

# Impact of the Thoracotomy Approach on Bleeding Events Prior to Hospital Discharge: A Comparison of the HeartWare™ HVAD™ System LATERAL and Bridge to Transplant-Continued Access Trials

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# Disclosures

- Sangjin Lee, MD, MSc: Consultant Medtronic
- Edwin McGee, Jr., MD : Consultant Medtronic
- Anson Cheung, MD: Consultant Medtronic, Abbott
- Theodore Boeve, MD: None
- Matthew R. Danter, MD: None
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# Bleeding in VAD Therapy

- Bleeding is among the most common adverse events following HVAD implantation<sup>1-3</sup>.
- Improved protocols regarding anti-thrombotic management have reduced reports of early major bleeding rates from ~50% to ~19%<sup>4-6</sup>.
  - However, bleeding complications can persist following LVAD implantation.
- Current literature is focused primarily on GI and neurological bleeding
  - Evidence regarding early, surgical bleeding is limited.

1. Rogers, et al. 2017. *N Engl J Med*.

2. Milano, et al. 2018. *JACC Heart Fail*.

3. McGee, et al. 2019. *J Heart Lung Transplant*

4. Miller, et al. 2007. *N Engl J Med*.

5. Aaronson, et al. 2012. *Circulation*.

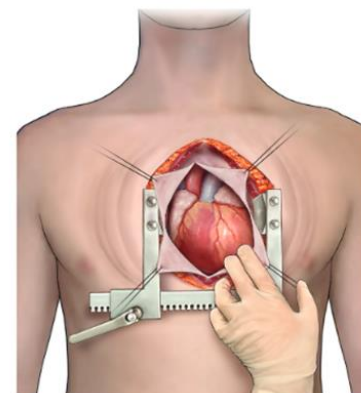
6. Netuka, et al. 2015. *J Am Coll Cardiol*.

# Purpose

- To explore further the bleeding events that occurred prior to hospital discharge in the LATERAL Trial HVAD patients compared to the ADVANCE BTT+CAP patients
- To further define the adverse event burden for the two surgical approaches, thoracotomy versus sternotomy

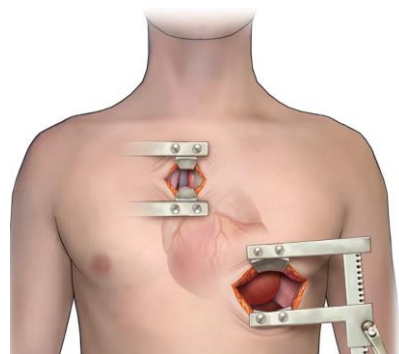
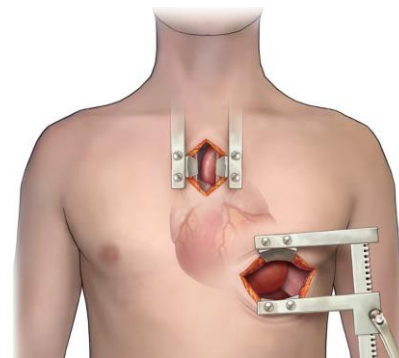
# ADVANCE BTT+CAP Bridge to Transplant Trials

- ADVANCE: prospective, multi-center study evaluating safety and efficacy of HeartWare™ HVAD™ System for BTT, using a contemporaneous control from the InterMACs Registry
  - 140 US pts enrolled from Aug 2008 – Aug 2010
  - Continued Access Protocol enrolled an additional 242 pts from May 2010 – Nov 2012
- Combined 382 pt cohort revealed **91% 6-month survival** on original device or transplanted or explanted for recovery, with improved QOL and comparable or lower adverse event rates



# LATERAL Clinical Trial

- Prospective, single-arm, multi-center trial evaluating the thoracotomy surgical approach for BTT patients implanted with the HeartWare HVAD System
- 144 Canadian and US pts enrolled from Jan 2015 – April 2016 at 26 sites; data entry: Intermacs Registry
- **Primary endpoint success achieved in 88.1%** (alive on original device and free from disabling stroke,\* or transplanted or explanted for recovery at 6 months) compared to performance goal of 77.5%
- **87% overall 2-year survival** on original device



*\*modified Rankin Scale score > 3*

# Methods

- Post hoc comparative analysis of ADVANCE BTT/CAP vs LATERAL Trials
  - Identified patients with pre-hospital discharge bleeding event post-HVAD System implant
- Pre-DC bleeding events
  - Intermacs Version 3.0 Adverse Events Definitions
  - Internal and external bleeding resulting in death, reoperation, and/or blood transfusions
  - Gastrointestinal bleeding events (GIB)
- Qualifying PRBC transfusions
  - Within any 24 hours period during the 1st week post-implant:  $\geq 20$  cc/kg PRBC if  $< 50$  kg, or  $\geq 4$  units PRBC if  $\geq 50$  kg
  - Any PRBC transfusion  $>$  one week post-implant

# Baseline Demographics

	LATERAL (n=144)	BTT+CAP (n= 382)	p-value
Age (years)	54.2 ± 11.5	53.2 ± 11.7	0.37
Sex (% Female)	28.8%	22.2%	0.15
Race (%White)	62.5%	68.1%	0.25
Body Mass Index (kg/m <sup>2</sup> )	27.1 ± 5.1	28.2 ± 6.1	0.03
Ischemic Cardiomyopathy	32.6%	38.0%	0.27
Intermacs Patient Profile			0.52
1	3.5%	5.5%	
2	31.3%	34.8%	
3	47.2%	40.6%	
4-7	18.1%	19.1%	
Diabetes Mellitus	5.6%	35.1%	<0.0001
Hypertension (requiring medication)	16.7%	59.7%	<0.0001

	LATERAL (n=144)	BTT+CAP (n= 382)	p-value
History Atrial Fibrillation	30.6%	38.5%	0.10
Prior Stroke	4.9%	10.5%	0.06
History Tobacco	34.7%	51.8%	0.0006
Prior CABG	11.1%	10.2%	0.75
Serum Creatinine	1.3 ± 0.7	1.3 ± 0.4	0.96
ALT	36.5 ± 34.9	47.5 ± 65.1	0.01
AST	34.1 ± 26.1	38.7 ± 49.5	0.18
Hemoglobin	11.7 ± 1.8	11.7 ± 2.6	0.89
Platelets	204.4 ± 66.7	209.7 ± 74.4	0.43
CVP	10.4 ± 5.6	11.6 ± 7.4	0.21
RAP	9.7 ± 5.3	10.3 ± 6.5	0.39



# Perioperative Characteristics

	LATERAL (n=144)	BTT+CAP (n= 382)	p-value
Cardiopulmonary Bypass Time (minutes)	69.7 ± 48.6	83.5 ± 35.3	0.002
Intensive Care Unit Length of Stay (days)	7.8 ± 9.8	10.8 ± 16.5	0.01
Hospital Length of Stay (days)	17.8 ± 11.7	26.6 ± 21.9	0.005

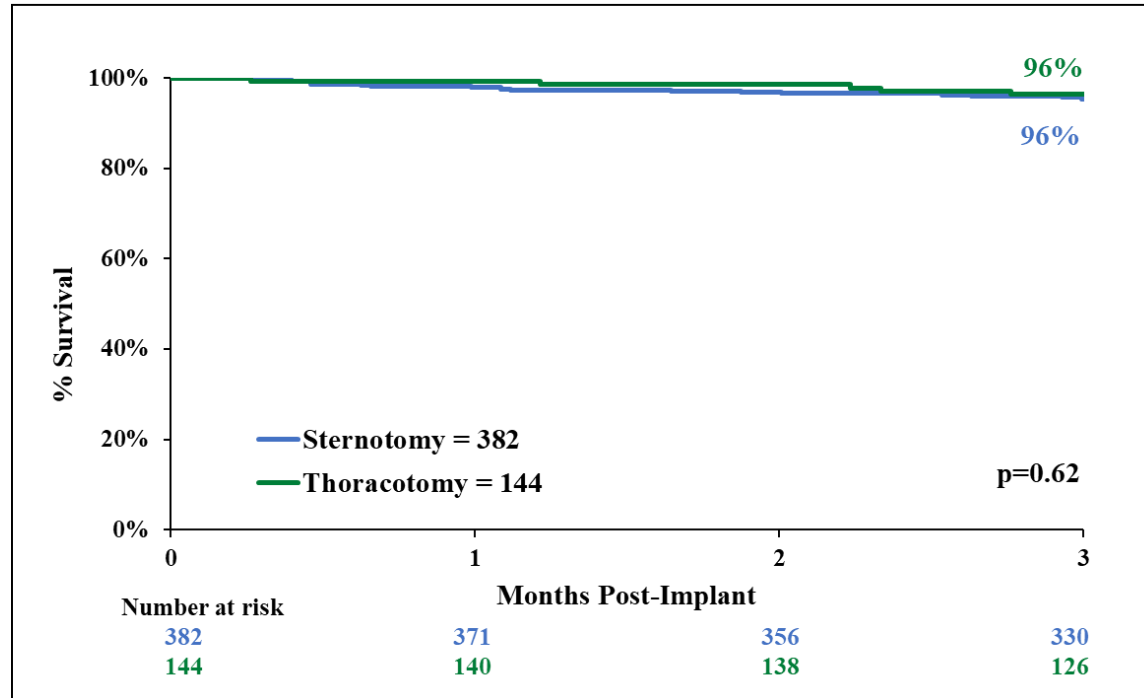
# Pre-Discharge Bleeding Events

Major Bleeding Events Pre-Hospital Discharge	Lateral (n=144)			BTT+CAP (n=382)			EPPY* P-Value
	Patients with Event N (%)	Number of Events	EPPY*	Patients with Event N (%)	Number of Events	EPPY*	
Bleeding Overall†	10 (6.9)	11	1.6	118 (30.9)	182	6.6	<b>&lt;0.001</b>
Re-Operation	5 (3.5)	5	0.7	44 (11.5)	49	1.8	0.06
Transfusion	10 (6.9)	11	1.6	54 (14.1)	59	2.2	0.46
GIB	3 (2.1)	4	0.6	16 ( 4.2)	16	0.6	>0.99

\*EPPY = events per patient year

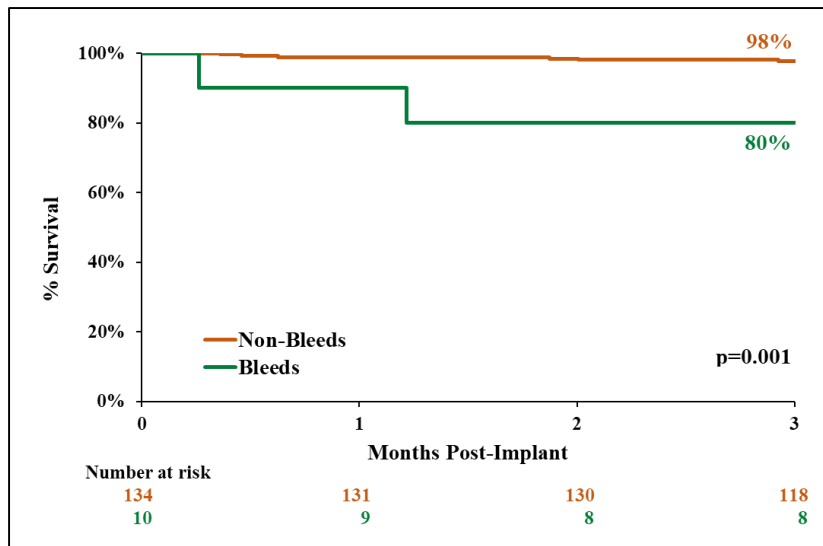
†Patients in Bleeding Overall cohort may be represented in one or more or no sub-category cohort.

# 3-Month Post-Implant Survival: Lateral vs BTT+CAP



# 3-Mo. Post-Implant Survival: Non-Bleeders vs Bleeders

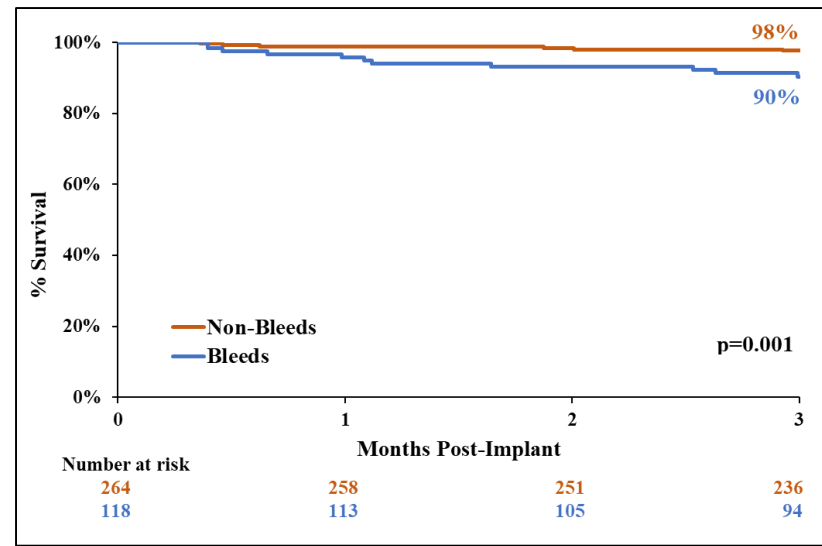
## Thoracotomy Approach



3-months Cause of Death (n=2)

- ISCM
- Neurological event

## Sternotomy Approach



3-months Cause of Death (n=11)

- Bleeding
- Neurological event
- Hepatic dysfunction
- MSOF
- Respiratory

# Summary

- Post hoc analysis comparing thoracotomy (Lateral) versus sternotomy (BTT+CAP) in advanced heart failure BTT patients with HVAD System support revealed:
  - Significantly shorter CPB time, as well as ICU and hospital LOS
  - Significant reduction in pre-discharge bleeding events overall
    - Trend toward reduced reoperations for bleeding
    - Similar GIB event rates
- Post-operative bleeding regardless of surgical approach remains associated with significantly higher mortality, although the numbers are small in the thoracotomy cohort.

# Limitations

- This is a post hoc analysis comparing two different clinical trials
- Due to the eras of the clinical trials, there is a potential temporal affect

# Conclusion

- These data continue to support the potential benefits of implanting the HeartWare HVAD System using the thoracotomy approach
- Future prospective studies will help to refine the patient selection for the thoracotomy approach, including minimizing the risk for early bleeding.

# Thank You !!

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