Fall 2014
TCT Takeaways

VALVES | RENAL DENERVATION | DRUG-ELUTING TECHNOLOGIES

NEWSLETTER

TCT 2014 - Key Takeaways

- TAVR is becoming an established technique - the future is improved durability; new technologies; new indications
  - Mitral valve repair is getting more attention - Abbott's MitraClip is still the only mitral transcatheter valve repair approach approved in the US
- Renal Denervation is not dead - physician excitement, more pre-clinical and clinical research is needed; randomized studies
- Drug-eluting technologies - tried and true mechanism of action
  - DES - well established
  - Bioresorbable Scaffolds are getting more data to what works and what doesn't; careful placement
  - Drug-Coated Balloons - the first DCB got FDA panel thumbs up in June this year; FDA approval may change the PAD market in the US
- FDA's Town Hall focused on the state of clinical research in the US
  - global delays in clinical study approvals: Brazil - 6-9 months, traditional European countries - 6 months
  - opportunity to bring clinical studies back to the US
  - FDA's initiatives to improve the clinical trial approval process in the US

What is new and what is tried and true?

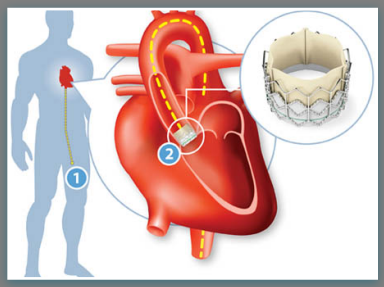
- reduce time from submission to full IDE approval to 30 days for at least 50% of submissions in 2015
- new guidances to facilitate the regulatory process
- move clinical studies to post-marketing

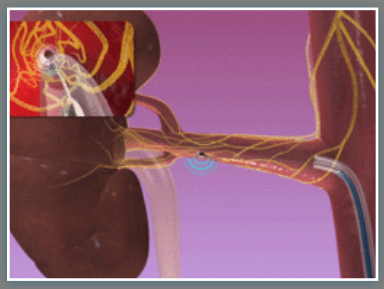
In Detail

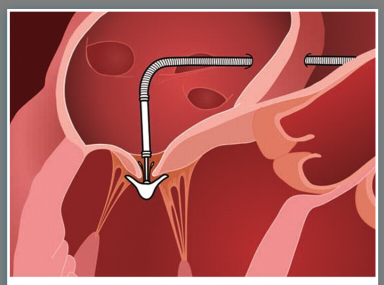
Valves

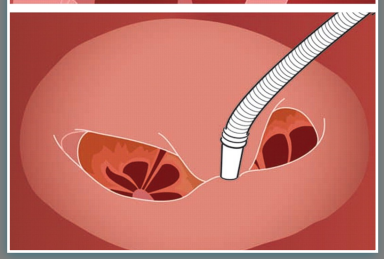
- TAVR - during the FDA Town Hall, Dr. Martin Leon gave a fantastic summary of the field
  - the technology is improving
  - it is an alternative procedure for high-risk patients
  - requires an entire team to collaborate to select the right treatment
  - extensive clinical research - randomized studies and post-market registries
  - standardized endpoint definition
  - team training is key
  - good news - echocardiography data up to 5 years indicate no valve deterioration and excellent hemodynamics
  - still not clear - is this technology good for lower risk patients?
  - para-valvular regurgitation - improve screening and optimal sizing using 3D-imaging
  - stroke after TAVR - improve patient selection, sizing and operator experience
  - the future of TAVR - improved durability, new technologies; new indications
- Mitral valve repair is coming into the spotlight - during the FDA Town Hall, Dr. Gregg Stone eloquently presented a roadmap for mitral valve product development based on the past 16 years of research
  - mitral treatment is complex and could involve multiple techniques
  - stick to the trail design; patient selection; crossovers

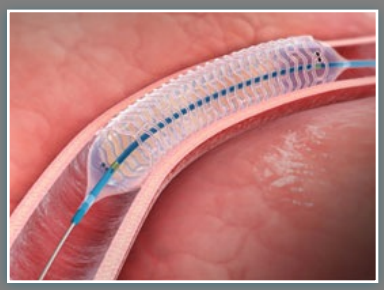
Key Takeaways in Pictures











- still only one transcatheter mitral valve repair product approved in the US
  - narrow indication
  - team of physicians to determine eligibility for the post-marketing study to widen the indications for use

Renal Denervation

- The RDN field is picking up again after the disappointing news in 2013
- Physicians are excited and eager to apply the technology on the right patients
  - consensus that there is a segment of the hypertensive population who benefits from RDN
  - patient selection needs to be improved
  - randomized studies are necessary to determine true effects
- The clinical outcome may have to be measured differently; how blood pressure is measured may have an impact on study outcome and demonstrating effectiveness
- Experts in the field recognize the need of better understanding the biology and pathology of the denervation process - where are the nerve bundles and how effective is the technology to deactivate them
  - conduct further pre-clinical studies
  - pay attention to the histopath to determine the effectiveness

Drug-Eluting Technologies

- Drug-Eluting Stents - thousands of patients treated world-wide; postmarking registries; establish objective performance criteria for clinical research
- Bioresorbable Scaffold
  - gaining traction OUS with more data and hands-on operator experience
  - improvement of vessel stenting (per Dr. Granada from CRF Skirball - http://www.tctmd.com/show.aspx?id=127101)
  - Abbott's IDE study is on-going (per www.ClinicalTrials.gov); other companies are coming up with their versions of BRS
  - FDA's review is complex due to the need to involve CDER
  - FDA reviewer provided nonclinical and clinical guidance for sponsors
  - consult the Agency early and often
- Drug-Coated Balloons
  - usage OUS is a fact - CAD and PAD (even bellow the knee)

- FDA's advisory panel voted unanimously in favor of the technology on June 12, 2014
- formulations have evolved to improve the therapy
- paclitaxel is the drug of choice - tissue retention
- distal tissue effects - not seen in general

FDA's 2-day Town Hall

- Challenges for clinical research and innovation in the US
  - US clinical research - regulatory and site challenges and opportunities
  - FDA's early feasibility initiative - first examples are in
  - FDA has shortened time for full IDE approval in the past 2 years since the enactment of FDASIA - from over 400 days to less then 200 days
  - The goal is to shorten time to full IDE approval to 30 days in 2015 - sponsors to work with the agency upfront; engage the review team early in the product development cycle
  - Guidance documents to support and to facilitate the initiative to strengthen clinical research in the US
    - IDE Decision Guidance
    - Pre-Submission Guidance
    - Guidance on Communications with the FDA - consult the Agency early and often
    - Guidance on Early Feasibility Studies in the US
    - Reality - in the US there are about 5,000 hospitals, 500 are enrolling, and of them, 200 are excellent centers
  - Reimbursement - parallel with marketing approval; FDA and CMS joint review initiative
- Novel Therapies - in addition to the devices discussed above, FDA's Town Hall discussed
  - Left Atrial Appendage occlusion - technology and clinical studies
    - FDA has convened a second advisory panel on October 8, 2014 to discuss recent safety data from clinical study with one device for LAA