CRT February 23, 2010 FDA Town Hall
Hot Topics Discussion Session 4: Barriers and Synergies in Japan-USA Device Evaluation

Summary of Session:

Lessons Learned: Past Present and Future Japan-USA DES Evaluation:

- There are several drug eluting stent (DES) and drug eluting balloon (DEB) trials in US and Japan now
- PLATINUM trial (Boston Scientific) is an example
    - Enrollment in Japan started almost at the same time as the US and EU
    - BSC plans to submit marketing application/PMA at the same time to both regulatory agencies
- SPIRIT III trial (Abbott) had a Japan arm, and some US data was leveraged for approval in Japan
    - There are different possible protocol types: single protocol, 2 separate protocols for each country, 2 separate protocols designed to complement each other
- Industry generally commented that HBD helped them decide to start a global trial– global clinical trials are possible

Building Synergy Between US and Japan: DES Clinical Trial Designs

- Angiographic follow-up is still needed in US studies
    - Having the angiographic arm in Japan may help enrollment, since procedural angiography is more common in Japan. This would also reduce confounding effects of "oculostenotic reflex" on the clinical endpoint.
    - Information needed to leverage angiographic cohort (data collected in another country) includes showing a similarity in vascular biology in patients from both countries
- Areas of future discussion/collaboration:
    - Similarities and differences in DES trial for small and large vessel evaluation
    - Gender vs body size effects
    - Pediatric devices
    - US and Japanese regulatory agencies have similar thought processes

Panel Discussion:

- Challenges:
    - Cost per patient is higher in Japan
        - How cost is calculated in Japan is unclear
        - Practice of paying up front for patients in Japan also drives cost up (i.e. sites are paid up front for a set number of patients regardless of whether they meet that enrollment number or not)
        - Sometimes there is a lack of a clinical research coordinator in house (Japan)

    - Industry perception of risk—recent increased speed of review in Japan has been helpful
- FDA and PMDA are committed to the Collaborative Scheme and HBD
- Going from Japan to US
    - There are niche devices marketed in Japan that may have a market/be beneficial in the US (smaller balloons, less invasive technologies, transradial accessory devices for interventions, etc)
        - Regulatory hurdle to come to the US may be high for a small Japanese manufacturer
    - For DES, PK levels tend to be higher in the Japanese population. Data may potentially be leveraged in the US, but consideration should also be given to potential differences in drug interactions due to different approved drugs in both countries.