

# A Prospective, Multicenter Trial of the VentrAssist Left Ventricular Assist Device for Bridge to Transplant: Safety and Efficacy

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- Background:** The increasing prevalence of chronic heart failure has stimulated the ongoing development of left ventricular assist devices (LVADs) for both bridge-to-transplant (BTT) and destination therapy (DT). The aim of this prospective, multicenter clinical trial was to determine the efficacy and safety of a third-generation LVAD, the VentrAssist, in a BTT cohort.
- Methods:** Patients (n = 33) with end-stage chronic heart failure who required circulatory support as BTT therapy were implanted with a VentrAssist device. The primary outcome was survival until transplant or transplant eligibility with the device in situ at trial end-point (Day 154 after implant). The secondary outcomes were pump flow index and end-organ function. Safety, patient functional status and resource use were also assessed.
- Results:** At trial end-point, the success rate was 82% (39.4% transplanted, 42.4% transplant-eligible). The LVAD pump flow index (median  $\geq 2.7$  liters/min/m<sup>2</sup>) was sufficient to maintain an adequate circulation and significantly improve end-organ function. Of the 77 protocol-defined serious adverse events, most occurred within 30 days of implantation. No patients died as a direct result of pump failure or malfunction. After implantation, patient functional status improved, with 70% of patients achieving hospital discharge, and resource use was reduced.
- Conclusions:** This trial demonstrated a favorable efficacy and safety profile for use of the VentrAssist LVAD in BTT patients. *J Heart Lung Transplant* 2008;27:579–88. Copyright © 2008 by the International Society for Heart and Lung Transplantation.

Chronic heart failure (CHF) is a major public health problem associated with considerable morbidity, mortality and resource use.<sup>1–3</sup> As the population ages, the number of elderly patients with CHF is expected to double to 70 million within 25 years.<sup>4</sup> Although heart transplantation (HTx) remains the optimal treatment for eligible patients, the shortage of donor hearts limits this option.<sup>4,5</sup> The prevalence of CHF and the shortage of donor hearts have fueled the development of left ventricular assist devices (LVADs), particularly for bridge-to-

transplant (BTT) purposes.<sup>6–8</sup> Nearly 80% of LVADs have been implanted as BTTs<sup>9</sup> and earlier fears of increased panel-reactive antibodies or post-BTT morbidity or mortality are no longer considered significant.<sup>10</sup>

The VentrAssist is a novel, third-generation, continuous-flow LVAD designed to overcome earlier LVAD limitations such as size, noise, reliability and mechanical complexity.<sup>5,11</sup> The first implant of the VentrAssist occurred in 2003,<sup>11</sup> with an updated implant report published in 2006.<sup>13</sup> We now present the first full report from a prospective, international trial of the VentrAssist LVAD as BTT.

## METHODS

### Study Design and Sponsorship

This prospective, longitudinal, single-arm, multicenter clinical trial was designed to determine the efficacy and safety of the VentrAssist LVAD in BTT patients. The trial was approved by the ethics committees of the seven participating centers and performed according to the principles of the Declaration of Helsinki. The trial began in September 2004 and ended in August 2006, with final follow-up on May 31, 2007. The sponsor (Ventricor, Ltd.)

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**Table 1.** Inclusion and Exclusion Criteria for Trial Participation

Inclusion criteria	Exclusion criteria
Transplant-eligible (according to institutional policy or likely to become transplant-eligible after LVAD implant)	Cardiogenic shock, acute myocardial infarction or cardiac arrest within 48 hours of enrollment
Requirement for circulatory support until transplant	Primary right-sided heart failure confirmed by echocardiogram with central venous pressure greater than 15 mm Hg and pulmonary artery systolic pressure greater than 60 mm Hg
Negative pregnancy test	Hypertrophic obstructive cardiomyopathy or restrictive cardiomyopathy
Willing and able to give informed consent	A mechanical prosthetic valve
Availability of strong social and physical support	Greater than mild aortic regurgitation
Able to attend the hospital for all protocol procedures	Recurrent ventricular tachycardia or ventricular fibrillation
	Pulmonary hypertension
	Severe tricuspid regurgitation
	Intracardiac clot/thrombus unlikely to be removed at surgery
	Chronic renal or liver failure
	Severe chronic obstructive pulmonary disease
	Stroke within 90 days before enrollment or a history of cerebral vascular disease with significant extra cranial stenosis
	Evidence of significant untreated aortic aneurysm
	Active bleeding
	Ongoing substance abuse
	Active methicillin-resistant <i>Staphylococcus aureus</i> infection or sepsis
	Cardiotomy within 6 weeks of enrollment
	Major organ transplant surgery
	Cardiomyoplasty/left ventricular reconstruction
	Body mass index >35 kg/m <sup>2</sup>
	Weight >120 kg
	Body surface area <1.4 m <sup>2</sup>

did not impose any limitations on data collection, analysis, interpretation or any resulting publications.

### Patients

Patients with end-stage CHF requiring circulatory support were recruited from the seven centers. Patient eligibility was determined according to protocol-defined criteria (Table 1) and enrollment was sequential and competitive.

### Device, Implant Procedure and Post-operative Management

The VentrAssist device, implant procedure and post-operative management have been described previously.<sup>5,12,13</sup> Briefly, the pump (Figure 1) was implanted via a sternal incision in the posterior rectus sheath or in a pre-peritoneal position. The inflow cannula was connected to the left ventricular apex and the outflow cannula to the ascending aorta. The position of the implanted components and the external controller and battery pack are shown in Figure 2.

Patients received standard post-operative care. A minimal recommended anti-coagulation protocol was used: Unfractionated heparin was initiated 6 to 12 hours after surgery, when chest tube drainage was <50 ml/h, and was continued to maintain an activated partial thromboplastin time of 50 to 60 seconds. Warfarin replaced

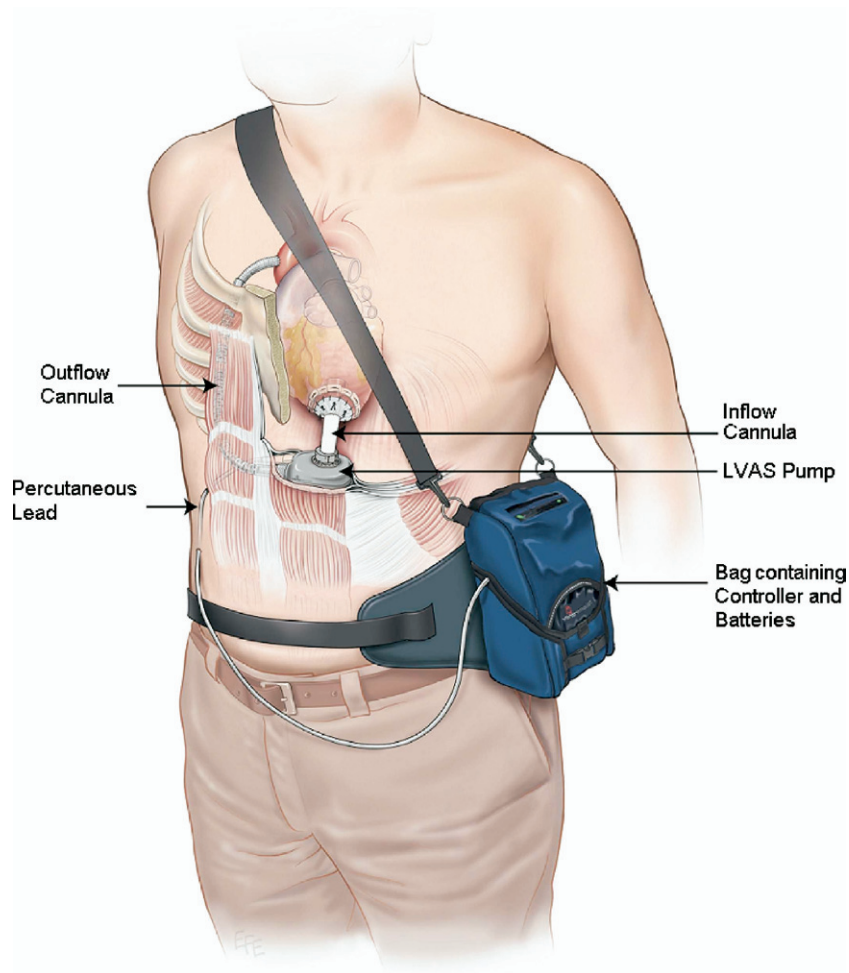
heparin when the patient became stable, intravenous lines had been removed, and gastrointestinal function had returned. Warfarin was adjusted to achieve an international normalized ratio (INR) of 2.0 to 2.5. Acetylsalicylic acid (100 to 160 mg/day) was initiated 24 hours after surgery.

### Outcome Measures

**Efficacy.** The trial primary outcome was survival until HTx or transplant-eligibility at post-operative day (POD) 154.



**Figure 1.** The VentrAssist blood pump.



**Figure 2.** The VentrAssist system in situ.

This end-point was selected because this was the median time from listing to transplant at three centers (The Alfred Hospital, St. Vincent's Hospital and Papworth Hospital). Success in the trial was defined as: (a) being transplant-eligible with the device in situ; or (b) being transplanted at or before POD 154. Survival and safety data were collected up until May 31, 2007 from all enrolled patients.

Secondary outcome measures included pump flow index, based on pre- and post-implant hemodynamics, and end-organ perfusion, based on measurements of renal (serum creatinine) and hepatic (total bilirubin) function.

**Safety.** Safety was assessed based on the incidence and severity of adverse events. Serious adverse events (SAEs) were classified as protocol-defined if they were known to be associated with the presence of an LVAD. Non-protocol-defined SAEs were coded using terminology from the *Medical Dictionary for Regulatory Activities* (MedDRA—registered trademark of the International Federation of Pharmaceutical Manufacturers and Associations).

All SAEs were reported to the relevant ethics com-

mittee and regulatory authority. An independent Data Safety Monitoring Board provided appropriate oversight of safety and a Morbidity and Mortality Committee adjudicated whether SAEs were device-related.

**Patient functional status.** Patient functional status was assessed based on quality-of-life measurements using the New York Heart Association (NYHA) class system<sup>14</sup> and the Rosser Utility Index.<sup>15</sup> This index is derived from questions based on distress (pain, feeling, anger, sleep), and disability (general mobility, self-care, usual activities, social/personal relationships).

**Resource use.** Resource use was assessed based on medication use and hospital re-admissions, quantified as days spent in an intensive care unit (ICU) or a non-ICU facility.

### Statistical Analyses

The a priori hypothesis was that the VentrAssist would provide adequate circulatory support for patients awaiting transplantation. This hypothesis would be supported if the lower boundary of the 95% confidence

interval for the proportion of successes was at least 65% that of the implanted patients. The sample size required was 30 patients. A 10% allowance (3 patients) was made for withdrawals. Based on the charts of Mehta and Cain,<sup>16</sup> at least 27 of 33 patients had to achieve trial success in order to obtain a  $\geq 65\%$  success rate (95% confidence limits: 65% to 93%).

## RESULTS

### Patient Disposition and Demographics

Of the 43 patients screened, 33 were enrolled and implanted with a VentrAssist (Figure 3). Reasons for patient exclusion were: septicemia (1), right heart failure (1), death (1), inflammatory bowel disease (1) and wanted an approved device (1), and 5 were excluded for unknown reasons. The 33 enrolled patients were predominantly white males, had a mean age of 52 years, and had severe end-stage CHF, as typified by a low cardiac index, low left ventricular ejection fraction and high pulmonary capillary wedge pressure (Table 2). All patients were in New York Heart Association (NYHA) Class IV.

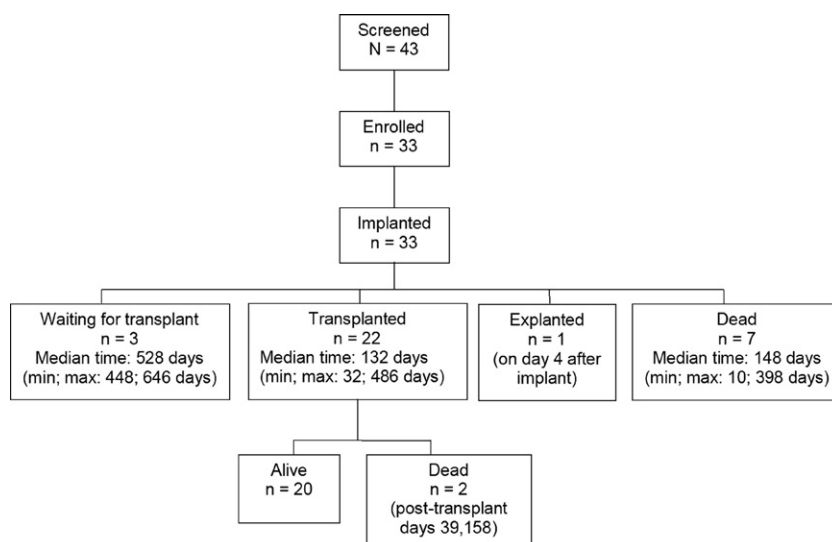
As of May 31, 2007, the device support time was  $197 \pm 173$  (mean  $\pm$  SD) days and the median support time was 142 days (range 4 to 646). Total support time across all patients was 6,499 days (17.8 years).

**Efficacy.** At trial end-point, 39.4% (13 of 33) of patients had been successfully bridged to transplant and 42.4% (14 of 33) of patients remained transplant-eligible (Figure 4). Thus, the success rate was 82% (95% confidence interval: 65% to 93%). This rate was maintained during follow-up; at Day 365, the success rate was 82%, with 60.6% (20 of 33) of patients transplanted and 21.2% (7 of 33) remaining transplant-eligible. Among patients

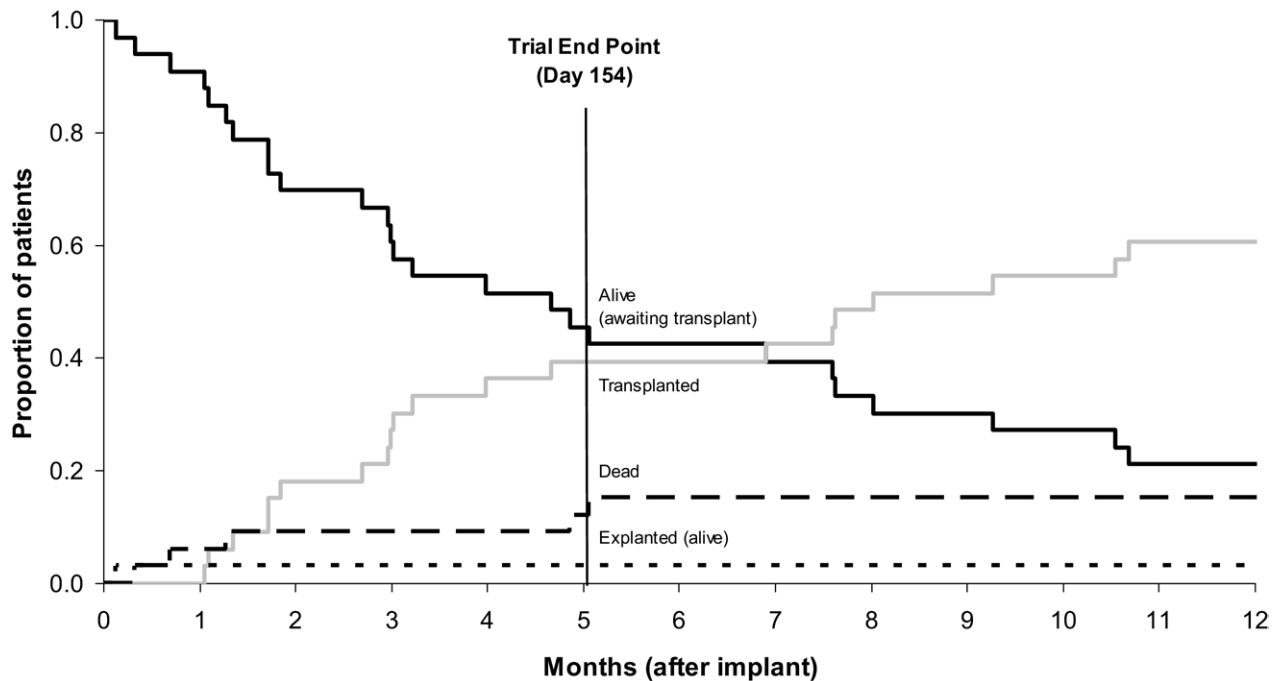
**Table 2.** Baseline Demographic and Clinical Characteristics of the Enrolled Patients ( $n = 33$ )

Characteristic	Data (mean $\pm$ SD)
Age (years)	52 $\pm$ 15.2
Male gender (%)	82
Ethnicity white (%)	91
Primary diagnosis	
Idiopathic/non-ischemic cardiomyopathy (%)	64
Ischemic cardiomyopathy (%)	36
Height (cm)	174.5 $\pm$ 12.2
Weight (kg)	78.9 $\pm$ 18.7
Body surface area (m <sup>2</sup> )	1.95 $\pm$ 0.29
Body mass index (kg/m <sup>2</sup> )	25.7 $\pm$ 4.8
Pulmonary arterial pressure	
Systolic (mm Hg)	47 $\pm$ 14.2
Diastolic (mm Hg)	24 $\pm$ 8.19
Pulmonary capillary wedge pressure (mm Hg)	23 $\pm$ 6.9
Central venous pressure (mm Hg)	13 $\pm$ 5.8
Cardiac index (liters/min/m <sup>2</sup> )	1.96 $\pm$ 0.7
Left ventricular ejection fraction (%)	16.5 $\pm$ 6.5
Intra-aortic balloon pump and/or extracorporeal membrane oxygenation treatment (%)	36
At least one inotrope agent (%)	64
Previous sternotomy (%)	15
New York Heart Association Class IV (%)	100

awaiting transplant, 5 died during the trial and 2 died >1 year after implantation (Figure 4). Causes of death for those who failed to reach transplantation were: cerebral hemorrhage (1); sepsis (1); ischemic bowel (1); multiple-organ failure (1); and "elective treatment withdrawal due to poor prognosis" (1). As of May 31, 2007, 2 of the 22 transplanted patients had died. After 282 days on VentrAssist support, 1 patient was transplanted but died 30 days afterwards from an ischemic



**Figure 3.** Disposition of patients during the trial and outcomes as of May 31, 2007.



**Figure 4.** Competing, mutually exclusive outcomes occurring during the 12 months after patients ( $n = 33$ ) were implanted with a VentrAssist device.

bowel. After 56 days on VentrAssist support, the other patient was transplanted, but died 158 days afterwards from fungal sepsis (not present at HTx).

Immediately after implantation, the mean pump flow index was 2.7 liters/min/m<sup>2</sup> (minimum 2.0 liters/min/m<sup>2</sup>, maximum 3.5 liters/min/m<sup>2</sup>; SD = 0.4;  $n = 24$ ), an improvement over the baseline cardiac index (mean 1.96 liters/min/m<sup>2</sup>; SD = 0.7;  $n = 33$ ). The pump flow index continued to improve, reaching a mean value of 2.9 liters/min/m<sup>2</sup> (2.2 to 4.2 liters/min/m<sup>2</sup>; SD 0.5;  $n = 30$ ) at 30 days after implantation and 3.0 liters/min/m<sup>2</sup> (2.1 to 3.9 liters/min/m<sup>2</sup>; SD 0.5;  $n = 14$ ) at trial end. The VentrAssist provided adequate circulatory support to restore end-organ function, as confirmed by improvements in plasma creatinine and bilirubin (Table 3).

**Safety.** The major types of device-related SAEs included infections, non-neurologic thromboembolic events, neurologic events and hemorrhage (Table 4).

At the trial end-point, there were 122 device-related and non-device-related SAEs; of these, 77 were protocol-defined SAEs (Table 4). Some patients had the same SAE more than once. As expected, the highest incidence of SAEs occurred during the first 30 days after implant (68% of protocol-defined SAEs, 51% of non-protocol-defined SAEs). As of May 31, 2007, 5 patients (15%) remained free from protocol-defined, device-related SAEs.

Of the device-related SAEs, only 6 were attributable to a system malfunction. No SAE was due to catastrophic pump failure. There were 2 SAEs related to outflow cannula leakage that occurred during implantation and were corrected immediately by the surgeon. A third SAE occurred in a patient with sarcoid heart disease who had early post-operative bleeding and right heart failure, the latter mandating urgent implantation of a right ventricular assist device (RVAD). After RVAD implantation, the VentrAssist initially failed to restart, but did so after removing a

**Table 3.** Indicators of End-organ Function at Baseline, 30 Days After VentrAssist Implantation and Within 7 Days Before Heart Transplantation

Indicator	Baseline mean [SD] ( $n$ )	Post-implant mean [SD] ( $n$ )	Pre-transplant <sup>a</sup> mean [SD] ( $n$ )	$p$ -value <sup>b</sup> [95% confidence limits]	$p$ -value <sup>c</sup> [95% confidence limits]
Creatinine ( $\mu$ mol/liter)	0.125 [0.054] ( $n = 33$ )	0.097 [0.039] ( $n = 30$ )	0.106 [0.026] ( $n = 25$ )	0.01 [0.006, 0.044]	0.18 [-0.005, 0.026]
Bilirubin ( $\mu$ mol/liter)	34.14 [26.65] ( $n = 29$ )	19.60 [16.56] ( $n = 30$ )	14.13 [9.31] ( $n = 24$ )	0.02 [2.09, 24.76]	0.01 [7.47, 38.43]

<sup>a</sup>Data from 22 patients just before transplant and from last data point for 3 ongoing patients.

<sup>b</sup>Comparison between baseline and post-implant values.

<sup>c</sup>Comparison between baseline and pre-transplant values.

**Table 4.** Protocol-defined and Non-protocol-defined Serious Adverse Events Occurring During VentrAssist Support

Serious adverse event (SAE)	≤30 days after implant		>30 days and ≤154 days after implant		Throughout duration of VentrAssist support		
	No. of SAEs	Linearized rate (rate/patient-month)	No. of SAEs	Linearized rate (rate/patient-month)	No. of SAEs	No. of patients	Linearized rate (rate/patient-month)
<b>Protocol-defined SAEs</b>							
Arrhythmia							
Atrial fibrillation	1	0.03	0	0.00	1	3%	0.00
Ventricular tachycardia/fibrillation	3	0.10	4	0.05	15	18%	0.07
Cardiac tamponade	15	0.49	0	0.00	15	30%	0.07
Hemolysis	1	0.03	0	0.00	1	3%	0.00
Hemorrhage	8	0.26	1	0.01	9	24%	0.04
Hepatic dysfunction	1	0.03	0	0.00	1	3%	0.00
Infection							
Local							
Drive-line	1	0.03	5	0.06	11	18%	0.05
Pump pocket	1	0.03	3	0.04	6	15%	0.03
Other infection	0	0.00	1	0.01	2	6%	0.01
Systemic (sepsis)	2	0.07	6	0.07	16	30%	0.07
Neurologic event							
Transient	0	0.00	0	0.00	0	0%	0.00
Stroke	5	0.16	1	0.01	9	24%	0.04
Psychiatric disease	0	0.00	0	0.00	2	3%	0.01
Renal dysfunction	2	0.07	1	0.01	3	9%	0.01
Right heart failure	4	0.13	0	0.00	4	12%	0.02
System-related malfunction	4	0.13	2	0.02	6	15%	0.03
Thrombosis and/or embolism	4	0.13	1	0.01	8	15%	0.04
<b>Non-protocol-defined SAEs</b>							
Blood and lymphatic system disorders							
Cardiac disorders	3	0.10	3	0.04	9	21%	0.04
Gastrointestinal disorders	2	0.07	2	0.02	4	6%	0.02
General disorders and administration site conditions	2	0.07	1	0.01	4	12%	0.02
Investigations	3	0.10	2	0.02	8	24%	0.04
Metabolism and nutrition disorders	0	0.00	1	0.01	1	3%	0.00
Nervous system disorders	0	0.00	1	0.01	1	3%	0.00
Psychiatric disorders	0	0.00	3	0.04	4	9%	0.02
Psychiatric disorders	1	0.03	0	0.00	4	6%	0.02
Respiratory, thoracic and mediastinal disorders							
Surgical and medical procedures	1	0.03	2	0.02	5	12%	0.02
Vascular disorders	0	0.00	1	0.01	2	6%	0.01
Other	6	0.20	1	0.01	7	15%	0.03
Other	5	0.16	5	0.06	10	21%	0.05
<b>Total</b>	<b>75</b>	<b>2.44</b>	<b>47</b>	<b>0.57</b>	<b>168</b>	<b>NA</b>	<b>0.79</b>

NA, not applicable.

surgical extension lead. Given the complex clinical scenario the decision was made to explant the VentrAssist and replace it with a Thoratec LVAD, resulting in successful biventricular VAD support. Post-operative examination of the VentrAssist pump revealed a fibrinous clot, hypothesized to have formed as a result of the low-flow state during right heart failure. The patient was successfully bridged to transplant after 46 days. The fourth and fifth SAEs occurred when the VentrAssist alarm system was

activated despite the absence of any underlying condition. A change in software corrected this problem. The sixth SAE occurred when the percutaneous power lead was accidentally transected on the day of implant; however, the pump was successfully replaced.

Another SAE occurred when a patient with an ongoing hypercoagulable state (despite Reteplase therapy) had the VentrAssist electively replaced with a second VentrAssist 10 days after implant.

**Table 5.** Quality of Life<sup>a</sup> at Baseline, 30 Days After Implant and at Trial End-point (Day 154)

	Baseline mean [SD] (n)	After implant mean [SD] (n)	Trial end-point mean [SD] (n)	p-value <sup>b</sup> [95% confidence limits]
Utility-based Quality of Life—Heart Questionnaire score	0.251 [0.918] (n = 23)	0.693 [0.591] (n = 23)	0.884 [0.279] (n = 25)	0.01 [−0.830–0.162]

<sup>a</sup>Based on the Rosser Utility Index.

<sup>b</sup>Comparison between baseline and trial end-point values.

Of the 6 neurologic events, 2 patients had a hemorrhagic event and 4 patients had an embolic event. The hemorrhagic events resulted in 2 deaths: 1 from the event itself and the other 35 days after the event. The embolic events resulted in no clinical sequelae for 2 patients, minor motor deficit in 1 patient, and some sensory deficit in another patient. Of these 4 patients, 3 were transplanted (32, 52 and 325 days after implant, respectively) and 1 patient is ongoing. Non-central nervous system thromboembolic events were all resolved without long-term sequelae.

Observed instances of (early) RV failure were seen in patients with marginal RV function at implant and, except in the 1 case of (irreversible) sarcoid disease, RV function was successfully managed medically.

**Patient functional status.** VentrAssist implantation improved patients' quality of life. Significant increases occurred in the Utility-based Quality of Life Heart Questionnaire score (Table 5) and, by POD 154, 81% of the trial's successful patients achieved NYHA Class I or II status.

**Resource use.** Use of cardiac medication, particularly inotropes and diuretics, was reduced after VentrAssist implantation (Table 6). Only anti-arrhythmic and calcium channel blocker use increased during the trial. The increase in anti-arrhythmic agents was in the setting of both atrial and ventricular arrhythmias: the former being present before implant, the cause of the latter events is unknown.

Most (70%) patients implanted with the VentrAssist could be discharged from hospital (Table 7 and Figure 4). However, 74% of patients discharged required re-admission. Causes of re-admissions included infections (drive-line, pocket, sepsis), wound-related complications (discomfort, breakdown, collection), low INR, nausea/vomiting, lethargy, syncope, arrhythmias, dehydration, splenic infarct, peripheral edema and shortness of breath. The mean duration of hospital stay during re-admission was 9 days (Table 7). No patients required re-admission to an ICU (Figure 5).

## DISCUSSION

This trial has demonstrated the efficacy and safety of the VentrAssist LVAD in providing adequate circula-

tory support to BTT patients. A year after VentrAssist implantation in 33 BTT patients, >80% of patients achieved a successful outcome, having been either transplanted or remaining transplant-eligible. Implantation resulted in improved end-organ function, enhanced quality of life and reduced medication use. The incidence of SAEs was acceptable and similar to rates for other LVADs.<sup>9,17,18</sup>

The success rate of the VentrAssist matched or surpassed success rates reported for other LVADs. At this time, there is only one other publication on the use of a third-generation LVAD (DuraHeart) as a BTT.<sup>19</sup> The DuraHeart maintained circulatory support for 84 to 202 days before transplant.<sup>19</sup> In a recent trial of the second-generation HeartMate II device,<sup>18</sup> 100 of 133 (75%) BTT patients were supported to transplant or remained transplant-eligible at 180 days, a success rate comparable to that of this trial. At the end of our follow-up, the VentrAssist remained implanted in 3 patients at 448, 528 and 646 days after implantation, surpassing the longest support time in the HeartMate II trial (600 days).<sup>18</sup> In 70 patients implanted with first- or second-generation LVADs, 52% survived (either transplanted or awaiting transplant) for 1 year.<sup>17</sup> Similarly, a success rate of 50% was reported in the survey by the International Society for Heart and Lung Transplantation.<sup>9</sup>

**Table 6.** Cardiac Medications Taken by Patients at Baseline and at Trial end-point (Day 154)

Medication	Patients (%)	
	Baseline (n = 33)	Trial end-point (n = 33)
Angiotensin-converting enzyme inhibitor/ angiotensin receptor blocker	52%	39%
Anti-arrhythmic	39%	42%
Beta-blocker	33%	27%
Calcium channel blocker	0%	6%
Digoxin	45%	30%
Diuretic	82%	33%
Inotrope	64%	12%
One intravenous inotropic agent	30%	3%
Two intravenous inotropic agents	18%	3%
Three or more intravenous inotropic agents	15%	6%
Vasodilator/nitrate	0%	0%
Vasopressor	12%	0%

**Table 7.** Duration of Hospital Stays for Patients Discharged After Implant ( $n = 23$ ) and for Patients Re-admitted After Initial Discharge ( $n = 17$ ; 35 Re-admissions)

Time period	Mean $\pm$ SD	Median (min, max)	Total patient-days
Days in the trial	106 $\pm$ 54.2	142 (4, 154)	3,513
From implant to initial discharge			
Time spent in the hospital (days)			1,551
In intensive care unit	20 $\pm$ 27.4	11 (1, 154)	
Not in intensive care unit	27 $\pm$ 25.5	20 (0, 126)	
Time to initial discharge (days)	43 $\pm$ 22.8	42 (14, 109)	
After initial discharge			
Time spent out of the hospital (days)	50 $\pm$ 44.9	48 (0, 135)	1,648
Re-admission duration (days)	9 $\pm$ 9.4	5 (1, 32)	

Therefore, the VentrAssist appears to perform well as a BTT, compared with earlier generation LVAD designs, and may be particularly suitable for patients requiring prolonged circulatory support. Despite the poor clinical status of our patients, these favorable results suggest that even better results might be obtained if the VentrAssist was used in earlier stages of advanced heart failure.

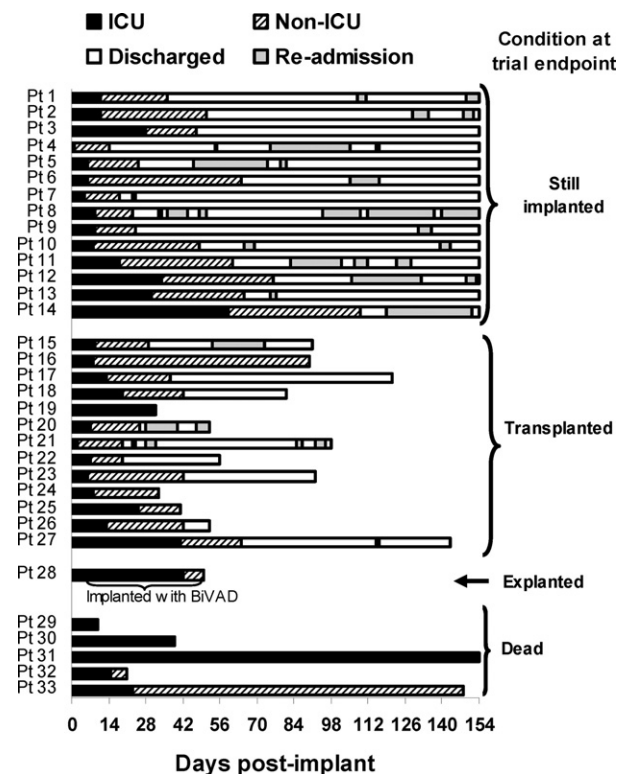
As reported for other LVADs,<sup>9,17,18,20,21</sup> the most prevalent SAEs in this trial included infectious, hemorrhagic, thromboembolic, neurologic and cardiovascular events. Except for arrhythmias and infections, most SAEs occurred within the first month, which is consistent with other reports.<sup>9,17,18</sup> However, the overall rate of SAEs during this early period (2.44 per patient-month) was lower than that reported by Sharples et al<sup>17</sup> (3.47 per patient-month) and Miller et al<sup>18</sup> (2.54 per patient-month). The rates of most individual protocol-defined SAEs were also lower in our study, especially for hemorrhage and respiratory and renal dysfunction. There was a relatively high incidence of early tamponade, although no tamponade events occurred after POD 30. All of these tamponades occurred in the first half of the trial and none of the reported tamponades were device-related. This probably reflects an early learning curve with the device and the intensity of anti-coagulation.

Notably, our results were favorable even in centers with limited VAD experience. The "learning curve" associated with this device was encouraging with patients and hospital staff, confirming that the VentrAssist was "user-friendly."

In terms of reliability, the use of any LVAD is not without risk. However, such risk is generally acceptable, given that patients are unlikely to survive without LVAD support. Device or system malfunction was rare in this trial and system design and software were changed as a direct consequence of some of these events. There were no instances of catastrophic device failure, reinforcing the robust and reliable design of the VentrAssist for out-of-hospital care.

The VentrAssist improved patients' quality of life and functional status. Although infrequently reported, quality of life is generally increased after LVAD implantation.<sup>3,18,20</sup> Similar to our findings, Sharples et al<sup>17</sup> and Miller et al<sup>18</sup> reported that LVAD implantation in BTT patients shifted patients from NYHA Class IV to Class I or II.

Implantation with the VentrAssist device reduced medication use and the burden on hospital resources. For our patients, the duration of the initial hospital stay after implantation was similar to that reported for other LVADs.<sup>17,18</sup> A greater percentage of our patients (70%)

**Figure 5.** Hospitalization profile, until the trial end-point, for each patient implanted with a VentrAssist device ( $n = 33$ ). Implant date is POD 0.

were discharged, compared to those implanted with first- and second-generation LVADs (66%),<sup>17</sup> and our results were comparable to those from the HeartMate II trial (75%).<sup>18</sup> Despite the intermittent need for further hospitalization, most of our patients spent lengthy periods at home, providing benefits in terms of medical costs and quality of life.

Although LVADs have been used successfully as BTT, ultimately, refinements in design and patient management may enable their wider use as destination therapy (DT) for transplant-ineligible patients. In the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) trial,<sup>20</sup> 129 transplant-ineligible patients were randomized to receive either LVAD (first-generation) implantation or optimal medical treatment. Significantly, the LVAD 1-year survival rate (52%) was higher than that of the medical treatment group (25%). Similar survival rates have been reported in BTT patients implanted with these early devices.<sup>9,17</sup> We reported the first successful use of the VentrAssist as DT in an elderly, transplant-ineligible man,<sup>12</sup> and further trials for this indication are underway.<sup>13</sup>

We studied a diverse patient group, with the age, body size and clinical needs of our patients varying widely. Nevertheless, favorable results were obtained in the extremes of both younger, smaller patients and older, larger patients.

As with other LVAD trials (apart from the REMATCH trial<sup>20</sup>), ours was not a randomized trial with a medically treated, control group. Other study limitations include relatively small numbers and limited elapsed time for follow-up of patients. To address these issues, a new European study, "BRACE" (Better Results and Clinical Effectiveness), was initiated immediately after this trial's last enrollment. This study will be the first in Europe to report long-term (2-year) follow-up on LVAD patients without a specific intention to treat (BTT, DT or recovery) being specified at implant.

In conclusion, this prospective, longitudinal, multicenter, international clinical trial of the VentrAssist LVAD in 33 BTT patients has demonstrated the device's favorable efficacy and safety profile. VentrAssist implantation enhanced patient functional status, facilitated hospital discharge, and reduced medication use. Notably, favorable outcomes were achieved at centers with limited LVAD experience. These results indicate that the VentrAssist may offer advantages over devices currently approved for BTT, particularly for longer-term circulatory support.

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