 (21.9%)
On Device	0 (0.0%)	13 (5.3%)
Overall Survival	43 (89.6%)	180 (76.9%)

The efficacy in the post-approval cohort was slightly inferior to the IDE cohort, 76.9% vs. 89.6% respectively.
However comparing the post-approval cohort to the more similar IDE compassionate use cohort, the post-approval cohort proved to be superior with an overall survival of 76.9% vs. 70.6%.



Efficacy Outcomes: IDE compassionate use vs. Post-Approval Phase Cohort

Outcome	IDE compassionate use (n = 204)	Post-Approval Phase (n = 247)
Transplanted	138 (67.7%)	172 (69.9%)
Successfully Weaned	6 (2.9%)	8 (3.2%)
Died or Unsuccessfully Weaned	60 (29.4%)	54 (21.9%)
On Device	0 (0.0%)	13 (5.3%)
Overall Survival	144 (70.6%)	180 (76.9%)

Similar survival rates and an improved adverse event profile were shown in the post-approval setting in patients compared to the selected IDE-patient cohort demonstrating the clinical efficacy and safety of EXCOR® Pediatric in commercial setting.

Review of the Bad Oeynhausen Experience

Sandica et al., Long term mechanical circulatory support in pediatric patients: The Bad Oeynhausen experience, oral communication EACTS 2014

During the study period (January 2008 to April 2014), 29 pediatric patients were supported with EXCOR® Pediatric.
Median age of EXCOR® Pediatric patients was 3.4 years, whereof 29% of the patients were younger than 1 year.

Patient characteristics

Variable	EXCOR® Pediatric patients (n=29)
Age in years, Median (range)	3.4 (0.25 - 16.5)
Weight in kg, Median (range)	13 (4.2 - 67.2)
Preoperative cardiac arrest (%)	18
Preoperative inotrope infusion (%)	93
Preoperative mechanical ventilation (%)	28
Preoperative renal failure (%)	7
Ratio male/female sex (%)	62 / 38

Primary diagnosis

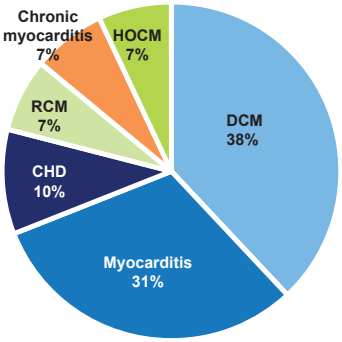


FIGURE 11 Primary diagnosis
Within the CHD cohort, there were 3 patients, all with single ventricle physiology. 2 of the 3 patients were supported at the Fontan stage, and 1 of the patients was supported at the Glenn stage. 1 of the 2 Fontan patients had a mechanical mitral valve.

Type of support

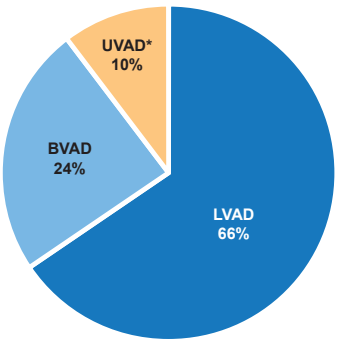


FIGURE 12 Type of support
*Of the 29 patients, 3 presented with single ventricle physiology and were supported with an UVAD.

Outcome

The overall mean support time was 126 days (4 - 619 days), with a cumulative experience of 3,647 days of cardiac support. 4 patients were supported for more than 6 months, 3 patients were on EXCOR® Pediatric support for more than 12 months. Longest time on support was 619 days.

Overall survival was 90%, whereof 66% of the patients were transplanted, 21% were weaned and 3% were still on support.
All single ventricle physiology patients were successfully supported until transplantation. There were no deaths after heart transplantation or after explantation in any of the EXCOR® Pediatric patients.

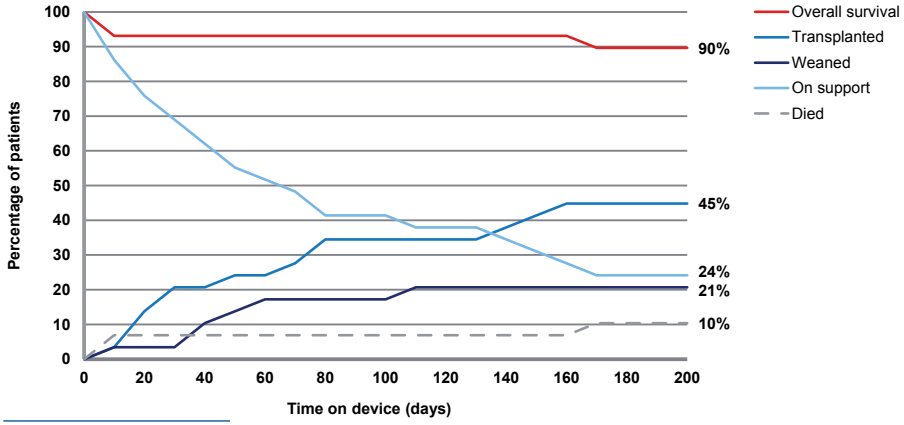


FIGURE 13 Competing outcome with overall survival at 195 days (n=29)
At 195 days, 45% of the patients were transplanted, 21% had been weaned, 24% were still on support and 10% died on support. Survival at 195 days was 90%.

Timing of EXCOR® Pediatric implantation is critical. Early implantation should be performed before irreversible end-organ dysfunction is evident. Accurate surgical technique during EXCOR® Pediatric implantation is of high importance[1].

With increasing experience and proven safety with long-term circulatory support in children, it is presumed that a higher proportion of patients can be weaned from EXCOR® Pediatric support, thus in some cases avoiding the need for cardiac transplantation[1]. Due to a shorter duration of pre-existing illness and comorbidities, and the higher regenerative capacity in the pediatric population, bridge to recovery can present a more frequent option in the future for the pediatric VAD population[1].
However the Bad Oeynhausen experience demonstrates that this strategy needs to be associated with early implantation of EXCOR® Pediatric.

Serious adverse events

14 blood pumps in 9 patients were changed within the study period. An aggressive policy to change the EXCOR® blood pumps when fibrin deposits that may initiate thrombus formation are observed, may positively influence the rate of neurological complications[1].

In this series, neurological complications without any major deficit were reported in 10% of the patients. Of these patients, 7% suffered from a cerebral embolism and 3% of intracranial bleeding. All patients recovered well without any major neurological deficit.
Superficial infections were reported in 14% of the patients. Meticulous hemostasis and primary chest closure in the operating room allowed for early extubation and dramatically decreased the risk of infections in this EXCOR® Pediatric cohort[1].

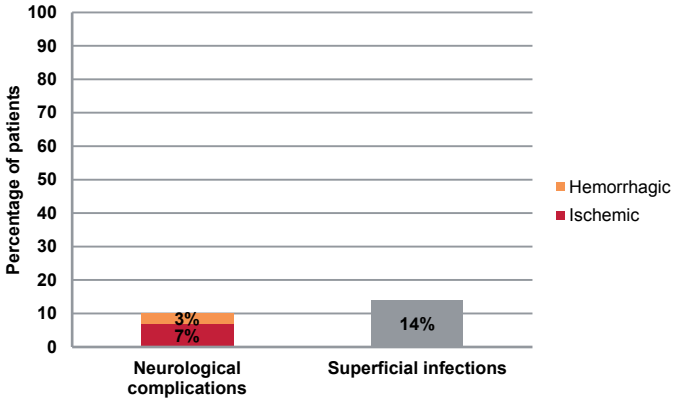


FIGURE 14 Rate of neurological complications and superficial infections
Neurological complications and superficial infections were reported in 10% and 14% of the EXCOR® Pediatric patients, respectively.

The Bad Oeynhausen experience has proven that long-term EXCOR® Pediatric support with a low rate of adverse events is possible.

[1] Sandica et al., Safety of Long-Term Mechanical Support With Berlin Heart EXCOR in Pediatric Patients, World J Pediatr Congenit Heart Surg. 2012 Jan 1;3(1):72-6

Horst Wackerbarth: „The Red Couch - A Gallery of Mankind“
Tobias R. & Dr. Eugen S. Herz- und Diabeteszentrum NRW Bad Oeynhausen, Deutschland 2011

Review of the Berlin Experience

Hetzer et al., Single-center experience with treatment of cardiogenic shock in children by pediatric ventricular assist devices, J Thorac Cardiovasc Surg 2011;141:616-23

In February 1990, the first pediatric patient was supported with an EXCOR® VAD at the German Heart Institute Berlin.
Continuous improvement of the system and adaption to the pediatric population as well as an increasing experience in pediatric VAD management and anticoagulation resulted in improved survival. The German Heart Institute Berlin data details the early experience with the EXCOR® Pediatric system.

During the study period (January 2002 to April 2009), 49 children were supported with EXCOR® Pediatric.

Patient characteristics

Variable	EXCOR® Pediatric patients (n=49)
Age in months, Median (range)	72 (12 - 204)
Weight in kg, Median (range)	19 (3.6 - 80)
Preoperative cardiac arrest (%)	29
Ratio male/female sex (%)	51 / 49
Preoperative ECMO (%)	14
Preoperative mechanical ventilation (%)	27

Primary diagnosis

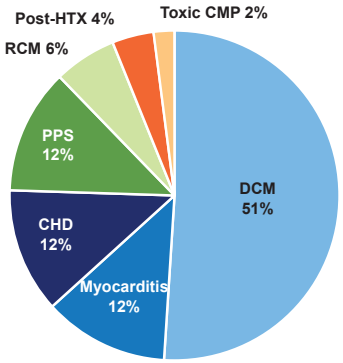


FIGURE 15 Primary diagnosis

Type of support

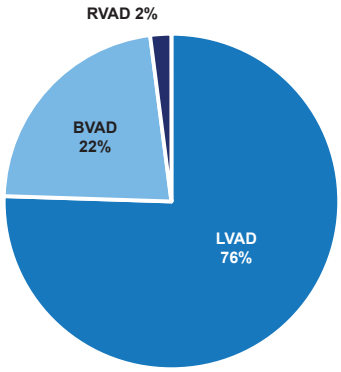


FIGURE 16 Type of support

Outcome

The median support time was 40 days (0 - 420 days), with a cumulative experience of 3,303 days of cardiac support.

Overall survival was 69%. Of the patients younger than 1 year 93% were supported successfully until transplantation or recovery.

Outcome per patient age

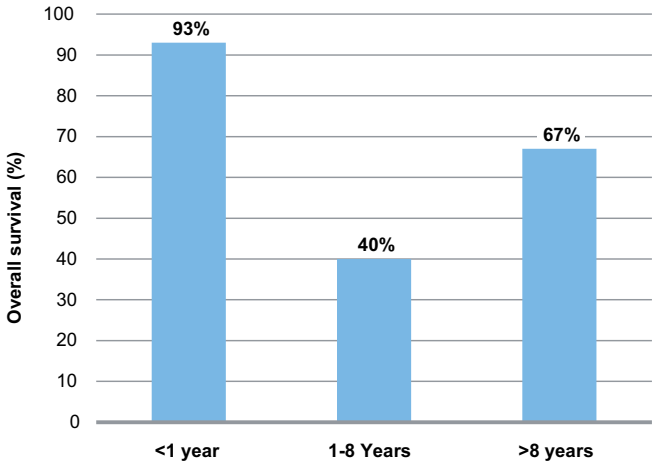


FIGURE 17 Outcome per patient age (n=49)
EXCOR® Pediatric treatment of infant younger than 1 year (n=15) was successful in 93% of the patients. 40% and 67% of the patient aged 1-8 (n=14) and older than 8 years (n=30) were successfully supported until transplantation or recovery, respectively.

Outcome per diagnosis

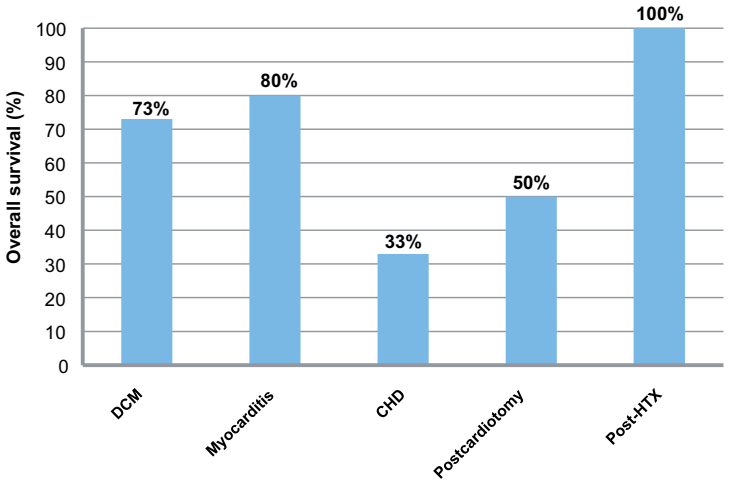


FIGURE 18 Outcome per diagnosis (n=49)
Highest survival rates have been demonstrated in patients diagnosed with graft failure after heart failure and myocarditis (100 and 80%, respectively). CHD is the most challenging diagnosis, 33% survived until transplantation or recovery.

Serious adverse events

Overall 46 pumps had been exchanged.
Thereof 12 pump exchanges were performed during a 3-months period in a single patient with HIT type II.

Serious adverse event	EXCOR® Pediatric patients (n=49)
Bleeding requiring re-thoracotomy	22%
CVA	12%

The EXCOR® Pediatric VAD offers a valuable option as a bridge to transplant or recovery for children with cardiogenic shock.


CHAMP

Weaning after Long-term Support of Pediatric Patients with EXCOR®

Review of the Erlangen Experience

R. Cesnjevar, A. Purbojo & A. Rüffer, Weaning after Long-term Support, oral communication EPUG 2014

During the study period (September 2008 to April 2014), 11 children diagnosed with either myocarditis or dilative cardiomyopathy were supported with EXCOR® Pediatric.

Patient characteristics

Variable	EXCOR® Pediatric patients (n=11)
Age in months, Median (range)	50.4 (6 - 192)
Weight in kg, Median (range)	18 (6.6 - 61)
Ratio male/female sex (%)	64 / 36
Preoperative ECMO (%)	36.4

Type of support

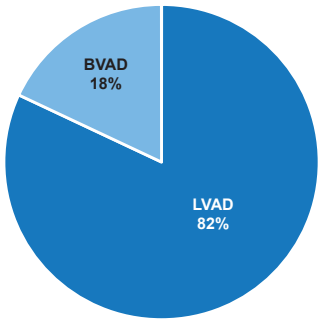


FIGURE 19 Type of support

Pediatric

Outstanding survival rates after EXCOR® Pediatric support in the setting of myocarditis and DCM have been demonstrated. High weaning rate of 36% was observed with EXCOR® Pediatric support in this single center experience.

Outcome

The median support time was 133 days (3 - 877 days), with a cumulative experience of 2,290 days of cardiac support.

Overall survival was 91%. 46% of the patients were transplanted, 36% were weaned and 9% are still on support.

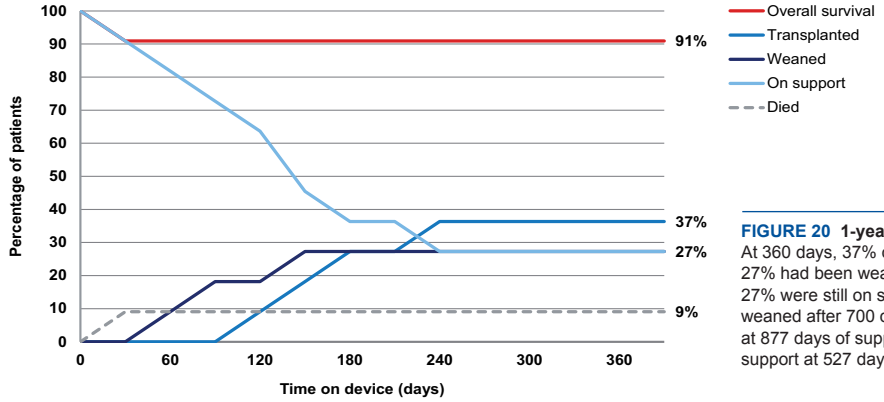


FIGURE 20 1-year survival (n=11)
At 360 days, 37% of the patients were transplanted, 27% had been weaned and 9% died on support. 27% were still on support. Thereof, one patient was weaned after 700 days, one patient transplanted at 877 days of support and one patient was still on support at 527 days.

A 3-year old girl diagnosed with DCM was supported for 877 days before successful transplantation. For a toddler, this is the longest time on support worldwide. It is important to note that no blood pump replacement was required anytime during the 877 days of support. Additionally, no major complications occurred during EXCOR® Pediatric support.

Long-term EXCOR® Pediatric support does not preclude recovery of the failing ventricle and weaning. A 1-year old girl was diagnosed with myocarditis and pulmonary edema. After implantation of the EXCOR® Pediatric VAD significant improvement of the LVEF was observed. The patient was successfully weaned after 700 days on EXCOR® Pediatric support.

Review of the United Kingdom Experience

Cassidy et al., A longer waiting game: bridging children to heart transplant with the Berlin Heart EXCOR device – the United Kingdom experience, J Heart Lung Transplant. 2013 Nov;32(11):1101-6

During the study period (December 2004 to December 2011), 102 children were supported with EXCOR® Pediatric with a cumulative experience of 5,247 days of support.

Patient characteristics

Variable	EXCOR® Pediatric patients (n=102)
Age in months, Median (range)	30.5 (0 - 202.8)
Weight in kg, Median (range)	11.6 (3 - 90)
Preoperative cardiac arrest (%)	23.5
Preoperative mechanical ventilation (%)	93
Preoperative ECMO (%)	24.5

Primary diagnosis

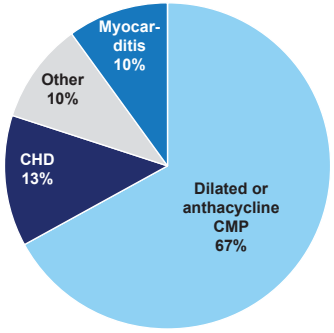


FIGURE 21 Primary diagnosis

Type of support

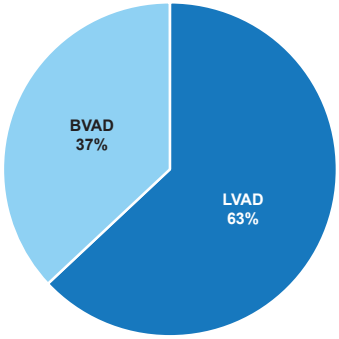


FIGURE 22 Type of support

Type of support

The overall median support time was 39 days (range 1 - 252 days). The median support time was longer in children who weighed ≤20 kg compared to whose weighing >20 kg (43 vs. 24 days). The median length of support is considerably longer compared with a median waiting time of 7 days (longest 22 days) in the 1998 to 2003 era due to a static transplant rate and gradual increase in transplant candidates.

Overall survival was 84%, 72% survived to transplantation and 12% demonstrated sufficient recovery of myocardial function for explantation.

Variability of survival was noted between diagnostic groups. Children with CHD had the lowest survival (69%) of any individual group. The CHD subpopulation included 5 patients with single ventricle physiology and ventricular failure after Glenn shunt.

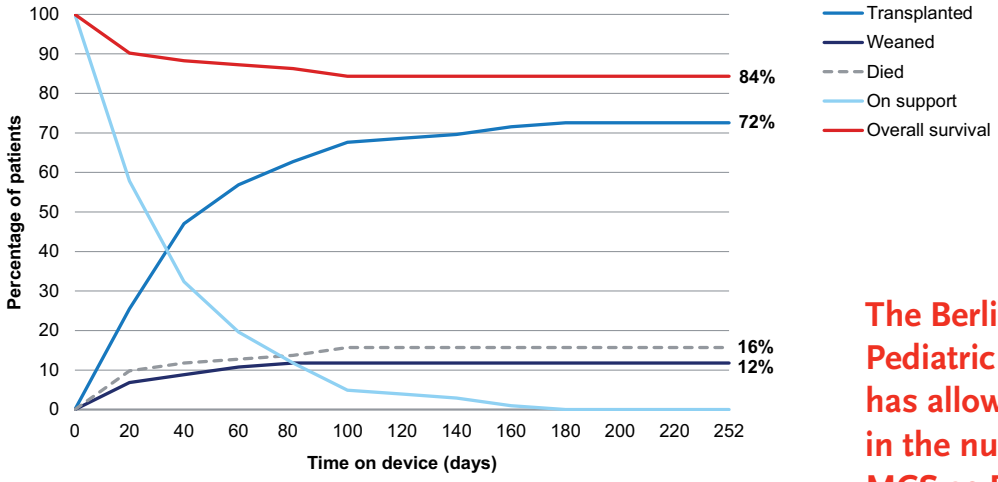


FIGURE 23 **Competing outcome with overall survival**
At 253 days, 72% of the patients were transplanted, 12% had been weaned and 16% died on support.

The Berlin Heart EXCOR® Pediatric experience in the UK has allowed significant increases in the number of children offered MCS as BTT and the length of time that they can be safely supported. Although younger children ≤20 kg have significantly longer waiting times on VAD support, their outcomes are comparable to older children.

Review of the Initial Experience in Poland

Kansy et al., First Multicenter Experience with EXCOR Pediatric in Poland - Successful introduction of pediatric VAD therapy, oral communication AEPC 2015

A total of 24 patients were implanted between December 2009 and March 2015.

Patient characteristics

Variable	EXCOR® Pediatric patients (n=24)
Age in years, Mean (range)	6.1 (0.2 - 15.0)
Weight in kg, Mean (range)	21.8 (4.9 - 57.0)
BSA in m^2, Mean (range)	0.8 (0.24 - 1.71)
LVEF in %, Mean (range)	17.7 (8 - 47)
INTERMACS profile 1 2 3 ≥ 4	 8.5% 50.0% 33.0% 8.5%
Preoperative inotrope infusion	100
Preoperative ECMO (%)	16.7
Preoperative mechanical ventilation (%)	37.5

Primary diagnosis

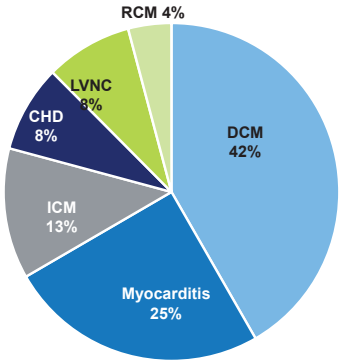


FIGURE 24 Primary diagnosis

Type of support

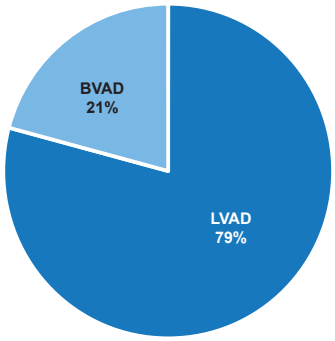


FIGURE 25 Type of support

Introduction of Pediatric VAD Therapy

Outcome

Mean support time was 165 days (range 16 - 1,097). Mean support time to heart transplantation was 160 days (range 69 - 433 days). Long-term support of more than 3 years on VAD reflects the overall trend of extended waiting time until heart transplantation.
Overall survival was 79 %, whereof 41.5 % survived to transplantation, 16.5 % demonstrated sufficient recovery of myocardial function for explantation and 21 % were still on support. One patient required re-implantation 7 days after weaning, he is still on EXCOR® support.

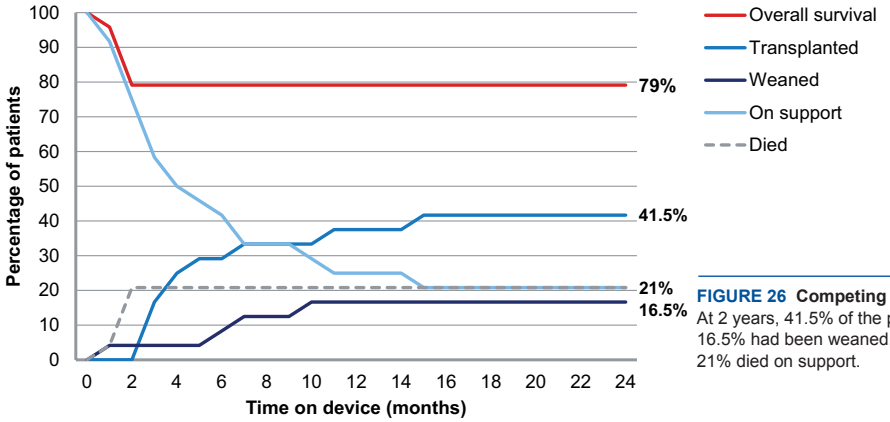


FIGURE 26 **Competing outcome with overall survival**
At 2 years, 41.5% of the patients were transplanted, 16.5% had been weaned, 21% are still on support and 21% died on support.

Serious adverse events

Serious adverse events	EXCOR® Pediatric patients (n=24)
Major bleeding	8.3% (0.18 EPPY)
Severe neurological events	12.5% (0.28 EPPY)
Transient neurological events	8.3% (0.18 EEPY)
Local infection	20.8% (0.46 EPPY)

Despite overcoming a learning curve, the device technology was applied with remarkable outcomes and a low complication rate.

Long-term VAD support of more than 2 years reflects the overall trend of extended transplant waiting time.

The EXCOR® Pediatric VAD has been successfully introduced in Poland with excellent results comparable to other experienced centers throughout the US and Europe.

Initial Clinical Experience in Japan

Review of the interim results of the EXCOR® Pediatric clinical study in Japan

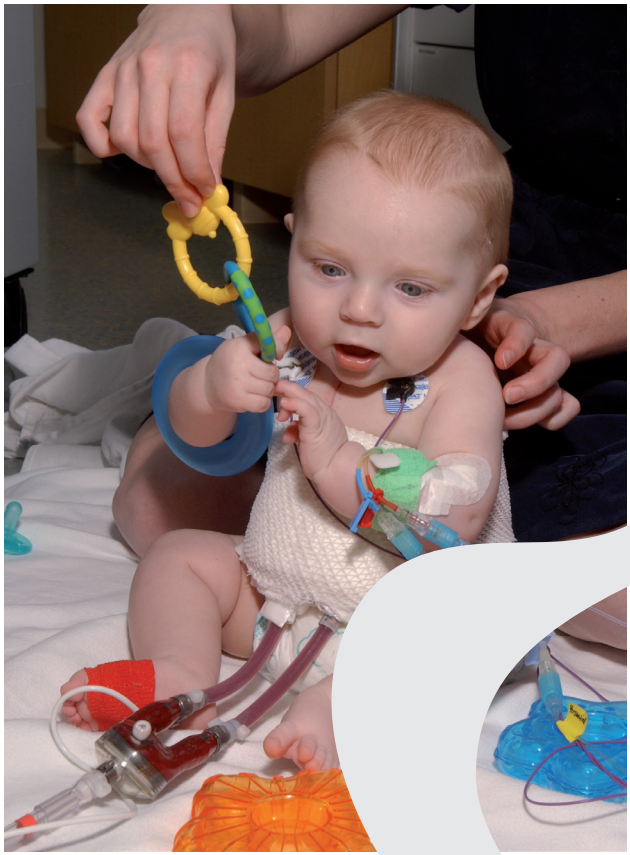
S. Kyo, What future will bring?, oral communication at ASCVTS 2014

In 2010, the organ transplant laws in Japan were revised and organ donation in children less than 15 years of age became possible. However, organ donation overall is extremely limited in Japan especially in the pediatric population. Longer bridge to transplantation support times with VADs is required for the pediatric population.

A pediatric VAD offering safe support for a prolonged period was urgently needed. Since 2012, 4 patients have been supported with the EXCOR® Pediatric VAD in Japan within a clinical study.

Patient characteristics

Variable	EXCOR® Pediatric patients (n=4)
Age in months, Median (range)	78 (4 - 156)
Weight in kg, Median (range)	11 (5 - 25)
INTERMACS level 1 or 2 (%)	100
Preoperative ECMO (%)	50
DCM preoperative diagnosis (%)	100
LVAD type of support (%)	100



Outcome

The overall median support time was 254 days (146 - 422 days). The Japanese patients were supported with EXCOR® Pediatric for a cumulative time of 1,110 days.
Overall survival was 100%, 50% were transplanted and 50% were still on support.

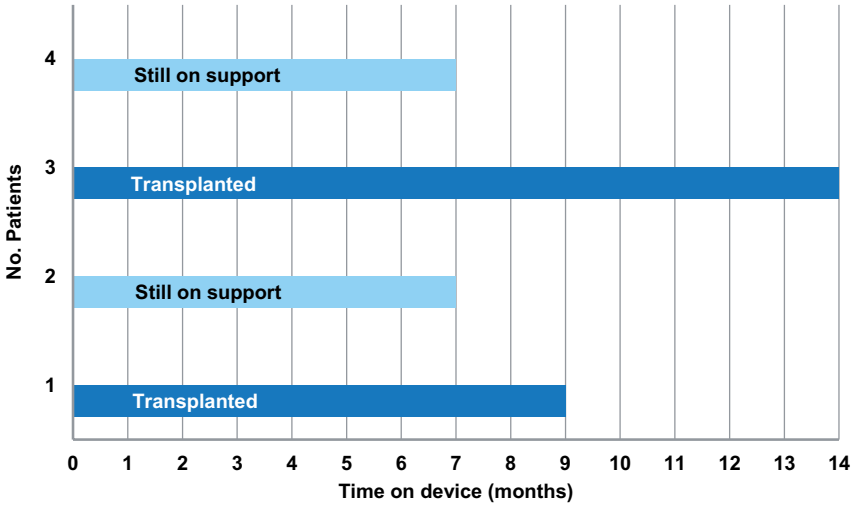


FIGURE 27 Time on device of Japanese patients
Two patients have been transplanted and two patients are still on support at 7 months.

The initial clinical experience with EXCOR® Pediatric in Japan is promising. All patients were either successfully transplanted or are still on support at 7 months.

Berlin Heart®

The availability of the Berlin Heart at BC Children's Hospital in Vancouver is incredibly exciting. The wait for suitable donor organs in Western Canada can be long. We are now able to bridge children with end-stage heart failure successfully and safely with this wonderful technology. We are very thankful to Berlin Heart for their tremendous support during the infancy of our surgical heart failure program.

Sanjiv K. Gandhi, MD, Chief, Pediatric Cardiothoracic Surgery, BC Children's Hospital

Berlin Heart GmbH
Wiesenweg 10
12247 Berlin · Germany
Phone +49 30 81 87 - 26 00
Fax +49 30 81 87 - 26 01
info@berlinheart.de
www.berlinheart.de

Berlin Heart Inc.
200 Valleywood
Suite B-100
The Woodlands · Texas 77380
Phone +1 281 863 - 97 00
Fax +1 281 863 - 97 01
info@berlinheart.com
www.berlinheart.com

The Berlin Heart EXCOR® Pediatric Ventricular Assist Device (EXCOR® Pediatric) is approved for use by the FDA under a Humanitarian Device Exemption.

Version MFE41.2
September 2015