Which “roadmap” in patient with advanced or refractory heart failure, eligible for LVAD and Heart transplantation?

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Background

Heart transplant (HTx) is the gold standard for eligible patients with advanced heart failure, but hearts supply is much lower than demand, and time in waitlist is getting longer. “Bridge” strategies to keep patients alive, clinically stable and eligible for HTx are needed. Left ventricular assist devices (LVADs) improve survival in inotrope-dependent patients and can revert type II pulmonary hypertension and end-organ damage, but device-related complications are frequent. In Italy, stable LVAD patients have no priority for organ allocation, and therefore LVAD is often a long-term therapy.
We report on patients treated with LVAD or repeated infusions of the inodilator Levosimendan as a bridge to HTx or candidacy at our center.

Methods

Retrospective analysis of 115 patients treated with LVAD (iLVAD) or levosimendan (LEVO) between January 2006 and February 2016, based on medical choice and patients' preferences. Baseline characteristics, 1-year survival on original therapy (freedom from death, emergency HTx or delayed LVAD implant), 1 and 5-years overall survival were evaluated in HTx eligible patients.

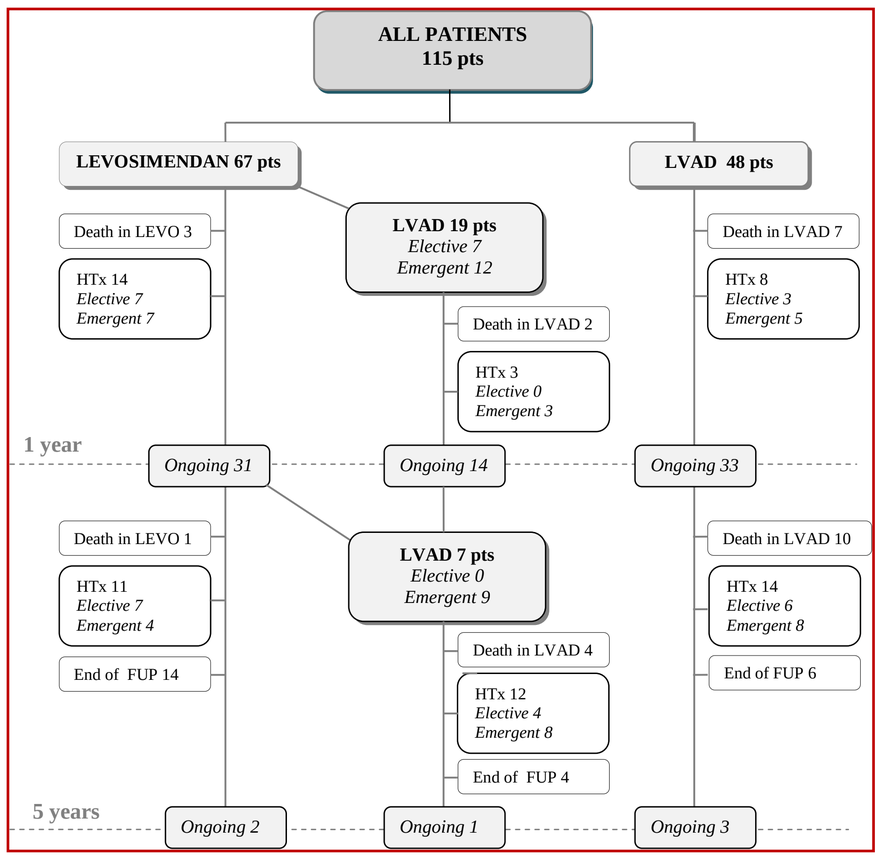
Results

67 patients (58%) were initially treated with Levosimendan (LEVO) and 48 (42%) with LVAD (iLVAD). LEVO patients were less compromised and smaller than iLVAD patients (Intermacs >4 60% vs 37%, p<0.001; BMI 24 ± 4 vs 27 ± 4.5 kg/m2, p=0.004), had smaller left ventricles and worse right ventricular function (p<0.05 for all).

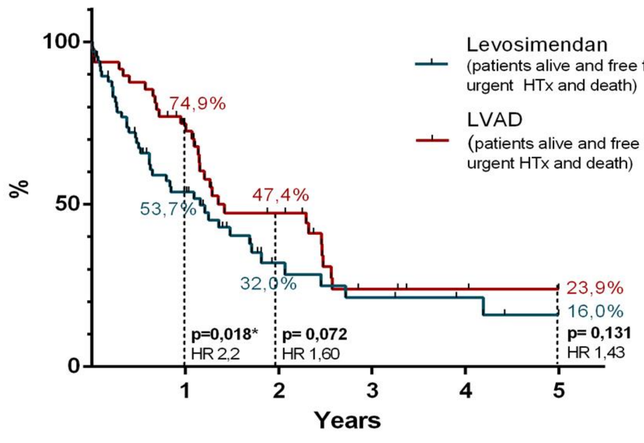
In the first year there were 3 deaths, 19 delayed LVAD implants (*d*LVAD), 7 emergency plus 7 elective HTx in LEVO pts *vs* 7 deaths, 5 emergency plus 3 elective HTx in *i*LVAD pts, with 51% LEVO *vs* 75% *i*LVAD pts surviving on original therapy (p <0.02).
Median follow-up at May 31, 2017 was 1526 days, IQR 1025-2262.

26/67 LEVO pts (39%) underwent *d*LVAD (median delay 173 days, IQR 82-377) with 69% 1-year survival on LVAD. Median time on original treatment was 186 days (IQR 84-436) for LEVO and 420 days (IQR 263-838) for *i*LVAD pts (p= 0,02).

Despite shorter time on original therapy, LEVO pts had similar 1-year (85% *vs* 77%) and superior 5-years overall survival (68% *vs* 50%, p<0.02) compared to *i*LVAD pts.

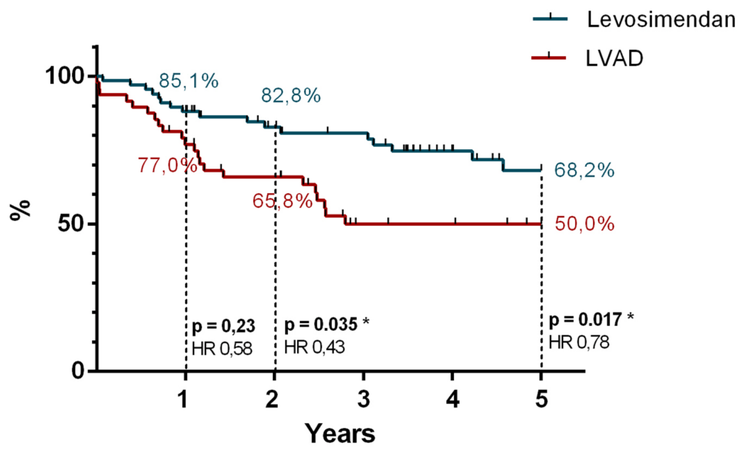


LEVO vs iLVAD- survival on original therapy



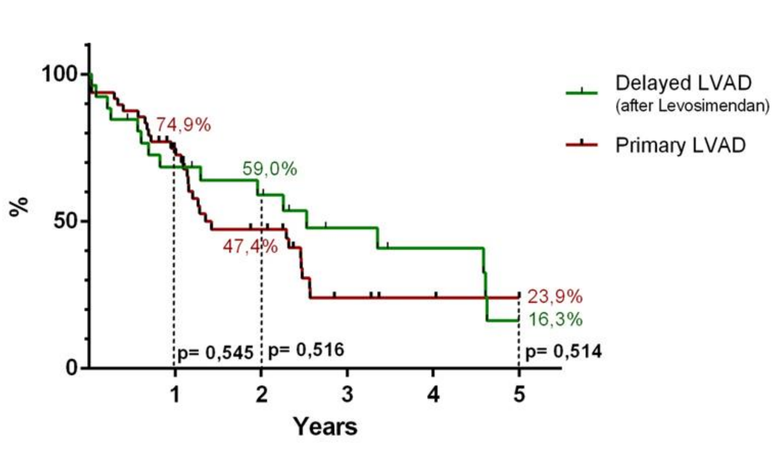
No. at Risk		1y	2y	3y	4y	5y
LEVOSIMENDAN	67	31	9	6	4	2
LVAD	48	33	17	6	4	3

LEVO vs iLVAD- overall survival



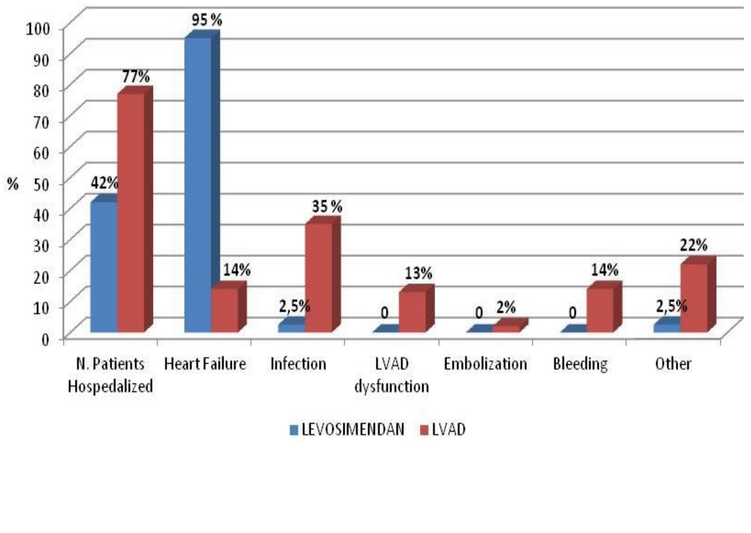
No. at Risk		1y	2y	3y	4y	5y
LEVOSIMENDAN	67	59	44	40	26	19
LVAD	48	36	28	16	15	12

iLVAD vs dLVAD – survival free of events

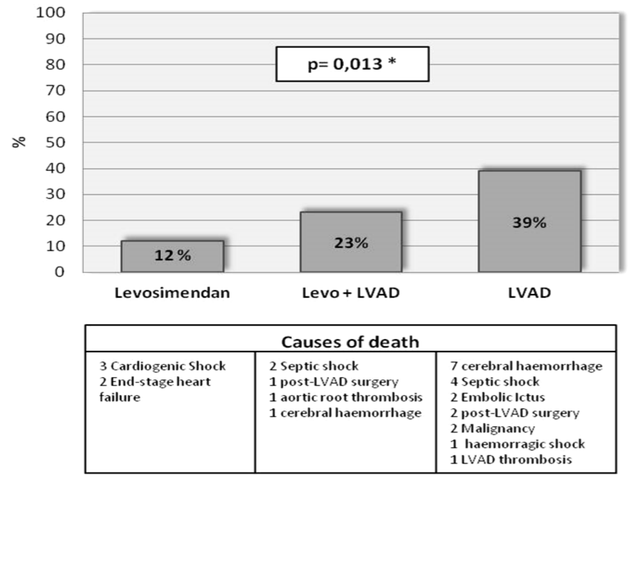


No. at Risk		1y	2y	3y	4y	5y
Delayed LVAD	26	17	12	7	5	2
Primary LVAD	48	35	17	6	3	3

Hospitalizations – 1 year

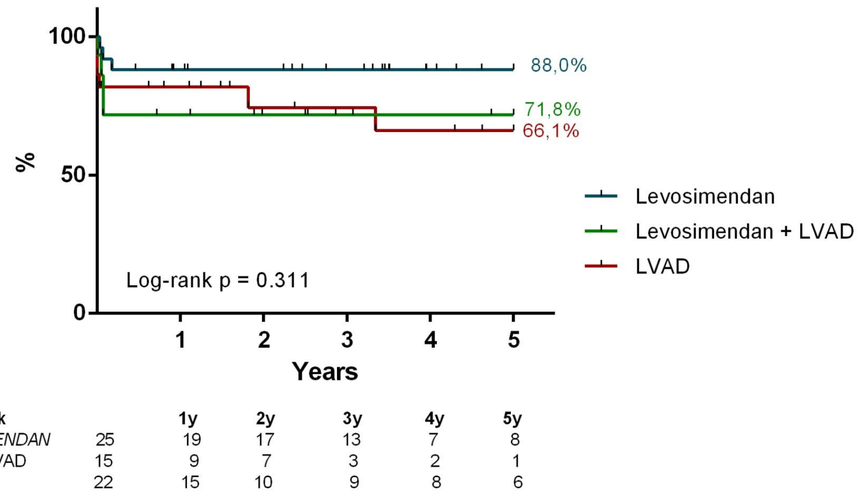


Death before HTx



Causes of death		
3 Cardiogenic Shock 2 End-stage heart failure	2 Septic shock 1 post-LVAD surgery 1 aortic root thrombosis 1 cerebral haemorrhage	7 cerebral haemorrhage 4 Septic shock 2 Embolic Ictus 2 post-LVAD surgery 2 Malignancy 1 haemorragic shock 1 LVAD thrombosis

Post-HTx survival



No. at Risk		1y	2y	3y	4y	5y
LEVOSIMENDAN	25	19	17	13	7	8
LEVO + LVAD	15	9	7	3	2	1
LVAD	22	15	10	9	8	6

Conclusions

In LVAD- and HTx-eligible pts, repeated Levosimendan infusions may serve as temporary treatment, until HTx or until patients recognize the need for additional therapy.
LVAD pts deserve some priority for HTx to prevent late device-related complications and deaths.

The authors discuss off label use of the drug Levosimendan
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