Performance of Helix transendocardial biotherapeutic delivery system after 300 cases

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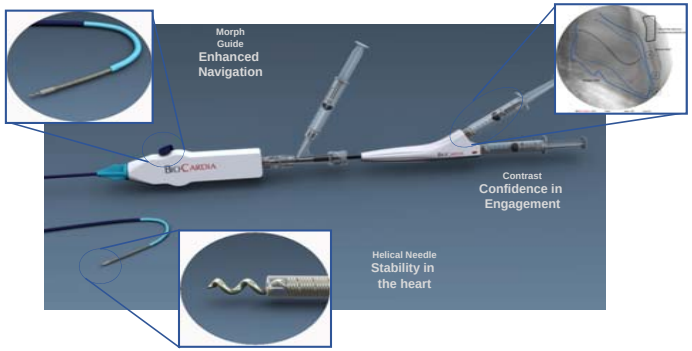
Background

Comprehensive approaches to local cardiovascular biologic therapy require a dedicated delivery system and may be regulated as combination products. FDA recent guidance has been towards performing sham-controlled trials, suggesting that there may be concern with delivery system safety. One leading trial using a placebo controlled trial design excluded events related to catheterization or injection procedure in the primary analysis. There is a need for understanding the overall MACE rate associated with different delivery platforms currently in use. Here we report on the safety experience of the Helix transendocardial delivery system after 300 clinical cases and compare results to those reported in the literature with other leading platforms.

The Helix Infusion System



The Helix Catheter System is comprised of the Helix Transendocardial Delivery Catheter used in combination with the Morph® Universal Deflectable Guide Catheter. The Morph® Universal Deflectable Guide is advanced through the aortic valve over a guide wire and provides the ability to guide the Helix Catheter. This catheter has been used in more than 5000 clinical procedures. The Helix Catheter for transendocardial delivery is advanced through the Morph guide via a hemostasis valve. The therapeutic lumen discharges at the distal tip of the helical needle. A second lumen discharges from the base of the helix for delivering contrast to confirm engagement and positioning. The helical needle allows for active fixation.

Clinical Experience

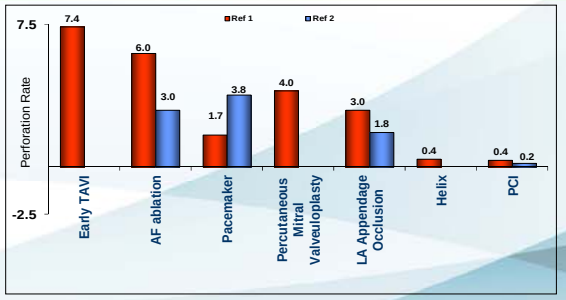
Publications of cell and gene delivery clinical trials over the past ten years utilizing different catheter based delivery systems have been reviewed for details on safety reporting and frequency of major adverse cardiac events including stroke/ ischemic events, myocardial infarction/vascular obstruction, cardiac perforation, vascular dissection, and death. Papers included delivery via intracoronary artery infusion using the STOP FLOW technique (N=907), and transendocardial intramyocardial delivery using the JNJ Myostar straight needle catheter (N=632), the BioCardia Helix catheter (N=300), and the Celyad C-Cath curved needle catheter (N=120). Primary articles on trials were supplemented by reports from the FDA Manufacturer and User Facility Device Experience of reported events, although for investigational trials there is no requirement to report anticipated adverse events. VT have been excluded in MACE due to the variability of reporting.

Safety Profile of various intramyocardial injection catheters

Year completed, Sponsor, Trial Name, ClinicalTrials.gov Identifier	ClinicalTrials.gov Identifier:	IM Catheter	Patients Treated	Stroke, MI, Perforation, Dissection, Death	Procedure Reported MACE	Procedure Reported Mace	Procedure Death
2016, Celyad, CHART 1, NCT01768702	NCT01768702	C-Cath	120	1/0/4/1/1	6	5,00%	1
TOTAL w C-Cath (Celyad)			**120**		**6**	**5,00%**	**0,83%**
2016, Vericel, lvCELL DCM, NCT01670981	NCT01670981	JNJ Myostar		Not Reported - Potentially in backup			Not reported
2014 Cytori ATHENA, NCT02052427	NCT02052427	JNJ Myostar	31	3/?/?/?/?	3	9,68%	
2013 Celyad C-Cure , NCT0081023	NCT0081023	JNJ Myostar	21	1/?/?/0/0	1	4,76%	
2013, Pilar Jimenez Quevedo, PROGENITOR	NCT00694642	JNJ Myostar	19	0/0/1/0/1	1	5,26%	1
2012, FOCUS, CCTRN	NCT00824005	JNJ Myostar	83	0/0/0/1/0	1	1,20%	
2012, Aldagen, FOCUS BR	NCT00314366	JNJ Myostar	20	1/0/0/0/0	1	5,00%	
2011, Mesoblast, Phase II REVASCOR	NCT00721045	JNJ Myostar	45	?/?/1/?/0	1	2,22%	
2011, Baxter, ACT34	NCT00300053	JNJ Myostar	167	?/?/2 /?/1	2	1,20%	1
2010, Meshalkin Research Institute of Pathology of Circulation, ESCAPE	NCT00841958	JNJ Myostar	55	0/0/0/0/0	0	0,00%	
2010 Cytori, The PRECISE Trial	NCT00426868	JNJ Myostar	27	1/?/0 /?/0	1	3,70%	
BM CMI 2009			50	1/0/1/0/0	2	4,00%	
TOTAL intramyocardial inj w straight needle (MyoStar, J&J)			**518**		**13**	**2,51%**	**0,39%**
2018 BioCardia CardiAMP Ongoing	NCT02438306		13	0/0/0/0/0	0		
2016, BioCardia/U Miami, TRIDENT	NCT02013674		30	0/0/0/0/0	0		
2014, U Milan, RECARDIO - Not Published	NCT02059681		10	0/0/0/0/0	0	0,00%	
CellProThera - NOT PUBLISHED	NCT02669810		11	0/0/0/0/0	0	0,00%	
ALSTER 2012*	NCT00939042		9	0/0/0/0/0	0	0,00%	
Stop HF 2012*	NCT01643590		93	0/0/0/0/0	0	0,00%	
2013, BioCardia/U Miami, TACHFT	NCT00768066		67	0/0/0/0/0	0	0,00%	
2012, BioCardia/U Miami/NIH, POSEIDON	NCT01087996		30	0/0/0/0/0	0	0,00%	
JVS-100 2012	NCT01082094		17	0/0/1/0/0	1	5,88%	
2011, BioCardia, TABMMI	NCT00507468		20	0/0/0/0/0	0	0,00%	
TOTAL using Helical shaped needle catheter (Helix/Morph, BioCardia)			**300**		**1**	**0,33%**	**0,00%**
ZEIHER 2012 - which strangely excludes REPAIR AMI.			775	0/4/0/7/0	11	1,42%	0,50%
TIME	NCT00684021		75	0/0/0/0/0	0	0,00%	
LATE TIME	NCT00684060.		57	0/0/0/0/0	0	0,00%	
TOTAL using intracoroanry infusion			**907**		11	**1,21%**	**0,43%**

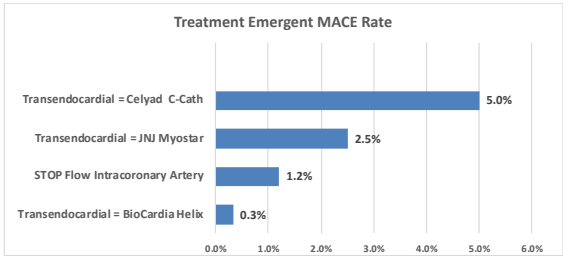
- In more than 300 clinical cases and over 5000 deliveries performed by 40 interventional cardiologists in 30 centers around the world, no death, MI or stroke related to the Helix Transendocardial Delivery Catheter has been reported thus far.
- Interpretation of results is nontrivial, as there is potential for both underreporting and over reporting of MACE events. The primary cause of MACE with all transendocardial catheters was cardiac perforation. The primary cause of MACE for the Stop Flow technique was reported as arterial obstruction.

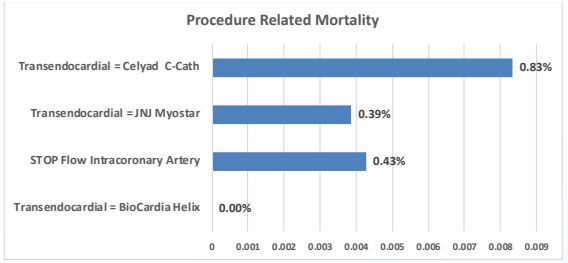
Safety Profile is comparable to PCI procedure



Comparison of perforation rates for various percutaneous procedures showed transendocardial delivery using the Helix Infusion Catheter System approaching the safety profile of conventional percutaneous coronary intervention (PCI).

Safety Profile of various intramyocardial injection catheters





Conclusions

The Helix Transendocardial Delivery System is currently the safest biotherapeutic intramyocardial delivery system based on currently available data among the leading delivery systems in clinical trial use today. Procedural safety in a real world multicenter experience remains to be established with all biotherapeutic delivery systems.

References

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