

# Stent Thrombosis: The Implications of Broader DES Use

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# Broader Use of DES and its Implications

- Earlier discussions focused on the risk of DES thrombosis associated with CYPHER® and TAXUS™ *when used in accordance with their approved indications.*
- However, since their approval in 2003 and 2004 (respectively) they have been implanted in an expanding number of patient and lesion subsets for which they are **not** currently indicated.

# Broader Use of DES and its Implications

- Current data (i.e., post market studies) suggest that the majority of DES are implanted in patients and lesion subsets that are not indicated in their label
- This use-pattern can be typical of promising and rapidly adopted medical interventions
- Can be difficult to determine whether an observed problem is inherent to the **device** or whether it resulted from **inappropriate use**

# Broader Use of DES and its Implications

- FDA does not regulate the practice of medicine
- While physicians can decide to use a device “off-label” for a particular patient, manufacturers may not promote such use
- If a manufacturer wants a new indication added to the device’s label, they must provide FDA with data to support that expanded use

# Ongoing Trials

Several important studies with broad public health implications are currently underway:

- **SYNTAX** (Boston Scientific)
    - Randomized trial comparing PCI with TAXUS stents to CABG for patients with complex coronary disease (Left main and 3-vessel disease)
  - **FREEDOM** (NIH)
    - Randomized trial comparing Cypher/Taxus vs. CABG in diabetics
  - **HORIZONS AMI** (Cardiovascular Research Foundation)
    - Randomized trial comparing TAXUS to BMS and two different anticoagulation regimens in patients having a heart attack (STEMI).
- \* Additional randomized, controlled studies are needed to better understand the risks and benefits of broader DES use, as well as to support additional indications for use.**

# Broader Use of DES and its Implications

Specific *patient* subsets that may influence the risk of stent thrombosis:

- Diabetes (insulin and non-insulin dependent)
- Renal dysfunction
- Multi-vessel disease

# Broader Use of DES and its Implications

Specific *lesion* subsets that may influence the risk of stent thrombosis:

- Left Main disease
- Bypass Grafts
- Chronic Total Occlusions
- In-Stent Restenosis
- Bifurcation lesions
- Long Lesions and Overlapping DES
- Small Vessels (<2.5mm diameter)
- Acute Myocardial Infarction (thrombus containing)
- Multiple Stents per Vessel

# Broader Use of DES and its Implications

Risk of stent thrombosis may be modified in these subsets

- Time-points at which patients are most at risk may vary (consider early *and* late)
- Uncertainty regarding the optimal duration and effectiveness of dual antiplatelet therapy in these subsets
- Long term follow-up data is needed

# Broader Use of DES and its Implications

- FDA has asked both Boston Scientific and Cordis to perform specific analyses on these patient and lesion specific subsets
- A standardized definition for stent thrombosis, developed by the Academic Research Consortium, were used for their analyses and presentations at the request of FDA.

# Broader Use of DES and its Implications

- Data for these patient and lesions specific subsets are available from a variety of potential sources:
  - Randomized controlled trials
    - Pivotal studies
    - Label expansion studies
    - Other: cost-effectiveness, delivery of care, head-to-head stent comparison studies, etc.
  - Registry studies
    - Condition of approval studies ( $n \geq 2000$ )
    - Other single-arm, consecutive, “all-comer” registries
  - *Meta-analyses*

# Challenges in Data Interpretation

1. Frequent overlap between subsets and their definitions
  - Multiple vessel disease ↔ multiple stents ↔ overlapping stents
  - Diabetes ↔ renal dysfunction
2. Variable and/or evolving clinical practice patterns
  - Anti-platelet therapy, procedural techniques, adjunctive treatments, etc.
3. Lack of adequate control arms
  - Comparative risk/benefit difficult to assess
  - Accepted standard of care may not exist (e.g., bifurcations)
  - Generally limited data on bare metal stents in complex lesions
4. Data may not capture adherence to anti-platelet therapy

# Challenges in Data Interpretation (cont'd)

5. Studies may be under-powered for patient- and lesion-specific subset analyses
6. Meta-analyses may fail to capture patient-level data
7. Definition of stent thrombosis is variable
  - Need for standardization
8. Length of follow-up varies across studies
9. Few long term data are available

# Conclusions

- Data on the risk of stent thrombosis come from a variety of studies, each having its own strengths and weaknesses, and each contributing its own unique piece to the larger picture.
- We need to understand what these studies are telling us about the risk of stent thrombosis in the broader population of patients who receive DES.