Berlin Heart®

Parent Booklet

EXCOR® Pediatric Ventricular Assist Device

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BACKGROUND

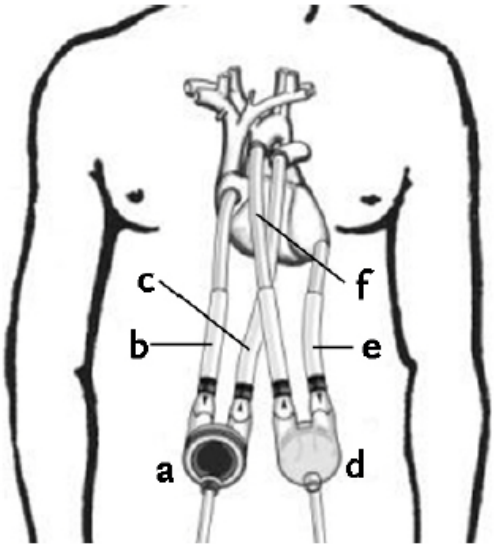
Your child's doctor has given you this booklet because the doctor has determined that your child's heart is having trouble pumping blood to the rest of his/her body. Your child's doctor will provide details specific to what caused your child's heart to have trouble pumping. This heart trouble is dangerous and your child's heart needs medical treatment to prevent damage to organs like the kidneys or to prevent your child from dying. Your child is a candidate for a heart transplant and since no organ is available right now, your child's doctor thinks a ventricular assist device might help your child's heart have the best chance for living until a donor heart becomes available. Your child's doctor has tried to help your child's heart pumping with the usual medical care. Unfortunately, this care has not been able to fix the pumping problems your child's heart has, something else to help improve his/her heart's pumping.

DEVICE DESCRIPTION

Devices are made that can possibly help a person whose heart function is not pumping enough blood to their body. One device is the Berlin Heart EXCOR® Pediatric Ventricular Assist Device (or simply "EXCOR® device"). The EXCOR® device has been approved by the Food and Drug Administration (FDA) with a Humanitarian Device Exemption (HDE). The

FDA and a team of doctors looked at the information from a clinical study that included 48 children that used the EXCOR® device and decided it was safe for use in children in the United States. More information is included in the back of this booklet about the Clinical Study reviewed by FDA.

The EXCOR® device has small pumps that can be used to support the left or right or both sides of your child's heart. The pump or pumps is/are connected to tubes (cannulas) that are sewn onto your child's heart. A machine outside of your child's body is used to make the pumps move the blood through your child's heart. This may help improve the blood flow to your child's body. A picture of the pumps attached to both sides of the heart is shown below.



a - Right pump *(pumps blood to the lungs)*

b - Right inflow cannula *(puts blood in the pump from the right side of the heart)*

c - Right outflow cannula *(sends blood to the lungs)*

d - Left pump *(pumps blood to the body)*

e - Left inflow cannula *(puts blood in the pump from the left side of the heart)*

f - Left outflow cannula *(sends blood to the body)*

Figure 1. EXCOR® Pump and Cannulas - Right and Left Heart Support

Blood Pump and Cannula Warnings

- Do not kink the tubes (cannula) to the heart needlessly. A kink could cause the blood to stop pumping through your child's body or cause the tubes (cannulas) to break that could lead to a leak in the tube.
- Do not pull, kink or do any activity that could put stress on the tubes to the heart. It is important to protect the cannnula and blood pump. Do not allow your child to belly flop, pull or stretch the cannula, as this may damage the cannula resulting in injury or death.
- Do not use pointed or sharp-edged objects near the EXCOR® device. The blood pump or tubes (cannulas) could be damaged causing a leak that could cause your child to not get enough blood.

IKUS Driver
(makes the pumps work by pushing the air into them)

Figure 2. The EXCOR® "IKUS" driver

Figure 2 shows the IKUS driver that is used to pump the blood through the blood pumps. The IKUS driver has three different sections that can provide air to the blood pump. The air is pumped through the tubes (drivelines) that connect to the machine and the blood pump shown in Figure 3. The IKUS is a heavy machine that may be rolled around on the wheels. It has a battery that will allow a short walk and outing from the hospital room when the doctors decide it is safe to let your child go out of the room. The IKUS has a backup system that will provide air and also has a manual air pump if needed. The IKUS must be plugged in; unless your child's clinical care team is with you and has a reason to unplug it. The care team is trained on the special programming and settings required for your child.

Driveline Warnings

- Do not kink the tubes (drivelines) to the IKUS. A kink could cause the blood to stop pumping through your child's body.

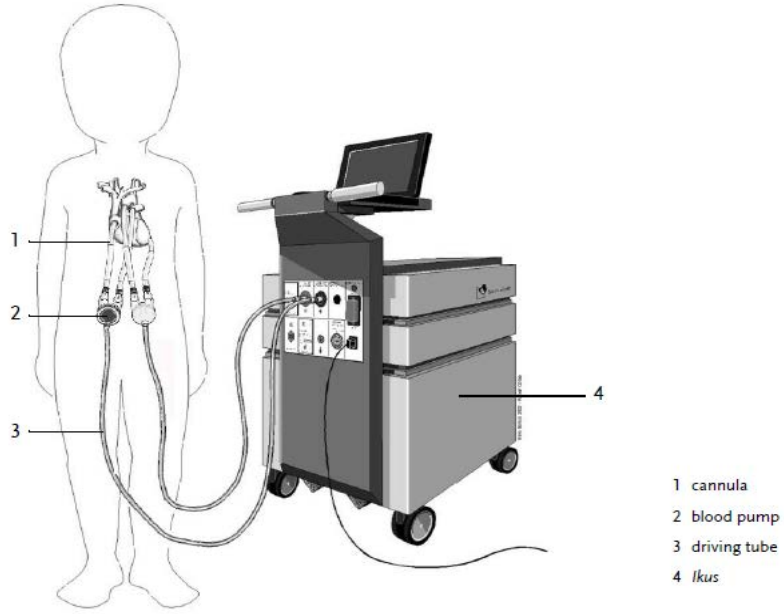


Figure 3. The whole system as it looks when on a patient that needs right and left pumps.

IKUS Driver Warnings

- Do not use water or fluids near IKUS. There is a risk of a short circuit or a malfunction of the device if it gets wet.
- Protect the IKUS from exposure to moisture and wetness. Never store or use the IKUS in a damp environment (e.g. bathroom, etc.). There is a risk of malfunction of the device in damp environments.
- Never unplug the IKUS, a hospital person trained on the EXCOR® will do that. If the IKUS has trouble or runs low on battery it could stop pumping, causing your child to not get enough pump output.
- Do not cover the air vents, they must not be covered or obstructed during operation. The IKUS could overheat if the vents are blocked and may have a malfunction in device operation that would cause your child to not get enough support from the EXCOR®.
- Place the IKUS driving unit on a firm and even surface. The IKUS is heavy and could roll away if not a firm, even surface. This could cause harm to your child or other people in the room.
- Never place other objects on top of an IKUS driving unit. The objects could fall causing damage to the IKUS that could lead to a problem with the IKUS.
- Avoid exposure to strong electromagnetic radiation (from items like a mobile/cell phones and cordless phones when switched on, electromagnetic security systems etc.). When using a cell phone in the immediate environment of an IKUS in operation

please make sure to keep a distance of at least at least 3 feet. The radiation from the devices could cause a problem with the IKUS.

- Protect the IKUS against extreme temperature changes and overheating (e.g. direct sunlight or from heaters). There is a risk that it could cause a problem with the IKUS that could lead to your child not having enough support from the EXCOR®.

WHAT ARE THE STEPS FOR GETTING AN EXCOR®?

If you allow your child to receive the EXCOR® device, your child's doctor will review the whole procedure with you and maybe with your child. A basic description of what will happen is listed here.

Before the Procedure:

Your child will have a physical exam and other tests before the EXCOR® device implant. Tests will include measuring your child's heart rate and blood pressure, urine output, blood tests, a CT Scan of the head (pictures of the brain), and possibly other tests for your child's heart. These tests will help the doctor know if your child is sick enough to receive the EXCOR® device or too sick to have the EXCOR® device. The doctors will also check if your child is able to take blood thinning medications that need to be used while on the EXCOR® device.

If the tests show that he/she can receive the EXCOR® device, the device will be implanted in the operating room using surgery with your child's chest open like regular heart surgery.

During the Implant Procedure:

For the surgery, your child will receive medication to help him/her relax, and anesthesia medications to prevent discomfort and pain by keeping your child asleep during the operation. A breathing tube will be placed in your child's throat to help your child's lungs receive oxygen from a machine called a ventilator. This tube will remain in place until your child's doctor determines your child is able to breathe on his/her own without the help of a ventilator. Your child's chest will be opened to get to his/her heart in order to insert the tubes (cannulas) that will be connected to the EXCOR® blood pump(s). The tubes (cannulas) will be secured to your child's heart and blood vessels with stitches. Once the tubes (cannulas) are sewn to the heart, they will be connected to the EXCOR® blood pump(s). The pumps will stay outside your child's body. Your child's doctor will start the pump(s) and after the pump(s) is/are started, your child's doctor will usually close his/her chest. Your child's doctor may decide to keep his/her chest open if needed. The chest may be left open if your child's tissue is swollen from the trauma or if there is a complication from surgery such as oozing or bleeding. The doctor will place a sterile patch over your child's chest until their chest is closed. After the surgery your child will be moved to the Pediatric Intensive Care Unit until he/she wakes up from the surgery.

After the Implant Procedure:

After the device is implanted, your child will be treated at the Pediatric Intensive Care Unit. He/she will be supported with a breathing machine and will have medications that will keep him/her comfortable and likely sleepy. Your child may have many wires attached to their body to monitor your child's heart, blood pressure and breathing; the hospital staff will explain each of those to you. The goal will be to wean your child from the breathing machine. The nurses and doctors will also be drawing blood to do lab tests to be sure your child is recovering as expected. One reason they need to draw blood is to be sure that your child has enough blood thinning medications to avoid blood clots.

The doctors and nurses will also have to check the sites where the tubes (cannulas) for the EXCOR® pumps come through the skin. These sites will be cleaned on a regular schedule to keep your child from getting an infection.

As your child recovers, the hospital staff may start several types of therapy, light school work, art projects, etc. as they do for other children in the hospital. Your child may get well enough to go for walks around the hospital to visit areas such as the playrooms, the cafeteria, etc. Each time your child is transported, you must have a hospital employee that is trained on the EXCOR® device to help care for the device. The device should never be unplugged to go out of the hospital room without a trained hospital employee there to help. Your child will not be able to leave the hospital while on the EXCOR device. The system is not approved for use outside of a hospital setting. It is possible that you may stay on the Pediatric Intensive Care Unit for an extended time or the whole time your child is supported with the EXCOR® device.

WHAT TESTING IS PERFORMED WHILE ON THE EXCOR®?

Your child will have a physical exam and tests before and after the EXCOR® device is implanted. These tests include: heart rate and blood pressure measurements, urine output, and blood tests. These tests will be done before the EXCOR® device is implanted and will be repeated during the time your child is on the EXCOR® device and after the device has been implanted. Your child may also have a video done of their heart called an echocardiogram. This video will help your child's doctor determine when it is time to adjust how the EXCOR® device is functioning to help your child's heart. The doctor will use the echocardiogram to check on your child's heart trouble.

HOW LONG WILL MY CHILD BE ON THE EXCOR®?

The situation for every child is different and that makes it difficult to predict how long your child will need the EXCOR® device. Some children are on the device for only a few weeks while others are on the device for many months. Unfortunately, there is no timeframe for finding a donor heart that matches your child. The longest time a child has been on the EXCOR® device in the United States is 435 days. The average time children were on the device in the United States was 58 days.

HOW IS THE DEVICE REMOVED?

The removal of the EXCOR® device must take place in the operating room. This procedure will require medications and other steps your child had when the pump was inserted. Your child will go back to the operating room and the pump will be stopped and removed. Typically, your child will receive a heart transplant at this time. In some cases, when the heart has regained enough strength so that a child doesn't still need a heart transplant, the pump will be removed. Prior to deciding whether to remove the pump, your child's doctors will make changes to the pump settings and your child's medications. More videos (echocardiogram) of the heart will be completed to ensure that the heart has regained strength. In this case, the holes where the tubes(cannulas) were located in your child's heart will be sewn up, and your child's chest closed without having a heart transplant performed.

WHAT ARE THE POSSIBLE RISKS?

The EXCOR® device is FDA-approved under a Humanitarian Device Exemption. This approval was based on a clinical study that showed that the device was safe compared to the other options. There are risks associated with this type of device that are similar to those risks identified with other heart assist devices and with heart surgery. It is possible that these risks could result in serious or permanent injury or disability.

In the back of this booklet are some tables that explain the likelihood of the risks for the EXCOR® and how these risks led to problems reported in the children in the Clinical Study reviewed by FDA.

Your child is at risk of having some of the same events, including:

- Death;
- stroke (blood clot in the brain) or other event including seizures;
- delayed time on breathing machine after surgery;
- blocked blood flow to organs such as lungs and/or blood vessels due to a blood clot, air bubble, fat deposit, or other unknown substance;
- trouble breathing;
- fluid in lungs or in the space around the lungs or other damage to lungs;
- the need to re-use the heart-lung machine;
- surgery to stop bleeding ;
- infection requiring surgery or medications;
- a blood infection;
- reduction or loss of kidney function, possibly requiring use of a machine to filter your blood;
- irregular heartbeats that may require an electrical shock or an electronic device ("pacemaker") to fix the heart beat;
- heart attack; too little blood flow, and/or fluid around heart;
- swelling of the sac around heart;
- changes in heart laboratory values;

- blood clot in blood vessels;
- blood vessel damage such as rupture, tearing, or forming a hole or connection between an artery and vein;
- allergic reaction to the EXCOR device;
- bleeding, possibly requiring blood transfusions, surgery or medicine;
- tissues experiencing swelling (inflammatory reaction);
- re-opening of the wound(s)
- right heart failure;
- blood disorders;
- psychiatric event;
- high or low blood pressure;
- fever or chills, abnormal liver function; digestion problems;
- organ failure or dysfunction;
- lack of oxygen to limbs or organs, possibly resulting in damage including loss of lower limb function and/or the need to remove the limb

Risks that may be specific to the EXCOR® device include:

- not being able to place the EXCOR® device in the heart;
- putting the EXCOR® device in the wrong place or movement during surgery;
- heart wall damage; heart valve damage or lowered heart function;
- the pump not pumping enough blood for the body;
- difficulty stopping use of the EXCOR® pump if the heart is pumping or other organ function is not adequate, possibly needing to use a heart support machine;
- device breakage or failure;
- the need to change to another EXCOR® device; of the 48 children implanted with the EXCOR® device in the FDA study, 24 children had their blood pumps exchanged for another EXCOR® blood pump because of blood deposits forming in the blood pumps; the average time to the first blood pump exchange in these children was 24 days from the time of implantation;
- damage to blood cells, that may appear as a reddish color in the urine;
- air bubbles in blood;
- and tissue or organ damage due to the pumping action.

The back of this booklet will help explain how these risks led to problems reported in the children in the Clinical Study reviewed by FDA. It will also explain more of the information from the study such as how many children were transplanted or that died while on support.

The implant procedure may involve more risks that are unknown at this time. Precautions will be taken to avoid harmful side effects including close monitoring of your child during and after pump placement by the medical staff trained in procedures like these. In addition, this procedure may involve unforeseeable risks to your child's fetus if she is pregnant. Therefore, pregnant women should not receive the EXCOR® device. Should your child become pregnant after receiving the device, you or your child should notify your child's doctor right away.

WHAT ARE THE POTENTIAL BENEFITS OF THE EXCOR® SUPPORT?

Possible benefits from this device may include:

- providing enough support to your child's heart to allow your child to have a heart transplant operation;
- protection from further heart and organ damage due to lack of blood flow;
- reduced work load on your child's heart;
- increased blood flow and oxygen delivery and supply to other parts of your child's body;
- providing enough support to your child's heart to allow your child's heart to regain strength to allow removal of the device without a need for a heart transplant.

In the back of this booklet are some tables that explain how these benefits led to outcomes or success reported in the children in the Clinical Study reviewed by FDA.

ARE THERE ANY ALTERNATIVE PROCEDURES AND TREATMENTS?

You may choose for your child to have no treatment performed. If your child does not receive this device your child will still have the same medical treatment options your child had before. Options that are available to your child may include: placement of another device such as a ventricular assist device (VAD) which requires placement and removal with an operation, intra-aortic balloon pump (IABP), and/or extracorporeal membrane oxygenation (ECMO); heart transplant surgery if your child is a candidate, and medications. There may be other options specific to your child's case; you, and if appropriate your child, should discuss these options with your child's doctor.

WHO DO I CONTACT FOR QUESTIONS?

For more information concerning risk or injuries you or your child may contact your child's primary doctor. You or your child may also want to discuss items such as rehabilitation, play time or social issues with team members listed here:

AREA OF SUPPORT	NAME	PHONE NUMBER
Primary Doctor		

GLOSSARY

Ventricular Assist Device – a pump that connects to the ventricles of the heart to help the heart pump.

Humanitarian Device Exemption – an FDA approval for a device that is intended for use in less than 4000 people.

FDA (Food and Drug Administration) – the US government agency that helps decide if certain foods, medications, or devices are safe for use.

Blood pump – the main part of the pump that keeps the blood moving through the heart and the body.

Cannula – the tube that connects the pump to the heart.

Right side of the heart – the side of the heart that pumps blood through the lungs and into the left side of the heart.

Left side of the heart – the side of the heart that pumps blood to all of the body including the brain.

IKUS Driver – the machine that pushes air in and out of the blood pumps to get the blood through the heart and to the body.

Driving Tube – the air line from the blood pump to the IKUS driver that carries air to the blood pump.

Anesthesia – drug used by doctors to keep a person asleep, free of pain and not moving during surgery.

Infection – when someone gets sick or when a certain virus or bacteria starts growing in a certain area of the body.

Ultrasound or ECHO – a video of the heart for doctors to see how well it is working.

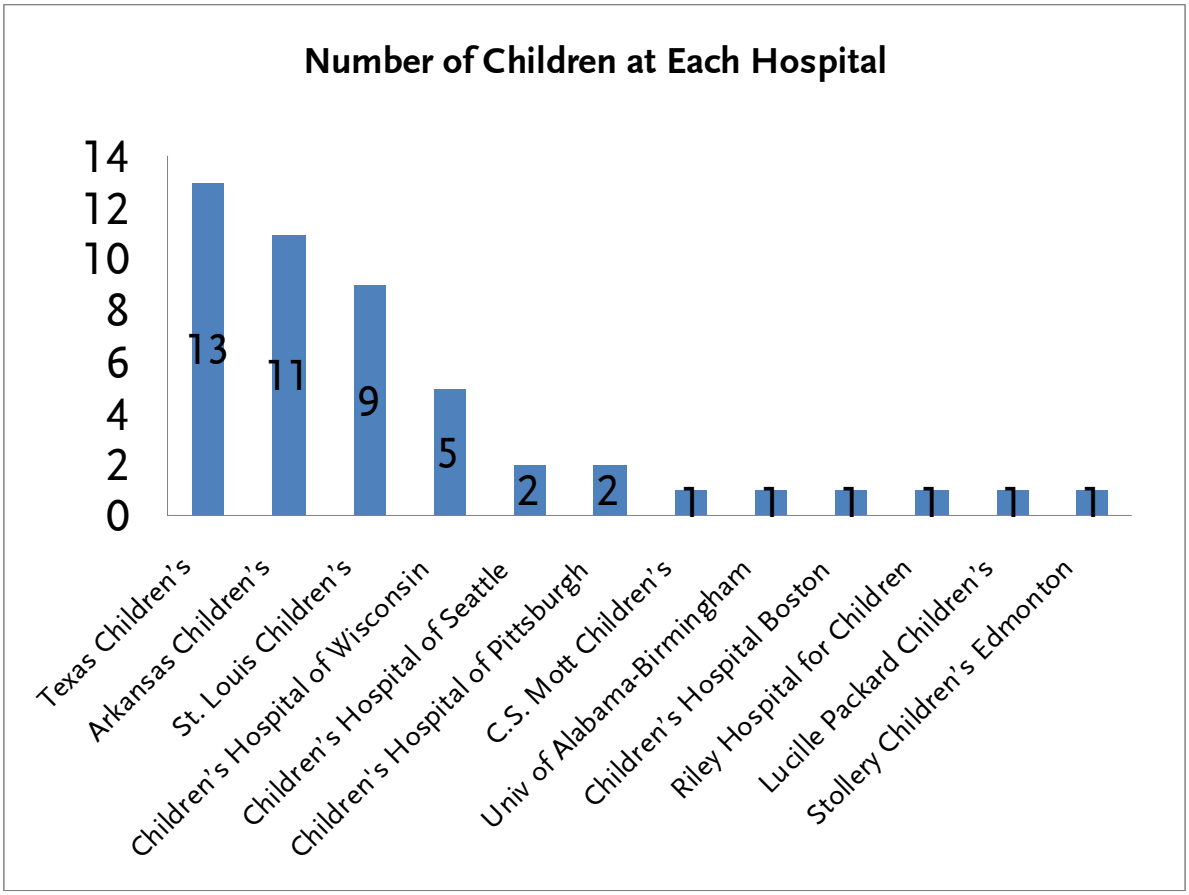
CT Scan – a video of the brain for doctors to decide if the brain is normal.

Inflammatory reaction – a reaction that causes swelling or a lab value to be out of range.

ECMO(Extracorporeal membrane oxygenation) – a device that supports the heart and lungs that is like the heart-lung machine used in surgery.
Intra-aortic balloon pump – a balloon on a long wire that is put into the body close to the heart to help the heart pump.

CLINICAL STUDY SUMMARY REVIEWED BY FDA

There were 48 children implanted with EXCOR® device during the clinical study. This shows where the children had their device implanted.



This table shows basic information on the 48 children.

Characteristic	Category	Number
Sex	Girls	23
	Boys	25
Age	0 - 30 days	0
	30 days to 2 years	20
	2 to 10 years	18
	10 to 16 years	10
Weight	3 to 10 kg	16
	10 to 30 kg	20
	30 to 60 kg	12
Primary Reason for needing the EXCOR® implant	Cardiomyopathy (Diseases of the heart muscle)	31
	Myocarditis (Irritation of the heart muscle)	8
	Congenital Heart Disease (Heart problems that the child was born with)	9
Children on ECMO prior to EXCOR®		14
Children on Ventilator prior to EXCOR®		32
Children on Ultrafiltration prior to EXCOR®		4
Children on a different VAD prior to EXCOR®		2
Children fed using Feeding tube prior to EXCOR®		17
Children had a heart attack (cardiac arrest) prior to the EXCOR® implant		12
Type of VAD implanted	Left side	31
	Both Left and Right sides	17
Children had another surgery at the same time as the EXCOR® implant (such as repairing another heart problem)		25
Children had a pump exchange due to thrombus		38

The 48 children implanted during the study were on the EXCOR® device from as little as less than one day to as much as 192 days (or a little over 6 months).

Half the children were on less than 38 days and half were on more than 38 days. The time that the children were supported depended on their health and the availability of a heart for them to receive.

This table shows the range of times that the children were on the device.

Time on EXCOR® Pediatric Device	Number
1 week (0 to 7 days)	6
Up to 1 month (8 days to 30 days)	13
Up to 2 months (31 days to 60 days)	11
Up to 3 months (61 days to 90 days)	6
Over 3 months (90 days to 192 days)	12

Each of the children implanted with an EXCOR® device either went on to get a heart transplant, were taken off the EXCOR® and found that they did not need a heart transplant (weaned) or died before they could receive a heart transplant.

This table shows what happened to all of the children who received the EXCOR® device in this clinical study.

Outcome of the Child	Number
Received heart transplant	42
Explanted/Weaned from EXCOR®	1
Explanted/Weaned from EXCOR® but had other problems	1
Died before receiving heart transplant	4

Of the 48 children implanted during the study, 4 died before they could receive a heart transplant. Two of these died because of a stroke (blood clot in the brain) and one because of a large blood clot in the body. Another child died during the operation to implant the EXCOR®.

Of the 48 children implanted during the study, 43 were supported long enough so that a heart transplant could be performed or recovered so that they didn't need to receive a heart transplant. This means that you would expect 90 out of every 100 children to have a successful outcome. The other 10 out of every 100 children may not be successful.

Of the 48 children implanted during the study, 14 had a blood clot in the brain that could also be called a stroke. The doctors continued to follow-up on these children to see how well they recover or if more support was needed.

Of the 14 children, 2 died due to the brain problem and before they had a chance to get a heart transplant and another 4 children were transplanted then an exam found that they had severe effects. But 3 of those 4 children are still alive and are working with physical therapists to improve.

The children were followed very closely during their stay in the hospital while on the EXCOR® device. Some of the children had minor or major issues due to the device or their own health. The following events were reported during the clinical study. All of the events had an effect that is listed in the table. Some children might have had more than one event so that there are less "children with an event" than the total number of events.

Adverse Event	Total Events	Children with an event		Effects of the Event (note: some children were sedated and so the doctors were not able to determine the effect)
Major Infection-Localized Non-Device	43	22	45.8%	Antibiotics given
Major Bleeding	37	22	45.8%	Transfusion given or operation performed to stop bleeding
Hypertension	20	20	41.7%	High blood pressure
Neurological Dysfunction-Ischemic CVA	15	14	29.2%	Weakness, Speech problems
Major Infection-Sepsis	12	11	22.9%	Antibiotics given
Respiratory Failure	12	9	18.8%	Tube placed
Right Heart Failure	5	5	10.4%	Need for support of the right ventricle
Renal Dysfunction-Acute	5	4	8.3%	Kidney not functioning properly
Pericardial Fluid Collection-Without Tamponade	4	4	8.3%	Pressure on the heart
Major Infection-Percutaneous Site or Pocket	4	4	8.3%	Antibiotics given
Cardiac Arrhythmia-Sustained SVT	4	3	6.3%	Medications given to control the fast heart beat
Cardiac Arrhythmia-Sustained VT	3	3	6.3%	Medications given to control the fast heart beat
Pericardial Fluid Collection-With Tamponade	3	3	6.3%	Drainage of fluid
Hemolysis-Late	2	2	4.2%	Lower level of red blood cells in blood

Adverse Event	Total Events	Children with an event		Effects of the Event (note: some children were sedated and so the doctors were not able to determine the effect)
Hepatic Dysfunction	2	2	4.2%	Bilirubin not being sent out from body
Neurological Dysfunction-Hemorrhagic CVA	2	2	4.2%	Issues with thinking and talking
Renal Dysfunction-Chronic	2	2	4.2%	Kidney not functioning properly
Psychiatric Episode	1	1	2.1%	Agitation, feeling of panic
Arterial Non-CNS Thromboembolism	1	1	2.1%	Blood clot in an artery with no effect
Venous Thromboembolism Event	1	1	2.1%	Swelling
Other	25	12	25.0%	Depends on event

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