The first experience of Inclisiran treatment after heart transplantation

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Conflict of interest: no disclosures.

Aknowledgements:
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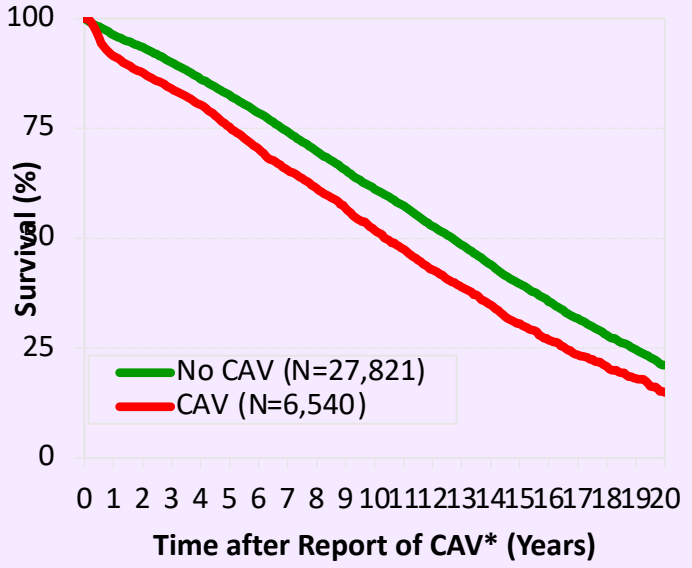
Causes of death after adult heart transplantation

Cause of Death (Deaths: January 1995 – June 2018)

Cause of Death	0-30 Days (N=6,871)	31 Days - 1 Year (N=5,980)	>1-3 Years (N=4,211)	>3-5 Years (N=3,630)	>5-10 Years (N=9,441)	>10-15 Years (N=7,108)	>15 Years (N=5,695)
Cardiac Allograft Vasculopathy	83 (1.2%)	190 (3.2%)	456 (10.8%)	449 (12.4%)	1,153 (12.2%)	859 (12.1%)	598 (10.5%)
Acute Rejection	268 (3.9%)	474 (7.9%)	412 (9.8%)	171 (4.7%)	176 (1.9%)	67 (0.9%)	29 (0.5%)
PTLD	2 (0.0%)	57 (1.0%)	94 (2.2%)	105 (2.9%)	305 (3.2%)	189 (2.7%)	121 (2.1%)
Malignancy (non-PTLD)	4 (0.1%)	137 (2.3%)	517 (12.3%)	712 (19.6%)	2,081 (22.0%)	1,525 (21.5%)	1,103 (19.4%)
CMV	3 (0.0%)	51 (0.9%)	19 (0.5%)	5 (0.1%)	8 (0.1%)	6 (0.1%)	2 (0.0%)
Infection, Non-CMV	958 (13.9%)	1,904 (31.8%)	561 (13.3%)	394 (10.9%)	1,023 (10.8%)	788 (11.1%)	702 (12.3%)
Graft Failure	2,716 (39.5%)	1,052 (17.6%)	1,112 (26.4%)	884 (24.4%)	1,838 (19.5%)	1,231 (17.3%)	944 (16.6%)
Technical	494 (7.2%)	94 (1.6%)	30 (0.7%)	28 (0.8%)	93 (1.0%)	85 (1.2%)	73 (1.3%)
Multiple Organ Failure	1,274 (18.5%)	1,006 (16.8%)	268 (6.4%)	209 (5.8%)	650 (6.9%)	599 (8.4%)	530 (9.3%)
Renal Failure	32 (0.5%)	53 (0.9%)	56 (1.3%)	113 (3.1%)	512 (5.4%)	569 (8.0%)	562 (9.9%)
Pulmonary	183 (2.7%)	235 (3.9%)	179 (4.3%)	163 (4.5%)	445 (4.7%)	336 (4.7%)	292 (5.1%)
Cerebrovascular	538 (7.8%)	332 (5.6%)	158 (3.8%)	119 (3.3%)	446 (4.7%)	387 (5.4%)	319 (5.6%)
Other	316 (4.6%)	395 (6.6%)	349 (8.3%)	278 (7.7%)	711 (7.5%)	467 (6.6%)	420 (7.4%)
Total Deaths (N)	7,759	6,912	5,223	4,607	12,586	10,268	8,531

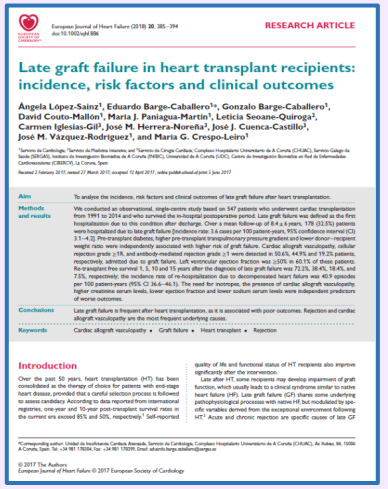
Survival After Report of CAV Within 3 Years of HTx and Survival In Patients Without CAV*




REVIEW ARTICLE

Cardiac Allograft Vasculopathy

Advances in Diagnosis


RESEARCH ARTICLE

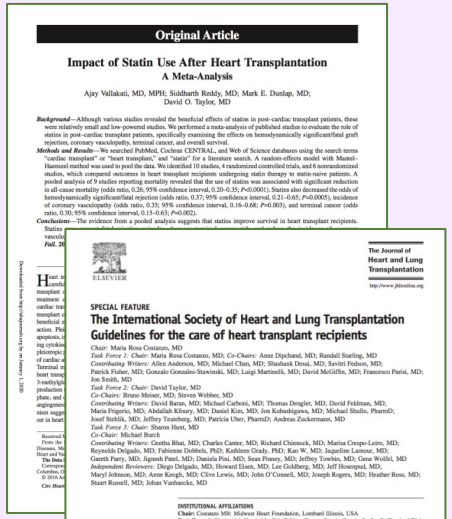
Late graft failure in heart transplant recipients: incidence, risk factors and clinical outcomes

ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2019
JHLT. 2019 Oct; 38(10): 1015-1066

Percentages represent % of deaths in the respective tim period. Total number of deaths includes deaths with unknown causes.

Lipid-lowering therapy after heart transplantation

The use of statins after HTx is recommended regardless of cholesterol levels. Due to pharmacological interactions and risk for toxicity, statin doses should generally be lower than those recommended for hyperlipidemia.



Original Article

Impact of Statin Use After Heart Transplantation
A Meta-Analysis

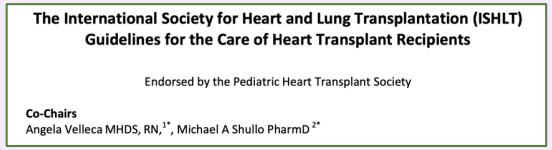
Ajay Vallakati, MD, MPH; Siddharth Reddy, MD; Mark E. Dunlap, MD; David O. Taylor, MD

ELSEVIER

The Journal of Heart and Lung Transplantation

SPECIAL FEATURE

The International Society of Heart and Lung Transplantation Guidelines for the care of heart transplant recipients



The International Society for Heart and Lung Transplantation (ISHLT) Guidelines for the Care of Heart Transplant Recipients

Endorsed by the Pediatric Heart Transplant Society

Co-Chairs
Angela Velleca MHDS, RN,[1*], Michael A Shullo PharmD [2*]

ESC European Society of Cardiology

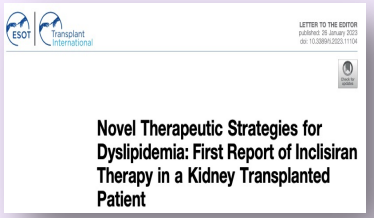
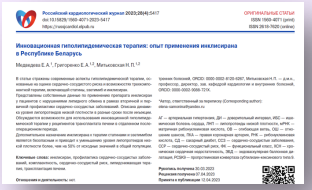
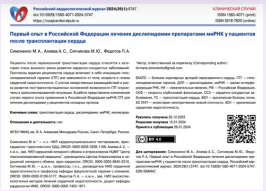
European Journal of Heart Failure (2024) doi:10.1002/ejhf.3185

POSITION PAPER

Prevention and rehabilitation after heart transplantation: A clinical consensus statement of the European Association of Preventive Cardiology, Heart Failure Association of the ESC, and the European Cardio Thoracic Transplant Association, a section of ESOT

Maria Simonenko[1*], Dominique Hansen[2,3], Josef Niebauer[4], Maurizio Volterrani[5], Stamatis Adamopoulos[6], Cristiano Amarelli[7], Marco Ambrosetti[8], Stefan D. Anker[9], Antonio Bayes-Genis[10], Tuvia Ben Gal[11], T. Scott Bowen[12], Francesco Cacciatore[13], Giuseppe Caminiti[5], Elena Cavaretta[14,15], Ovidiu Chioncel[16,17], Andrew J.S. Coats[18], Alain Cohen-Solal[19], Flavio D'Ascenzi[20], Carmen de Pablo Zarzosa[21], Andreas B. Gevaert[22,23], Finn Gustafsson[24], Hareld Kemps[25,26], Loreena Hill[27], Tiny Jaarsma[28,29], Ewa Jankowska[30], Emer Joyce[31,32], Nicolle Krankel[33], Mitja Lainscak[34], Lars H. Lund[35], Brenda Moura[36,37], Kari Nytrøen[38], Elena Osto[39,40], Massimo Piepoli[41,42], Luciano Potena[43], Amina Rakisheva[44,45], Giuseppe Rosano[46], Gianluigi Savarese[47], Petar M. Seferovic[48], David R. Thompson[27], Thomas Thum[49], and Emeline M. Van Craenenbroeck[22,23]

Inclisiran after solid organ transplantation

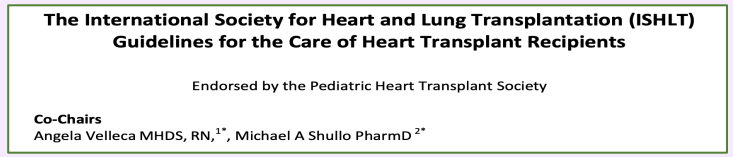
Kidney transplant  ESOT Transplant International LETTER TO THE EDITOR published: 28 January 2023 doi: 10.3389/ti.2023.11104 Novel Therapeutic Strategies for Dyslipidemia: First Report of Inclisiran Therapy in a Kidney Transplanted Patient	Male, 79 year-old - 12 year received a deceased donor kidney transplantation - Everolimus + Steroids - Metabolic syndrome (dyslipidaemia, hypertension, post-transplant diabetes, overweight), hyperuricemia, history of smoking (approximately 13 pack years), progressive peripheral artery disease (Fontaine IIB), coronary artery disease	Atorvastatin 80mg + Ezetimib 10mg Total cholesterol 5.18 mmol/l, LDL-C 2.46 mmol/l, triglycerides 1.79 mmol/l, + Inclisiran (1 year observation after 1st injection, received 3 injections)
Liver transplant  Российский кардиологический журнал 2023;28(4):5417 doi:10.15829/1560-4071-2023-5417 ОРИГИНАЛЬНЫЕ СТАТЬИ Инновационная гиполипидемическая терапия: опыт применения инклисирана в Республике Беларусь	18 patients, male - 15 63.5±12.5 year-old: from 39 to 77 year-old	Rosuvastatin 10-40 mg and/or Ezetimib 10mg + Inclisiran 8 patients – 3 injections 6 patients – 2 injections 4 patients – 1 injection
Heart transplant  Российский кардиологический журнал 2024;29(1):5747 doi:10.15829/1560-4071-2024-5747 КЛИНИЧЕСКИЙ СЛУЧАЙ Первый опыт в Российской Федерации лечения дислипидемии препаратами миРНК у пациентов после трансплантации сердца	4 patients: 2 male, 2 female	Patients who were on top of lipid-lowering therapy: 1 patient – 4 injections (15 months of follow-up) 2 patients – 3 injections (1 year of follow-up) 1 patient – 2 injections (9 months of follow-up)

Background

After heart transplantation (HTx) patients are at very high risk for developing cardiovascular diseases. Post-transplant management includes the initiation of lipid-lowering therapy (LLT) in all heart recipients.

Immune and non-immune risk factors for cardiac allograft vasculopathy

Age and sex of donor	Age and sex of recipient	**Dyslipidaemia**
Hypertension	Hyperhomocysteinemia	Diabetes
Allograft rejection	CMV	Histocompatibility


The International Society for Heart and Lung Transplantation (ISHLT) Guidelines for the Care of Heart Transplant Recipients

Endorsed by the Pediatric Heart Transplant Society

Co-Chairs
Angela Velleca MHDS, RN,[1*], Michael A Shullo PharmD [2*]

Objective: to analyze results of Inclisiran management in recipients after HTx.

Materials and methods

- From January 2010 to February 2024 HTx was performed in 244 patients, 13 of them were children (10-16-year-old).
- Early after HTx statins were prescribed in all of them.
- In long-term follow-up due not effectiveness statins were up-titrated (Atorvastatin, ≤20mg) and other LLT was added: Fenofibrate (145mg; n=55), Ezetimibe (10mg; n=23) and Alirocumab (75mg; n=5).
- From May 2023 to February 2024 indications for Inclisiran treatment have been determined in 4 recipients. We estimated their clinical characteristics and outcomes of Inclisiran management.

The use of Inclisiran after heart transplantation

№	Causes of heart failure	Age, year-old	Sex	Years after HTx when Inclisirant therapy was initiated	Immunosuppression	Dislipidaemia prior to HTx	LLT prior to Inclisiran management	Number of Inclisiran injections	Renal or liver dysfunction
1	Ischaemic heart disease + After HTx: generalized atherosclerosis	65	Male	12 years	Tacrolimus, Everolimus	+	Atorvastatin 20 mg + Ezetimib 10 mg. Fenofibrate 145 mg was discontinued due to CKD. Later Omega-3 fatty acids were prescribed.	4	CKD C4 CFR < 30 ml/min/1,73m^2
2	Hypertrophic cardiomyopathy	51	Male	10 months	Tacrolimus, Everolimus, Steroids	-	Atorvastatin 20 mg Later Omega-3 fatty acids were prescribed.	3	CKD C5 CFR < 30 ml/min/1,73m^2; October 2022 – October 2023 – renal replacement therapy
3 **	Non-compact myocardium, radiation-induced heart disease	40	Female	8 months	Tacrolimus, Mycophenolic acid, Steroids	-	-	3	CKD C4 CFR < 30 ml/min/1,73m^2; Toxic hepatitis developed 3 months after HTx
4	Ischaemic heart disease + After HTx: generalized atherosclerosis	65	Female	9 years	Tacrolimus, Everolimus	+	Atorvastatin 20 mg + Ezetimib 10 mg	3	CKD C4 CFR < 30 ml/min/1,73m^2;

There were no adverse events in analyzed patients. Serum levels of Tacrolimus and Everolimus, C-reactive protein and creatinine did not change after injections.

Risk factors and lipid profile

Patient	№6	№199	№211	№39
Risk factors of post-transplant CVD	- IHD, CABG prior to HTx - Hypertension - Age - Male - Dyslipidaemia - 1 peisode of 2R/3A (<1 year after HTx) - Smoking prior to HTx and after - Overweight	- Coronary artery stent implantation prior to HTx - BCA atherosclerosis prior to HTx - MI due to thromobosis on the 2nd day after HTx - Smoking prior to HTx - Hyperhomocysteinemia - Dyslipidaemia after HTx - Male - Age - Hypertension - Overweight	- HTx - High immunological risk, high risk of allograft rejection and CAV development - Drug-induced dyslipidaemia	- IHD, CABG prior to HTx - Hypertension - Age - Dyslipidaemia - Smoking prior to HTx
Lipid profile prior to Inclisiran injection and 6 months after 1st injection				
Total cholesterol	7.54 → 3.82 mmol/l	8.29 → 3.82 mmol/l	4.41 → 2.95 mmol/l	4.74 → 3.88 mmol/l
Triglycerides	7.92 → 3.07 mmol/l	3.5 → 3.07 mmol/l	0.78 → 1.41 mmol/l	2.57 → 1.90 mmol/l
Low-density lipoprotein cholesterol	3.62 → 1.53 mmol/l	5.58 → 1.53 mmol/l	2.53 → 0.93 mmol/l	2.63 → 1.84 mmol/l

Conclusion

- While initiation of LLT is obligatory to all heart recipients, decision on up-titration of it should be based on their lipid profile.
- Inclisiran is safe and effective lipid-lowering medication for transplant recipients.
- Limitations to up-titration of oral LLT is an indication to prescribe Inclisiran injections in transplant patients.