Performance of Helix transcatheter 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 delivery platforms currently in use. Here we report on the safety experience of the Helix transcatheter delivery system after 300 clinical cases and compare results to those reported in the literature with other leading platforms.

The Helix Catheter System is comprised of the Helix Transcatheter Delivery Catheter used in combination with the Morph® Universal Deflectable Guide Catheter. The Morph® Universal Deflectable Guide is advanced through the aortic valve via an over wire guide and provides the ability to guide the Helix Catheter. This catheter has been used in more than 5000 clinical procedures. The Helix Catheter for transcatheter 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 transcatheter intramyocardial delivery using the JNU Mystal straight needle catheter (N=632), the BioCardia Helix catheter (N=300), and the Celaya C-Cath curved needle catheter (N=120). Primary articles on trials were supplemented by reports from the FDA Manufacturer and User Facility 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

<table>
<thead>
<tr>
<th>Procedure Related Mortality</th>
<th>Treatment Emergent MACE Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transcatheter = Celaya C-Cath</td>
<td>0.3%</td>
</tr>
<tr>
<td>Transcatheter = JNJ Myostar</td>
<td>0.33%</td>
</tr>
<tr>
<td>STOP Flow Intracoronary Artery</td>
<td>0.43%</td>
</tr>
<tr>
<td>Transcatheter = BioCardia Helix</td>
<td>0.00%</td>
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</tbody>
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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 Transcatheter 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 transcatheter techniques was from 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 transcatheter delivery using the Helix Infusion Catheter System approaching the safety profile of conventional percutaneous coronary intervention (PCI).

Conclusions

The Helix Transcatheter 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

3. The Helix Infusion Catheter System has been used in ten clinical trials for adult stem cells and genes delivering patients with ischemic heart failure or acute myocardial infarction, including TAIMMY (NCT00657468), POSEIDON (NCT01087996), TAC-HFT (NCT00768006), ACXIR-100 Phase I (NCT01082094), STOP-HF (NCT01643500), TRIDENT (NCT02013674), RECARDIO (NCT02059681), EXCELLENT (NCT02069810), ALSTER-Helix (NCT00309442) and the CardiAmer HF trials (NCT02438006).

5. Bergman et al. Eurointervention 2012, 8 pg 732-742
6. Patel et al. TCT 2012
9. Hare et al. JAMA 2012, 308(22): 2369-2379