

Supplementary Appendix

Supplement to: Zimmermann WH, Ensminger S, Kutschka I, et al. Stem-cell–derived biologic ventricular assist tissue in heart failure. *N Engl J Med* 2026;394:1991-2001. DOI: 10.1056/NEJMoa2513525

This appendix has been provided by the authors to give readers additional information about the work.

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BioVAT-HF Investigators

University Medical Center Göttingen Investigators

Investigator	Department	Role
PD Dr. Sören Brandenburg	Department of Cardiology and Pneumology	Principal Investigator
Prof. Dr. Tim Seidler	Department of Cardiology and Pneumology	Principal Investigator - Former
Dr. Fawad Jebran	Department of Cardiothoracic and Vascular Surgery	Principal Investigator - Deputy
Prof. Dr. Ingo Kutschka	Department of Cardiothoracic and Vascular Surgery	Study physician
Dr. Birgit Gerecke	Department of Cardiothoracic and Vascular Surgery	Study physician
PD Dr. Kristian Hellenkamp	Department of Cardiology and Pneumology	Study physician
Dr. Bo Beuthner	Department of Cardiology and Pneumology	Study physician
PD Dr. Ruben Evertz	Department of Cardiology and Pneumology	Study physician
Dr. Niklas Bader	Department of Cardiology and Pneumology	Study physician
Dr. Laura Priesmeier	Department of Cardiology and Pneumology	Study physician
Dr. Gabriel Riedemann	Department of Cardiology and Pneumology	Study physician
Prof. Dr. Bernhard Danner	Department of Cardiothoracic and Vascular Surgery	Study physician
PD Dr. Monika Sadlonova	Department of Cardiothoracic and Vascular Surgery	Study physician
Dr. Lena Bosselmann	Department of Psychosomatic Medicine and Psychotherapy	Study physician
Prof. Dr. Joachim Lotz	Institute for Cardiac Imaging	Study physician
Prof. Dr. Wolfram-Hubertus Zimmermann	Department of Pharmacology and Toxicology	Study physician
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Prof. Dr. Hassina Baraki	Department of Cardiothoracic and Vascular Surgery	Study physician
PD Dr. Michael Didié	Department of Cardiology and Pneumology	Study Physician - Former
Dr. Stefanie Wehrhahn	Department of Cardiology and Pneumology	Study Physician - Former
Dr. Juliana Warneck-Telezki	Department of Cardiology and Pneumology	Study Physician - Former
Dr. Carolin Müller	Department of Cardiology and Pneumology	Study Physician - Former
Prof. Dr. Christian Ritter	Institute for Radiology	Study physician - Former
PD Dr. Johannes Kowallick	Institute for Radiology	Study physician - Former

University Medical Center Schleswig Holstein, Campus Lübeck Investigators

Investigator	Department	Role
Prof. Dr. Stephan Ensminger	Department of Cardiac and Thoracic Vascular Surgery	Principal Investigator
Prof. Dr. Ingo Eitel	Department of Cardiology, Angiology, and Intensive Care Medicine	Principal Investigator - Deputy
Dr. Dominik Jurczyk	Department of Cardiology, Angiology, and Intensive Care Medicine	Study physician
Dr. Tobias Graf	Department of Cardiology, Angiology, and Intensive Care Medicine	Study physician
PD Dr. Christina Paitazoglou	Department of Cardiology, Angiology, and Intensive Care Medicine	Study physician
Dr. Claudia Busch-Tilge	Department of Cardiac and Thoracic Vascular Surgery	Study physician
PD Dr. Buntaro Fujita	Department of Cardiac and Thoracic Vascular Surgery	Study physician
Prof. Dr. Thomas Pühler	Department of Cardiac and Thoracic Vascular Surgery	Study physician

Supplementary Methods

Inclusion Criteria

Part A

1. Heart failure with reduced ejection fraction (HFrEF with $EF \leq 35\%$) as assessed by high-resolution echocardiography and MRI or CT.
2. At least one hypo- or dyskinetic segment to demark the transplant target area.
3. Stable disease condition allowing for an elective left-lateral mini-thoracotomy.
4. 18-80 years of age
5. Previous implantation of an ICD or CRT-D with event recorder
6. New York Heart Association (NYHA) Class III or IV under optimal medical therapy
7. Willingness and ability to give written informed consent
8. Female subjects of childbearing potential must agree to use acceptable method(s) of contraception for the full study duration.

A total of 18 patients were recruited using the inclusion criteria for Part A of the study protocol.

Part B

1. Symptomatic heart failure (NYHA II-IV) with reduced ejection fraction (HFrEF with $LVEF \leq 35\%$) as assessed by echocardiography.
2. Patients on guideline-directed medical therapy
3. NT-proBNP >300 pg/mL for patients in sinus rhythm or >900 pg/mL if in atrial fibrillation
4. History of previous heart failure hospitalization in the past 12 months
5. At least one hypo- or dyskinetic segment or dilated heart chamber to demark the transplant target area.
6. Stable disease condition allowing for an elective left-lateral mini-thoracotomy
7. 18-80 years of age
8. Willingness and ability to give written informed consent
9. Female subjects of childbearing potential must agree to use acceptable method(s) of contraception for the full study duration.

A total of 2 patients were recruited using the inclusion criteria for Part B of the study protocol. These patients fulfilled completely (1 patient) or partially (1 patient was in New York Heart Association class II) the Part A study protocol inclusion criteria.

Exclusion Criteria

1. Contraindication to immunosuppressive drugs (e.g. known history of unresolved cancer, hepatitis B/C, HIV, HTLV1)
2. Contraindication to TachoSil (e.g. hypersensitivity to human fibrinogen, human thrombin, horse collagen, human albumin, riboflavin, sodium chloride, sodium citrate, L-Arginine-Hydrochloride)
3. Hypertrophic cardiomyopathy (HCM)
4. Terminal kidney failure (stage 4; GFR <30 ml/min) at the time of enrollment
5. Terminal liver failure (Child-Pugh stage C; score >10) at the time of enrollment
6. Autoimmune disease (removed as an exclusion criterion in Part B of the study protocol)
7. History of disabling stroke
8. Reduced life expectancy in the short term due to non-cardiac disease
9. Any condition that excludes adherence to study protocol (in particular lack of adherence to prescribed medication)
10. Simultaneous participation in another interventional trial
11. Pregnant or breastfeeding females
12. Known or suspected alcohol and/or drug abuse

Informed Consent Process

Potentially eligible patients were screened by the clinical investigators at the study centers. Interested patients were informed about the purpose of the clinical trial, procedures, potential risks and benefits as well as the possibility to at any time withdraw from the clinical trial. Participants were asked to consider clinical trial participation for at least 24 hours before signing the informed consent.

Informed consent forms were reviewed and approved by the German Center for Cardiovascular Research (DZHK) ethics group and the competent ethics committees.

All participants gave written informed consent to participate in the trial. A hard copy of the informed consent signed by the participant and the responsible clinical investigator are available at the study centers.

Dose Determining Committee (DDC) members

Prof. Dr. Tim Friede	University Medical Center Göttingen Department of Medical Statistics
Prof. Dr. Gerd Hasenfuß	University Medical Center Göttingen Department of Cardiology and Pneumology
Prof. Dr. Ingo Kutschka	University Medical Center Göttingen Department of Cardiothoracic and Vascular Surgery University Hospital Basel Department of Cardiac Surgery
Prof. Dr. Wolfram-Hubertus Zimmermann	University Medical Center Göttingen Department of Pharmacology and Toxicology

Data Safety Monitoring Board (DSMB) members

Prof. Dr. Stefan Janssens	University Hospital and KU Leuven Department of Cardiovascular Sciences
Prof. Dr. Philippe Menasché	Service de Chirurgie Cardio-vasculaire Hôpital Européen Georges Pompidou
Prof. Dr. Sarah Zohar	INSERM U1138, Equipe 22 Centre de Recherche des Cordeliers

Genome Safety Testing

For genome sequencing and the analysis of imbalanced and structural genomic alterations, genomic DNA was isolated using NucleoSpin Tissue Kits (Macherey-Nagel). A total of 3 µg of genomic DNA was submitted for genome sequencing at the Cologne Center for Genomics (CCG, Universität zu Köln) and processed with TruSeq DNA PCR-free Kits (Illumina) and sequenced on an Illumina NovaSeq6000-system. The sequencing data was analyzed with Varbank 2.0 (Cologne Center for Genomics) CNV-Seq software. Structural alterations of > 50 Kb were considered and analyzed for their clinical relevance.

Basic QC analysis of genome sequencing data is summarized below:

QC parameter	MCB	WCB	PPC
Total reads	923,888,026	866,246,934	886,825,792
Unique reads (% of total reads)	94.63	94.53	94.95
Unique mapped reads (% of total reads)	92.15	92.46	92.21
Mean coverage (x-fold)	40	37	38
Coverage > 2 (% of targets)	92.3	92.2	92.3
Coverage > 10 (% of targets)	91.7	91.5	91.6
Coverage > 30 (% of targets)	83.6	81.0	82.0
MAPQ ≥ 40 (% of total reads)	91.77	92.56	90.89
MAPQ 30-40 (% of total reads)	0.29	0.28	0.30
MAPQ 20-30 (% of total reads)	0.75	0.71	0.77
MAPQ 10-20 (% of total reads)	0.92	0.86	0.97
MAPQ 0-10 (% of total reads)	3.8	3.53	4.33
MAPQ not available (unmapped reads; % of total reads)	2.48	2.07	2.74

MAPQ denotes mapping quality score, MCB master cell bank, WCB working cell bank, PPC post production cells and QC quality control.

Exome sequencing was performed to identify point mutations and smaller insertions/deletions (indels). Genomic DNA was isolated using NucleoSpin Tissue Kits (Macherey-Nagel). Coding sequences as part of the Agilent Human All Exon V7-Panels (Exom) including intron-exon boundaries were enriched (SureSelect-QXT method), amplified, and sequenced on an Illumina NovaSeq6000-system. The sequencing data was analyzed with Varbank 2.0 (Version 3.4, Cologne Center for Genomics) and compared to a reference database (www.ensembl.org). Identified unknown variants were classified with the following software:

SIFT (www.jgvi.sift)

MutationTaster (www.mutationtaster.org)

PolyPhen-2 (www.genetics.bwh.harvard.edu/pph2)

M-CAP (<http://bejerano.stanford.edu/mcap/>)

Human Splicing Finder (<http://www.umd.be/HSF3/HSF.shtml>)

BDGP Splice Site prediction (http://www.fruitfly.org/seq_tools/splice.html)

Basic QC analysis of exome sequencing data is summarized below:

QC parameter	MCB	WCB	PPC
Total reads	135,512,662	92,470,670	175,174,824
Unique reads (% of total reads)	88.44	86.68	86.53
Unique mapped reads (% of total reads)	88.30	86.60	86.42
Mean coverage (x-fold)	54	54	58
Coverage > 2 (% of targets)	97.3	97.5	97.4
Coverage > 10 (% of targets)	93.9	94.1	94.5
Coverage > 30 (% of targets)	75.4	75.0	78.3
Coverage > 100 (% of targets)	9.2	9.2	10.8

MCB denotes master cell bank, WCB working cell bank, PPC post production cells and QC quality control.

Test: Genome sequencing/Exome sequencing	Results		
Focus	MCB (P14+2)	WCB (P19+4)	PPC (P19+7)
Cytogenomic analyses for copy number variation including structural and numerical alterations	Clinically relevant CNV & Indels not detected	Clinically relevant CNV & Indels not detected	Clinically relevant CNV & Indels not detected
Karyotype	46, XY	46, XY	46, XY
Tumor Panel analysis for mutations in 90 oncogenes ⁽¹⁾	Pathogenic/likely pathogenic alterations in TA genes not detected	Pathogenic/likely pathogenic alterations in TA genes not detected	Pathogenic/likely pathogenic alterations in TA genes not detected
Cardio Panel analysis for mutations in 232 genes ⁽²⁾ associated with hypertrophic, dilated, and arrhythmogenic cardiomyopathies	Pathogenic/likely pathogenic alterations in cardiac disease markers not detected	Pathogenic/likely pathogenic alterations in cardiac disease markers not detected	Pathogenic/likely pathogenic alterations in cardiac disease markers not detected

CNV denotes copy number variations, iPSC induced pluripotent stem cells, MCB master cell bank, WCB working cell bank, PPC post production cells, P passage and TA genes tumor-associated genes or oncogenes.

⁽¹⁾Genes analyzed: *APC, ATM, BAP1, BARD1, BMPR1A, BRCA1, BRCA2, BRIP1, CDC73, CDH1, CDKN1B, CDKN2A, CFTR, CHEK2, EDC3, EDC4, ENG, EPCAM, ERCC4, FAM175A, FAN1, FANCA, FANCB, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, FANCM, FH, FLCN, GALNT12, GREM1, KIT, MAP3K1, MAX, MEN1, MET, MLH1, MLH3, MRE11A, MSH2, MSH3, MSH6, MSR1, MUTYH, NBN, NF1, NF2, NTHL1, PALB2, PALLD, PDGFRA, PIK3CA, PMS1, PMS2, POLD1, POLE, PPM1D, PRSS1, PTEN, RAD50, RAD51C, RAD51D, RB1, RET, RINT1, RNASEL, RNF43, RPS20, SCG5, SDHA, SDHAF2, SDHB, SDHC, SDHD, SETD6, SLX4, SMAD4, SPINK1, STK11, TMEM127, TP53, TSC1, TSC2, UBE2T, VHL, ZNF276.*

⁽²⁾Genes analyzed: *ABCC9, A2ML1, ABCG5, ABCG8, ACADVL, ACTA1, ACTA2, ACTC1, ACTC1, ACTN2, AKAP9, ALG10B, ALMS1, ANK2, ANKRD1, APOA1, APOA4, APOA5, APOB, APOC2, APOE, BAG3, BRAF,*

CACNA1C, CACNA2D1, CACNB2, CALM1, CALM2, CALR3, CAP2, CASQ2, CASZ1, CAV3, CBL, CBS, CDC42, CETP, COL3A1, COL5A1, COL5A2, COX15, CREB3L3, CRELD1, CRYAB, CSRP3, CTF1, CTNNA3, DES, DMD, DNAJC19, DOLK, DPM3, DPP6, DSC2, DSG2, DSP, DTNA, EFEMP2, ELAC2, ELN, EMD, EPG5, EPHB4, EYA4, FBN1, FBN2, FGA, FGF12, FHL1, FHL2, FKRP, FKTN, FLNA, FLNC, FOXE3, FXN, GAA, GATAD1, GCKR, GJA5, GLA, GPD1L, GPIHBP1, HADHA, HCN4, HFE, HRAS, HSPB8, ILK, JAG1, JPH2, JUP, KCNA5, KCND2, KCND3, KCNE1, KCNE2, KCNE3, KCNE5, KCNH2, KCNJ2, KCNJ5, KCNJ8, KCNQ1, KLF10, KLHL24, KRAS, LAMA2, LAMA4, LAMP2, LDB3, LDLR, LDLRAP1, LEMD2, LMF1, LMNA, LMOD2, LOX, LPL, LTBP2, LTBP3, LZTR1, MAP2K1, MAP2K2, MAT2A, MFAP5, MIB1, MRPS14, MTM1, MURC, MYBPC3, MYH11, MYH6, MYH7, MYL2, MYL3, MYLK, MYLK2, MYO6, MYOZ2, MYPN, NDUFB11, NEBL, NEXN, NF1, NKX2-5, NODAL, NOTCH1, NPPA, NRAS, OBSCN, PCSK9, PDLIM3, PKP2, PLN, PPCS, PRDM16, PRKAG2, PRKAR1A, PRKG1, PTPN11, RAF1, RANGRF, RASA2, RBM20, RIT1, RPL3L, RRAD, RRAS2, RYR1, RYR2, SALL4, SCN10A, SCN1B, SCN2B, SCN3B, SCN4B, SCN5A, SCO1, SCO2, SDHA, SEMA3A, SEPN1, SGCB, SGCD, SGCG, SHOC2, SKI, SLC25A4, SLC2A10, SLC4A3, SLMAP, SMAD2, SMAD3, SMAD4, SMAD6, SNTA1, SOS1, SOS2, SPEG, SPRED1, SREBF2, SYNE1, TAB2, TAZ, TBX20, TBX3, TBX5, TCAP, TECRL, TGFB2, TGFB3, TGFB3R1, TGFB3R2, TJP1, TMEM43, TMPO, TNNC1, TNNT3, TNNT2, TPM1, TRDN, TRIM63, TRPM4, TTN, TTR, TXNRD2, VARS2, VCL, ZBTB17, ZHX3, ZIC3.

Study Design and Participants

The study was designed by the sponsor (University Medical Center Göttingen), reviewed and endorsed by the Clinical Study Group of the German Center for Cardiovascular Research (DZHK), and approved by the responsible regulatory authority (Paul-Ehrlich-Institute [PEI]; December 23, 2020) as well as the Competent Ethics Committee (January 12, 2021). Safety oversight was provided by an independent data safety monitoring board. Dose escalation steps were suggested based on clinical experience gained in the trial and data review by a Dose Determining Committee. Data were reported by the participating study centers in a central data base (DZHK eCRF; secuTrial) and monitored by the sponsor's clinical trial unit according to the monitoring manual (version 1.0, January 27, 2021). W.H.Z., G.H., and T.F. prepared a first draft of the manuscript.

A total of 26 patients were enrolled after signed informed consent and underwent a baseline investigation to confirm eligibility according to the inclusion and exclusion criteria. Twenty patients met the eligibility criteria for BioVAT transplantation. The following 6 patients were considered recruitment failures:

- 1) **pheno_549698654:** Diagnosed with dental disease after recruitment, which did not allow for administration of immunosuppression. The patient was re-considered for BioVAT transplantation after dental repair but decompensated with a requirement for a microaxial flow pump and extracorporeal membrane oxygenation and was thus excluded from the study. Subsequently, the patient received an orthotopic heart transplantation but died from postoperative complications including septic/cardiogenic/hemorrhagic shock.
- 2) **pheno_592166213:** Withdrew consent prior to implantation, decompensated and subsequently died.
- 3) **pheno_746598668:** Recruited after the baseline assessment by echocardiography confirmed a left ventricular ejection fraction (LVEF) of 32%. Subsequently, cardiac computed tomography identified a LVEF >35%, which resulted in the decision to exclude the patient, because the inclusion criterion of LVEF ≤35% was not met.
- 4) **pheno_194151297:** Could not be treated on the scheduled BioVAT transplantation date because of an engineered-heart-muscle unit production failure. The patient was rescheduled for a subsequent implantation date but decompensated with a requirement for extracorporeal membrane oxygenation and was thus excluded from the study. The patient was subsequently implanted with a left ventricular assist device and is listed for heart transplantation.
- 5) **pheno_968658240:** Right heart catheterization prior to the scheduled transplantation date indicated severe pulmonary hypertension. Based on this finding, the patient was considered not operable and listed for heart transplantation.
- 6) **pheno_679881560:** After informed consent and prior to the scheduled transplantation date, the patient was excluded because of a suspected lack of study protocol adherence.

This interim analysis reports safety and efficacy outcomes in 20 patients: 2 treated with the low dose (BioVAT assembled from 5 engineered-heart-muscle units), 2 treated with the middle dose (BioVAT assembled from 10 engineered-heart-muscle units), and 16 patients treated with the safe maximal dose (BioVAT assembled from 20 engineered-heart-muscle units) with a combined follow-up of 11.6 years in BioVAT-HF and additional 9 years in the VAT-Registry.

The VAT-registry (registered under DRKS00027292) was implemented according to regulatory expectations and as described in the clinical trial protocol to obtain information on long-term outcomes. Time to mechanical assist device implantation, time to heart transplantation, mortality, LVEF, New York Heart Association classification, and N-terminal pro-B-type natriuretic peptide plasma concentration are reported in the VAT-registry once a year. Patients are asked to enroll in the VAT-registry under a separate informed consent until end-of-life.

Statistical Analysis

The Gaussian linear mixed models for repeated measures (MMRM) included visit as factor and baseline values of the end point as covariate. The baseline value was included as linear term. The error terms are assumed to follow a multivariate normal distribution with unstructured covariance. If the numerical procedures did not converge, a Toeplitz matrix with heterogeneous variances was used instead of the unstructured covariance matrix. Model fit was checked visually by inspection of Pearson residuals plotted against predicted values. The degrees of freedom were determined by the Kenward-Roger approach. These analyses used all available data (even beyond 3 months, but hypothesis testing focused on 3 months follow-up), including patients with missing assessments; 9 out of 121 (7.4%) assessments of the primary efficacy end points are missing. The repeated measures model used is robust to missingness as long as it is not informative. No penalty for interim testing was applied, since the analysis of the full study will test assessments at the 12-month visit. Least square means are reported with 90% confidence intervals (CI). The observed baseline values were used in the computation of the least squares means. The secondary end point data and laboratory values are reported descriptively, summarizing continuous end points by means and standard deviations or median and interquartile range, as appropriate, and categorical outcomes by frequencies and percentages. Statistical analyses were performed with R software, version 4.3.1. The sample size calculation was carried out using nQuery 9, version 9.2.1.0.

Missing Data

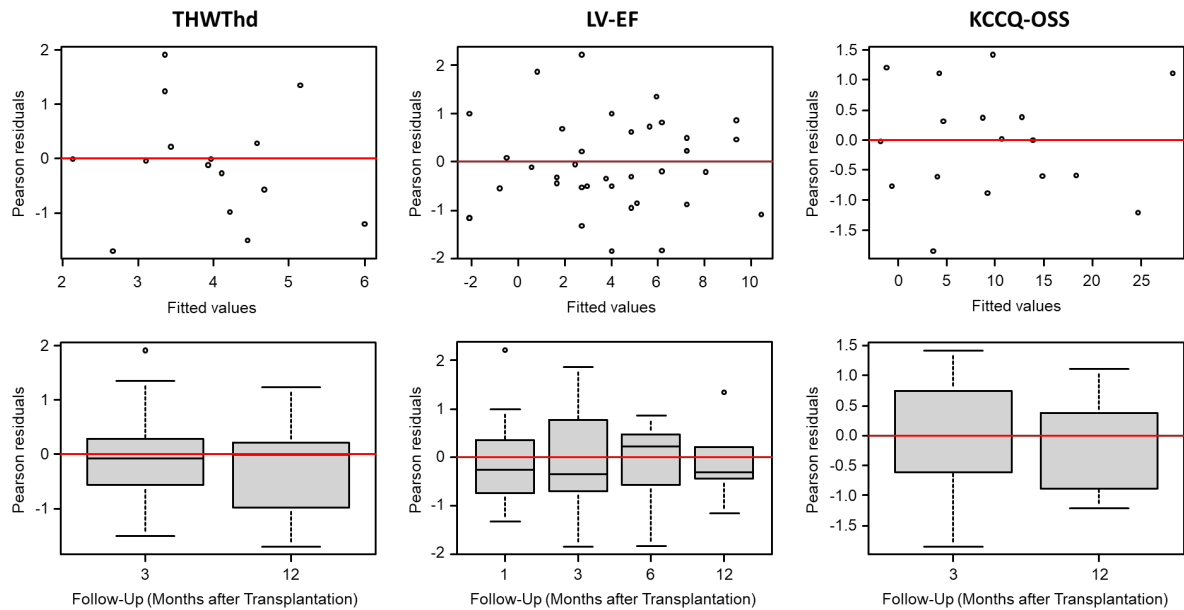
Extent of missingness for primary and secondary end point for the 16 patients transplanted with the safe maximal dose (20 EHM) is tabulated below:

	Baseline (N=16)	1 month FU (N=14)	3 months FU (N=12)	6 months FU (N=8)	12 months FU (N=5)
Primary efficacy end points — no. (%)					
TWThd	5 (31)	-	2 (17)	-	0 (0)
LVEF	0 (0)	2 (14)	0 (0)	0 (0)	0 (0)
KCCQ-OSS	0 (0)	-	0 (0)	-	0 (0)
Secondary efficacy end points — no. (%)					
NYHA class	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
6MWT distance	0 (0)	2 (14)	1 (8)	1 (13)	0 (0)
peak VO₂	6 (38)	8 (57)	6 (50)	2 (25)	3 (60)
Hand-grip strength	1 (6)	1 (7)	0 (0)	0 (0)	0 (0)
EQ-VAS	0 (0)	-	0 (0)	-	0 (0)
Medication adherence	0 (0)	-	1 (8)	-	0 (0)

FU denotes follow-up, TWThd target heart wall thickness in diastole, LVEF left ventricular ejection fraction, KCCQ-OSS Kansas City Cardiomyopathy Questionnaire – Overall Summary Score, NYHA New York Heart Association, 6MWT 6-minute walk test, VO₂ maximal oxygen consumption, and EQ-VAS EuroQoL Visual Analogue Scale.

Model Diagnostics

Model fit was evaluated using standard diagnostic tools appropriate for parametric mixed models with repeated measures (MMRM). In particular, we examined Pearson residuals. Residuals versus fitted values showed no systematic patterns, trends, or evidence of heteroscedasticity with residuals centered around zero across the range of fitted values. In addition, residuals were examined by follow-up visit; median residuals were approximately zero at each visit, and the spread of residuals was comparable across visits, indicating an adequate specification of both the mean structure and the covariance model. Refer to a summary of the data below:



Top panels: Pearson residuals from the mixed model for repeated measures (MMRM) plotted against fitted values for the three primary end points (target heart wall thickness in diastole [THWThd], left ventricular ejection fraction [LVEF], Kansas City Cardiomyopathy Questionnaire-Overall Summary Score [KCCQ-OSS]). Bottom panels: boxplots show Pearson residuals from the MMRM by follow-up visit. Boxes represent the interquartile range with median indicated by the horizontal line.

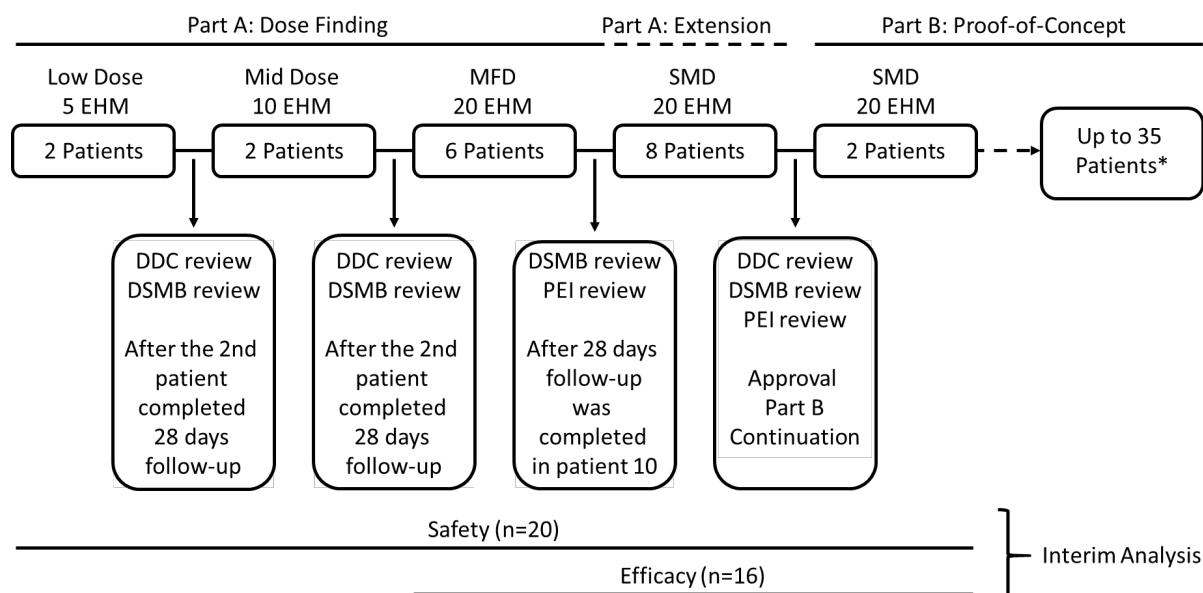
Estimated variance components of the MMRM model (diagonal elements of the estimated covariance matrix) are summarized below:

	covariance structure	1 month FU	3 months FU	6 months FU	12 months FU
TWThd	US	-	2.5	-	0.9
LVEF	TOEPH	26	36	60	36
KCCQ-OSS	US	-	136	-	251

FU denotes follow-up, KCCQ-OSS Kansas City Cardiomyopathy Questionnaire-Overall Summary Score, LVEF left ventricular ejection fraction, US an unstructured covariance matrix, TWThd target heart wall thickness in diastole, and TOEPH a Toeplitz heterogeneous covariance structure.

Supplementary Figures

Figure S1. Study design



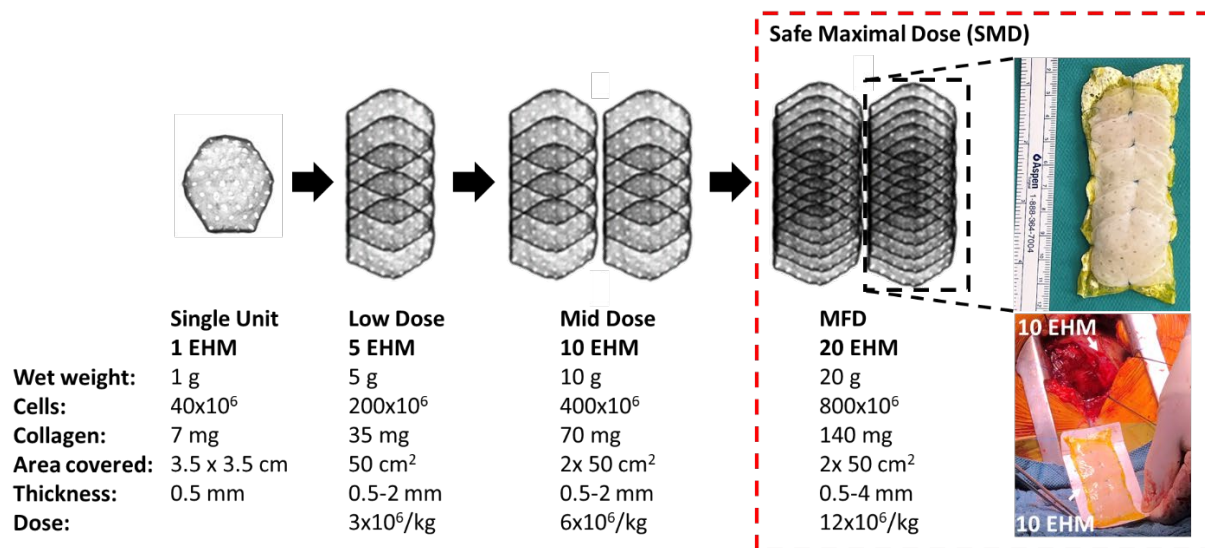
BioVAT denotes Biological Ventricular Assist Tissue, DDC Dose Determining Committee, DSMB Data Safety Monitoring Board, EHM engineered-heart-muscle, PEI Paul-Ehrlich-Institute, MFD maximal feasible dose, SMD safe maximal dose, and VAT Ventricular Assist Tissue.

The study protocol prespecified the maximal feasible dose (MFD) as 20 engineered-heart-muscle units. Dose escalation steps were suggested by the Dose Determining Committee and confirmed by the independent Data Safety Monitoring Board after data review. The Paul-Ehrlich-Institute approved the safe maximal dose (SMD) for the Part A extension and Part B of the trial.

*The BioVAT-HF study plans to include up to 35 patients in Part B of the study. In addition to transplantation of the engineered-heart-muscle units on the epicardium of the left ventricle, Part B also allows for transplantation of the engineered-heart-muscle units on the epicardium of the right ventricle in patients with right heart failure concomitant with an elective thoracotomy for a surgical intervention on the left ventricle. A minimum of 5 and a maximum of 30 patients are planned for treatment with engineered-heart-muscle units transplanted on the left or right ventricle to inform a subsequent pivotal study design. As of June 2025, patients only underwent transplantation of engineered-heart-muscle units on the left ventricle. The prespecified interim analysis was performed after completion of 3 months follow-up in the 16th patient transplanted with BioVAT formulated from 20 engineered-heart-muscle units.

Patients enrolled in BioVAT-HF are asked to enroll into the VAT-registry (registered under DRKS00027292) until end-of-life to obtain information on long-term outcomes. Time to mechanical assist device implantation, time to heart transplantation, mortality, LVEF, New York Heart Association classification, and N-terminal pro-B-type natriuretic peptide plasma concentrations are reported in the VAT-registry once a year.

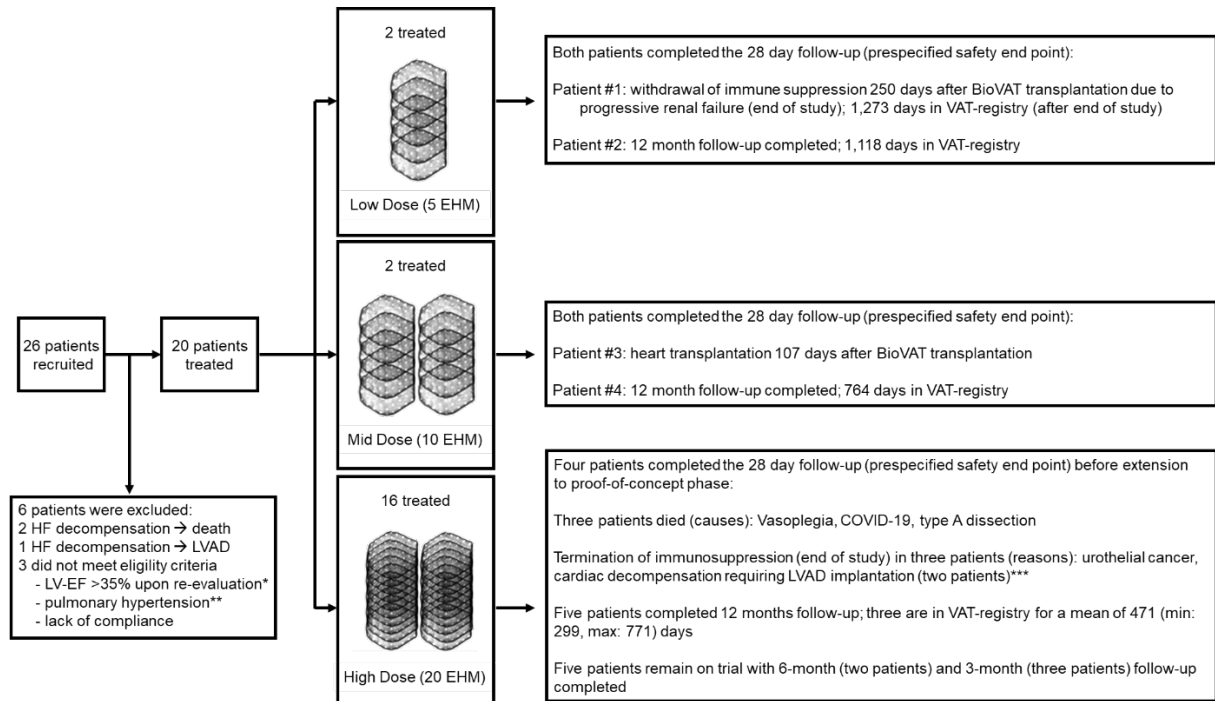
Figure S2. BioVAT dose levels, assembly, and transplantation



Schematic overview of BioVAT dose levels. Individual engineered-heart-muscle units (single units) are stacked as indicated to cover the surface of a TachoSil sponge (9.5 x 4.8 cm TachoSil, Corza Medical). At the low dose level, 5 engineered-heart-muscle units were sutured using Prolene 5-0 (Johnson & Johnson) to a single TachSil sponge. At the mid dose level, two 5 engineered-heart-muscle units per TachoSil assemblies were transplanted side-by-side. At the high-dose level (prespecified as the maximal feasible dose [MFD]), two 10 engineered-heart-muscle units per TachSil assemblies were transplanted side-by-side. The TachoSil sponge served as a security measure to stop epicardial bleeding, to reduce pericardial adhesions, and to ensure transfer and positioning of the engineered-heart-muscle units directly onto the target epicardium. A demonstration of spontaneous contractility of a single engineered-heart-muscle unit at the time of release for transplantation is shown in **Supplementary Video S1**.

SMD denotes safe maximal dose, MFD maximal feasible dose, and EHM engineered-heart-muscle.

Figure S3. CONSORT diagram



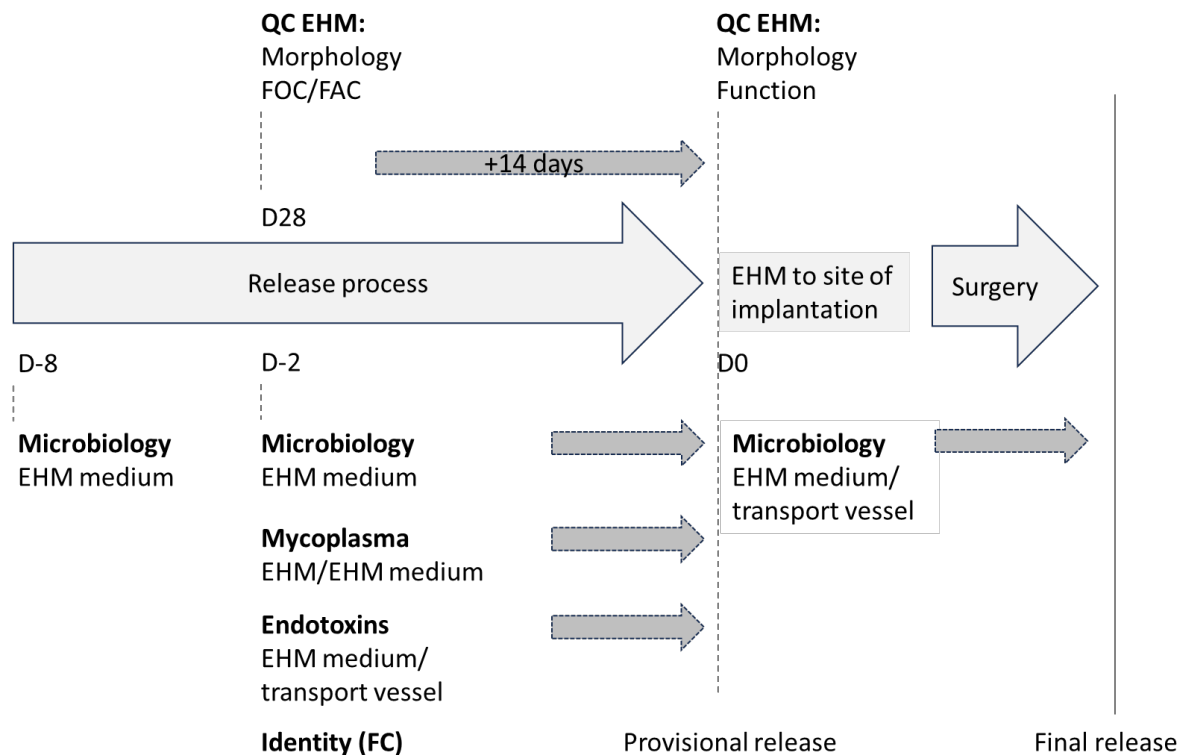
*Following echocardiography, where the left ventricular ejection fraction was 32% at the baseline investigation, cardiac computed tomography demonstrated a left ventricular ejection fraction of >35%; the patient did not meet the inclusion criterion “left ventricular ejection fraction \leq 35%” and was thus excluded from the study.

**Severe pulmonary hypertension was confirmed by right heart catheterization before treatment; the patient was deemed inoperable and excluded from the study.

***Left ventricular assist device implantation 41 and 172 days after BioVAT transplantation.

COVID-19 denotes Severe Acute Respiratory Syndrome Coronavirus Type 2 infection, EHM engineered-heart-muscle, LVAD left ventricular assist device, LV-EF left ventricular ejection fraction, and VAT ventricular assist tissue.

Figure S4. Engineered-heart-muscle release testing

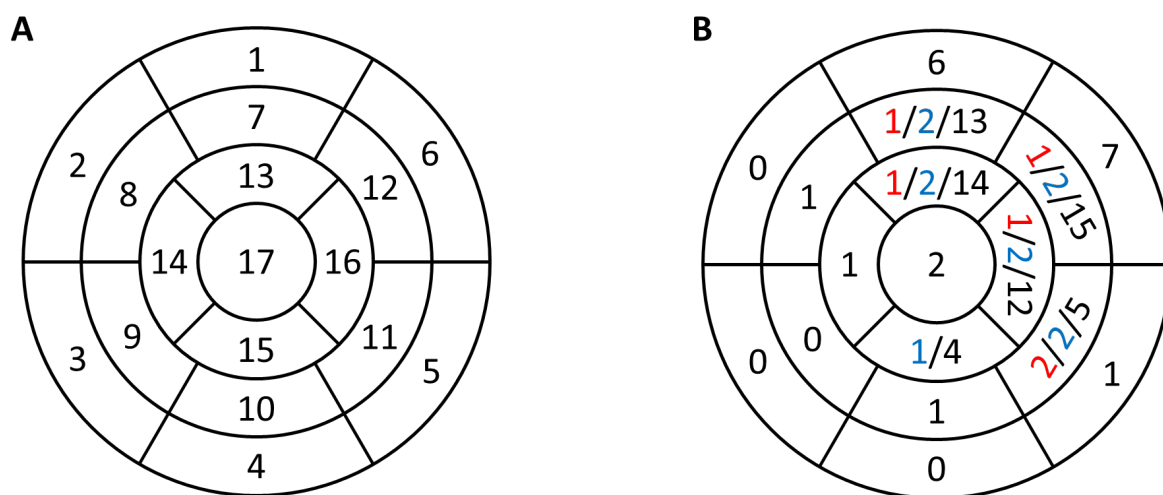


Engineered-heart-muscle units are prepared and cultured for a minimum of 28 days, which can be extended by 14 days. Upon release, engineered-heart-muscle units have to be transplanted within 72 hours (shelf-life at 15 to 25°C). Release testing starts 8 days (D-8) prior to dispatch to the study site with repeated microbiology (sterility) and endotoxin testing of the engineered-heart-muscle unit culture medium. Engineered-heart-muscle units are subjected to quality control testing at 2 days (D-2) before release, i.e., typically day 28 (D28) of culture. Quality control includes assessments of morphology and force of contraction in surrogate engineered-heart-muscle rings (mean \pm SD: 0.93 ± 0.57 mN; n=20 batches) and fractional area change in single engineered-heart-muscle units prepared for transplantation (mean \pm SD: $2.2 \pm 1.8\%$; n=20 batches; refer to Tiburcy et al. 2017 for details),¹ identity testing by flow cytometry to determine cardiomyocyte (ACTN2⁺; sarcomeric actinin) and stromal cell (VIM⁺; vimentin) content, and mycoplasma testing. After a provisional release and visual inspection of morphology and contractility at the point-of-care, engineered-heart-muscle units were transplanted. Additional sterility testing was performed with the spent engineered-heart-muscle unit culture medium and transport vessels for the final (post-transplant) release.

EHM denotes engineered-heart-muscle, FOC force of contraction (quantitative; cut-off: 0.3 mN; potency assay), FAC fractional area change (qualitative), FC flow cytometry, and QC quality control.

Figure S5. BioVAT transplant location

AHA 17 Segment Model

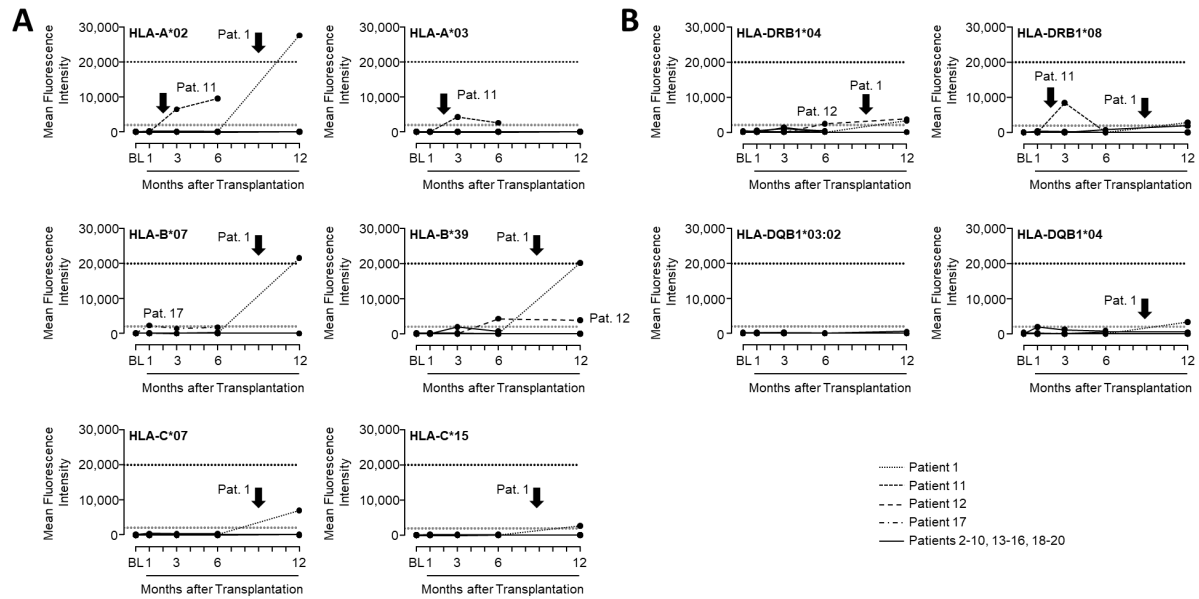


Panel A shows the American Heart Association (AHA) 17 Segment Model.² Panel B shows segments transplanted with BioVAT in a total of 20 patients: 2 patients transplanted with BioVAT assembled from 5 engineered-heart-muscle units (red), 2 patients transplanted with BioVAT assembled from 10 engineered-heart-muscle units (blue), and 16 patients transplanted with BioVAT assembled from 20 engineered-heart-muscle units (black).

AHA Segments:

1: basal anterior	7: mid anterior	13: apical anterior
2: basal anteroseptal	8: mid anteroseptal	14: apical septal
3: basal inferoseptal	9: mid inferoseptal	15: apical inferior
4: basal inferior	10: mid inferior	16: apical lateral
5: basal inferolateral	11: mid inferolateral	17: apex
6: basal anterolateral	12: mid anterolateral	

Figure S6. Donor specific antibodies

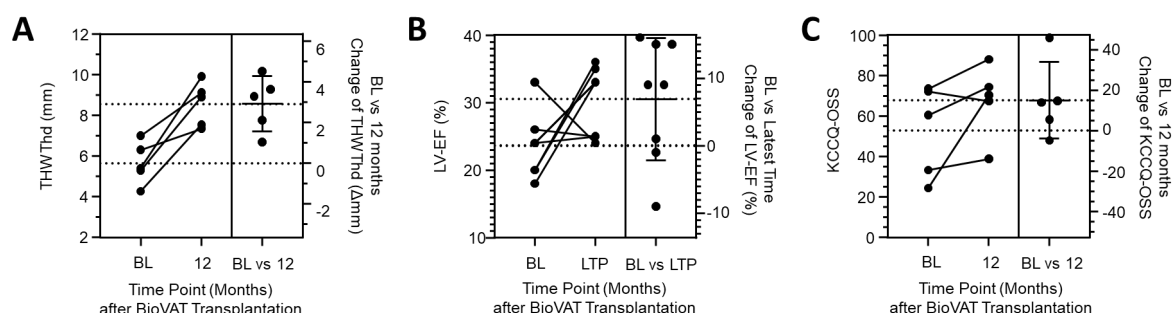


Donor specific antibody screening and differentiation was performed with Luminex microbead assays. Samples with a negative test result in the screening test were arbitrarily assigned the mean fluorescence intensity value 0. If the screening test was positive, single antigen assays were used to determine the mean fluorescence intensity value of beads representing the human leukocyte antigen pattern of induced pluripotent stem cell-derived engineered-heart-muscle. Antibodies bound to epitope-specific fluorescing microbeads were identified by fluorescence signal intensity. Striped lines indicate mean fluorescent intensity values of 20,000 (black) and 2,000 (grey) indicating strong and border line allograft immunization, respectively. Arrows indicate the termination of immunosuppression on day 250 (patient 1) and day 54 (patient 11) after BioVAT transplantation. Reason for termination of immunosuppression was worsening of renal function (patient 1) and diagnosis of a urothelial carcinoma (patient 11). Patients 12 and 17 showed signs of low level (mean fluorescent intensity values >2,000) allograft immunization to HLA-B*39, HLA-DRB1*04 and HLA-B*07, respectively. Patients 2-10, 13-16, and 18-20 presented with no evidence for allograft immunization.

To screen for allograft immunization and evidence for antibody mediated rejection, human leukocyte antigen-directed antibodies were detected using Luminex (LABScreen Multi, One Lambda/ThermoFisher). In case of a positive screening test, HLA antibodies were further differentiated with Luminex Single Antigen beads (LABScreen Single Antigen Class I and II, One Lambda/ThermoFisher).

HLA denotes human leukocyte antigen.

Figure S7. Long-term monitoring of primary efficacy end points



Panel A shows the target heart wall thickness in diastole assessed by cardiac computed tomography in individual patients before and 12 months after BioVAT transplantation at the safe maximal dose level (20 engineered-heart-muscle units); the change from baseline to 12 months follow-up is summarized in the right scatter dot plot with data presented as mean \pm SD. Panel B shows the left ventricular ejection fraction assessed by echocardiography in individual patients before and at the latest time point of follow-up (mean, 17 months; range, 6 to 41) after BioVAT transplantation at the safe maximal dose level (20 engineered-heart-muscle units); the change from baseline to the latest time point of follow-up is summarized in the right scatter dot plot with data presented as mean \pm SD. Panel C shows the Kansas City Cardiomyopathy Questionnaire-Overall Summary Score (scores range from 0 to 100 with higher scores indicating better health status) in individual patients before and 12 months after BioVAT transplantation at the safe maximal dose level (20 engineered-heart-muscle units); the change from baseline to 12 months follow-up is summarized in the right scatter dot plot with data presented as mean \pm SD.

BL denotes baseline, THWThd target heart wall thickness in diastole, LTP latest time point (mean, 17 months; range, 6 to 41), LV-EF left ventricular ejection fraction, and KCCQ-OSS Kansas City Cardiomyopathy Questionnaire-Overall Summary Score.

Supplementary Tables

Table S1. Overview of BioVAT doses in the treated patients

	pheno_#	EHM	Cells (x10 ⁶)	BW (kg)	EHM/kg bw	Cells/kg bw
Patient 1	pheno_712964436	5	200	100	0.05	2.00
Patient 2	pheno_203701612	5	200	109	0.05	1.83
Patient 3	pheno_094328810	10	400	76	0.13	5.26
Patient 4	pheno_581781390	10	400	130	0.08	3.08
Patient 5	pheno_585138723	20	800	100	0.20	8.00
Patient 6	pheno_557113172	20	800	71	0.28	11.27
Patient 7	pheno_291636687	20	800	78	0.26	10.26
Patient 8	pheno_344190045	20	800	105	0.19	7.62
Patient 9	pheno_707541394	20	800	68	0.29	11.76
Patient 10	pheno_413515017	20	800	80	0.25	10.00
Patient 11	pheno_165203545	20	800	63	0.32	12.70
Patient 12	pheno_810774493	20	800	89	0.22	8.99
Patient 13	pheno_935846536	20	800	105	0.19	7.62
Patient 14	pheno_081292356	20	800	107	0.19	7.48
Patient 15	pheno_307445008	19	800	65	0.29	11.69
Patient 16	pheno_769101790	20	800	84	0.24	9.52
Patient 17	pheno_932517408	20	800	105	0.19	7.62
Patient 18	pheno_552551884	20	800	84	0.24	9.52
Patient 19	pheno_240440030	20	800	114	0.18	7.02
Patient 20	pheno_424933903	20	800	79	0.25	10.13

Patient 15 was transplanted with a BioVAT assembled from 19 engineered-heart-muscle units due to a loss of an engineered-heart-muscle single unit during the production run. Note that patient 15 was included in the safe maximal dose cohort (n=16) with an above cohort average cells/bw dose (11.69 vs mean \pm SD: 9.4 \pm 1.8 cells/bw). Refer to **Figure S2** for an overview of the BioVAT formulations.

pheno_# denotes the unique identification from the trusted third party assigned patient identifier.

EHM denotes engineered-heart-muscle and BW or bw body weight.

Table S2. Summary of administered immune suppression

	pheno_#	Methylprednisolone	Tacrolimus	Everolimus	Mycophenolate mofetil
Patient 1	pheno_712964436 ¹	Yes	Yes	No	No
Patient 2	pheno_203701612	Yes	Yes	No	No
Patient 3	pheno_094328810	Yes	Yes	No	No
Patient 4	pheno_581781390	Yes	Yes	No	No
Patient 5	pheno_585138723	Yes	Yes	No	No
Patient 6	pheno_557113172	Yes	Yes	No	No
Patient 7	pheno_291636687	Yes	Yes	No	No
Patient 8	pheno_344190045	Yes	Yes*	Yes*	No
Patient 9	pheno_707541394	Yes	Yes*	Yes*	No
Patient 10	pheno_413515017	Yes	Yes	No	No
Patient 11	pheno_165203545 ²	Yes	Yes	No	No
Patient 12	pheno_810774493	Yes	Yes*	Yes*	No
Patient 13	pheno_935846536	Yes	Yes	No	No
Patient 14	pheno_081292356	Yes	Yes	No	Yes
Patient 15	pheno_307445008 ³	Yes	Yes*	Yes*	No
Patient 16	pheno_769101790 ⁴	Yes	Yes	No	No
Patient 17	pheno_932517408	Yes	Yes*	Yes*	No
Patient 18	pheno_552551884	Yes	Yes	No	No
Patient 19	pheno_240440030	Yes	Yes	No	No
Patient 20	pheno_424933903	Yes	Yes	No	Yes

¹⁻⁴Termination of immunosuppression: 250¹, 54², 172³, and 2⁴ days after BioVAT transplantation.

*Replacement of Tacrolimus by Everolimus after completion of wound healing.

Methylprednisolone: 0.15 mg/kg bodyweight per day
typically, 5 to 10 mg per day until 3 to 6 months after transplantation

Tacrolimus: target trough levels 5 to 15 ng/mL

10 to 15 ng/mL (7±3 days before until 2 months after transplantation)
8 to 12 ng/mL (3 to 6 months after transplantation)
5 to 10 ng/mL (until end-of-life)

revised with Clinical Trial Protocol Version 7

8 to 10 ng/mL (7±3 days before until 3 to 6 months after transplantation)
5 to 8 ng/mL (until end-of-life)

Everolimus: 3 to 8 ng/ml if combined with tacrolimus
6 to 10 ng/ml if administered in a calcineurin inhibitor-free protocol.

Mycophenolate mofetil: 1,000 mg bid
750 mg bid (50-75 kg)
500 mg bid (≤50 kg)

pheno_# denotes the from the trusted third party assigned patient identifier.

Table S3. Demographics and clinical characteristics at baseline of all BioVAT-treated patients

Characteristics	Total N=20
Baseline characteristics	
Age — yr	59 ± 12
Range (min, max)	(31, 77)
Male sex — no.	17
Weight — kg	90 ± 20
BMI — kg/m ²	28.2 ± 4.8
Heart rate — beats per minute	65 ± 8
Blood pressure — mmHg	
Systolic	104 ± 13
Diastolic	68 ± 8
Heart failure-related	
Living with heart failure before treatment — yr	4.8 ± 4.5
Left ventricular ejection fraction — %	25 ± 6
NYHA classification — no. (%)	
NYHA II	1 (5)
NYHA III	19 (95)
NT-proBNP median (IQR) — ng/L	1,227 (481 - 3,205)
Comorbidities — no. (%)	
Coronary heart disease	18 (90)
History of myocardial infarction	14 (70)
Non-ischemic cardiomyopathy	2 (10)
Type 2 Diabetes	5 (25)
Hypertension	11 (55)
Dyslipidemia	17 (85)
Renal function	
eGFR ≥90 mL/min/1.73 m ²	2 (10)
eGFR 60-89 mL/min/1.73 m ²	7 (35)
eGFR 31-59 mL/min/1.73 m ²	11 (55)
Atrial fibrillation	7 (35)

Plus-minus values are mean ± SD. Renal failure is defined as KDIGO stages 1 to 3.

Data from 20 participants treated with BioVAT formulated from 5 engineered-heart-muscle units (2 patients), 10 engineered-heart-muscle units (2 patients), and 20 engineered-heart-muscle units (16 patients).

BMI denotes body mass index, NYHA New York Heart Association, KDIGO Kidney Disease Improving Global Outcomes, and eGFR estimated glomerular filtration rate.

Table S4. Demographics and clinical characteristics at baseline of SMD-treated patients

Characteristic	Total N=16
Basic characteristics	
Age — yr	60 ± 11
Range (min, max)	(31,75)
Male sex — no.	15
Weight — kg	86 ± 18
BMI — kg/m ²	27.4 ± 4.9
Heart rate — beats per min	65 ± 6
Blood pressure — mmHg	
Systolic	105 ± 13
Diastolic	68 ± 8
Heart failure-related	
Living with heart failure before treatment — yr	5.5 ± 4.7
Left ventricular ejection fraction — %	24 ± 5
NYHA classification — no. (%)	
NYHA II	1 (6)
NYHA III	15 (94)
NT-proBNP median (IQR) — ng/L	1,242 (481 – 4,241)
Comorbidities — no. (%)	
Coronary heart disease	14 (88)
History of myocardial infarction	10 (63)
Non-ischemic cardiomyopathy	2 (12)
Type 2 diabetes	3 (19)
Hypertension	8 (50)
Dyslipidemia	13 (81)
Renal failure	
eGFR ≥90 mL/min/1.73 m ²	2 (12)
eGFR 60-89 mL/min/1.73 m ²	6 (38)
eGFR 31-59 mL/min/1.73 m ²	8 (50)
Atrial fibrillation	6 (38)

Plus-minus values are mean ± SD. Renal failure is defined according to KDIGO stages 1-3.

Data from 16 patients treated with BioVAT formulated from 20 engineered-heart-muscle units (safe maximal dose) and included in the interim efficacy analysis.

BMI denotes body mass index, NYHA New York Heart Association, KDIGO Kidney Disease Improving Global Outcomes, eGFR estimated glomerular filtration rate, and SMD safe maximal dose.

Table S5. Summary of guideline-directed medical therapy in BioVAT-treated patients

	pheno_#	Diuretic	ARB	ARNI	BB	MRA	SGLT2i	Vericiguat	ICD/CRT-D
Patient 1	pheno_712964436	yes	0	yes	yes	yes	yes	0	ICD
Patient 2	pheno_203701612	yes	0	yes	yes	yes	yes	0	ICD
Patient 3	pheno_094328810	yes	0	yes	yes	yes	yes	0	ICD
Patient 4	pheno_581781390	yes	0	yes	yes	yes	yes	0	ICD
Patient 5	pheno_585138723	yes	0	yes	yes	yes	yes	yes	ICD
Patient 6	pheno_557113172	yes	yes	0	yes	yes	yes	0	ICD
Patient 7	pheno_291636687	yes	0	yes	yes	yes	yes	0	ICD
Patient 8	pheno_344190045	yes	0	yes	yes	yes	yes	yes	ICD
Patient 9	pheno_707541394	yes	0	yes	yes	yes	yes	0	CRT-D
Patient 10	pheno_413515017	0	0	yes	yes	yes	yes	0	ICD
Patient 11	pheno_165203545	0	0	yes	yes	0	yes	yes	ICD
Patient 12	pheno_810774493	yes	0	yes	yes	yes	yes	0	ICD
Patient 13	pheno_935846536	yes	0	yes	yes	yes	yes	0	ICD
Patient 14	pheno_081292356	yes	0	yes	yes	yes	yes	yes	ICD
Patient 15	pheno_307445008	yes	0	yes	yes	yes	yes	0	ICD
Patient 16	pheno_769101790	yes	0	yes	yes	yes	yes	0	ICD
Patient 17	pheno_932517408	0	0	yes	yes	yes	yes	0	ICD
Patient 18	pheno_552551884	yes	0	yes	yes	yes	yes	0	ICD
Patient 19	pheno_240440030	yes	0	yes	yes	yes	yes	0	CRT-D
Patient 20	pheno_424933903	0	0	yes	yes	yes	0	0	ICD

ARB denotes angiotensin 1 receptor blocker (valsartan), ARNI valsartan and sacubitril, BB betablocker, MRA mineralocorticoid receptor antagonist, SGLT2i sodium-glucose co-transporter-2 inhibitor, ICD implantable cardioverter defibrillator, and CRT-D cardiac resynchronization therapy with a defibrillator.

ICD and CRT-D devices included event monitors, which were interrogated at every study visit.

pheno_# denotes the from the trusted third party assigned patient identifier.

Table S6. Representativeness of Study Participants

Category	Example
Disease, problem, or condition under investigation	Advanced stage C (symptoms present with structural heart disease) and D (advanced heart failure unresponsive to therapy) heart failure with reduced ejection fraction (HFrEF)
Special considerations related to	
Sex and gender	Men have a higher lifetime risk (18%) of developing HFrEF than women (12%). The overall representation of women in HFrEF trials is approximately 25%.
Age	The mean age of patients at the time of HFrEF onset is 71.6 years for men and 72.9 years for women. Approximately 5 to 10% of all patients with HFrEF are considered to be in advanced stage C and D heart failure. In advanced heart failure, implantation of left ventricular assist devices (LVAD) or heart transplantation are considered. Patients who have an LVAD implanted are predominantly male (85%) with a mean age of 60.
Race or ethnic group	White individuals are overrepresented in heart failure trials. Racial or ethnic groups of color are less likely to receive non-pharmacologic therapies such as an LVAD or heart transplantation for HFrEF than Whites.
Geography	Age and cause vary among countries. Patients with HFrEF in Eastern Europe and Asia are younger (<70 years) and patients in Western Europe are older (>70 years). Device therapy (ICD, CRT) is highest in North America and Western Europe. Hospitalizations for heart failure are more frequent in North America and Western Europe.
Other considerations	HFrEF in men is attributable to hypertension (23%), hypercholesterolemia (20%), myocardial infarction (18%), smoking (16%), obesity (10%), atrial fibrillation (5%), and diabetes (5%). HFrEF in women is attributable to hypertension (39%), hypercholesterolemia (28%), smoking (19%), myocardial infarction (10%), atrial fibrillation (10%), obesity (6%), and diabetes (5%).
Overall representativeness of this trial	A total of 23 of 26 participants (88%) enrolled in BioVAT-HF presented with a history of coronary heart disease. In 18 of 26 participants (69%) the area of BioVAT transplantation was demarcated by post myocardial infarction hypokinetic scarred left ventricular free wall segments. In the remaining 31% of the BioVAT-HF participants the left ventricular free wall was identified as globally hypokinetic. BioVAT were assembled from engineered-heart-muscle units to target the hypokinetic left ventricular heart wall with the intention to remuscularize the failing heart. The overrepresentation of male participants (23 of 26; 88%) relates to the higher incidence of HFrEF caused by ischemic heart disease in the target patient population. The overrepresentation of White patients (100%) is a consequence of the early clinical trial conducted in Germany and its demographics (>90% Caucasian population).

Data obtained from Morris et al. 2021,³ Mwansa et al. 2021⁴, van Essen et al. 2025,⁵ and Westerhout et al. 2025.⁶

Table S7. Summary of adverse events in all treated patients

Category	Patients with AEs N=20
Any adverse event (AE) — no. (%)	196 (100)
Adverse events by maximum severity — no. (%)	
Grade 1 / Mild	66 (34)
Grade 2 / Moderate	78 (40)
Grade 3 / Severe	30 (15)
Grade 4 / Life threatening	19 (10)
Grade 5 / Death*	3 (2)
Adverse events related to BioVAT — no. (%)	0 (0)
Adverse event related to underlying heart disease — no. (%)	48 (24)
Adverse events related to concurrent disease — no. (%)	44 (22)
Adverse events related to immunosuppression — no. (%)	41 (21)
Adverse events related to the procedure** — no. (%)	14 (7)
Adverse events related to concomitant medication — no. (%)	14 (7)
Adverse event related to other reasons — no. (%)	35 (18)
Discontinuation of trial due to adverse event*** — no. (%)	4 (10)

Data are obtained from all patients in the BioVAT-HF study at the time of the interim analysis. Data were collected between February 3, 2021 and October 6, 2025.

*Systemic inflammatory response syndrome with vasoplegia (considered a cardiovascular death), COVID-19 related, type A dissection (considered a cardiovascular death).

**Adverse events related to the procedure (arrhythmic events, worsening of disease progression, surgical events).

***Discontinuation defined as termination of immunosuppression due to progressive renal failure, urothelial carcinoma, or two instances of left ventricular assist device (LVAD) implantation after cardiac decompensation.

Table S8. Laboratory values

Laboratory values	Pre-transplant*	3 months follow-up	Latest time point**
Low dose (5 engineered-heart-muscle units) and mid dose (10 engineered-heart-muscle units)			
NT-proBNP median (IQR) — ng/L	1,804 (962 – 3,760); 3	5,514 (2,578– 8,105); 4	782 (745 – 2,389); 3
hsTnT — ng/L	17 ± 11; 4	52 ± 18; 4	43 ± 18; 3
Creatinine — ng/L	1.3 ± 0.3; 4	1.6 ± 0.3; 4	1.9 ± 0.7; 3
eGFR — ml/min/1.73 m ²	58 ± 29; 4	44 ± 13; 4	40 ± 21; 3
BUN — mg/dL	17 ± 7; 4	19 ± 4; 4	13 ± 3; 3
ALAT — U/L	24 ± 9; 4	32 ± 8; 4	18 ± 6; 3
ASAT — U/L	36 ± 14; 4	21 ± 4; 4	19 ± 2; 3
GGT — U/L	30 ± 4; 4	35 ± 12; 4	26 ± 5; 3
hsCRP — mg/L	1.0 ± 0.5; 4	3.1 ± 2.8; 4	1.9 ± 1.4; 3
Safe Maximal Dose (19/20 engineered-heart-muscle units)			
NT-proBNP median (IQR) — ng/L	6,063 (758 – 8,260); 14	2,397 (1,269 – 8,282); 12	1,773 (972 – 3,467); 8
hsTnT — ng/L	30 ± 27; 15	65 ± 45; 12	30 ± 11; 8
Creatinine — ng/L	1.5 ± 0.3; 15	1.5 ± 0.4; 12	2.0 ± 0.6; 8
eGFR — ml/min/1.73 m ²	53 ± 16; 15	57 ± 21; 12	44 ± 21; 8
BUN — mg/dL	23 ± 13; 15	24 ± 11; 12	14 ± 6; 8
ALAT — U/L	28 ± 17; 15	30 ± 20; 12	25 ± 12; 8
ASAT — U/L	24 ± 7; 15	25 ± 6; 12	23 ± 8; 8
GGT — U/L	89 ± 96; 15	74 ± 58; 12	48 ± 33; 8
hsCRP — mg/L	1.2 ± 1.3; 15	2.0 ± 1.6; 12	2.9 ± 5; 8

Plus-minus values are mean ± SD (if data is from ≥ 3 patients); patient number.

*24 hours before BioVAT transplantation and after the initiation of immunosuppression (7±3 days before transplantation); note that there was an increase of NT-proBNP from baseline values with no apparent change of renal function (creatinine baseline levels: 1.4 ± 0.3 ng/L; 20 patients) and cardiac troponin levels (hsTnT baseline levels: 43 ± 99 ng/L; 19 patients).

**Latest time point under observation on study or in VAT-registry, i.e., from an average of 22 months (range, 6 to 52 months) after BioVAT transplantation. In the VAT-registry, LVEF, NYHA class and NT-proBNP are reported every 12 months.

ASAT denotes aspartate aminotransferase, ALAT alanine aminotransferase, BUN blood urea nitrogen, GGT gamma-glutamyl transferase, hsCRP high-sensitivity C-reactive protein, hsTnT high-sensitivity troponin T, NT-proBNP N-terminal pro-B-type natriuretic peptide, and IQR interquartile range

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