The Dual Antiplatelet Therapy (DAPT) Trial:
An FDA Perspective

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FDA Assessment of Currently Approved Drug Eluting Stents (DES)

- Approximately 700,000 US patients a year are implanted with drug-eluting stents
  - Safe and effective when implanted in accordance with their indications for use
- Require the use of dual antiplatelet therapy: ASA + thienopyridine
- May be associated with a small but clinically important increased rate of stent thrombosis beyond 1 year
Public Health Implication

• Optimal duration of dual antiplatelet therapy to reduce the incidence of late stent thrombosis is currently unknown

• *Professional society recommendation* based on available data that dual antiplatelet therapy be administered for 12 months post-DES implantation
  – Consensus opinion based upon limited data rather than randomized clinical trials
Followed Think Tank Incubator Meeting:

- A need for a **large, pragmatic public health** trial exploring the benefit of extending thienopyridine treatment beyond one year (24 months vs. 12 months) in patients treated with DES needs to be done **expeditiously**

- FDA expects that the results of the study will change clinical practice and provide valuable new information in product labeling for DES.
The DAPT Study is a RCT with sufficient size and power to determine the appropriate duration for dual antiplatelet therapy to protect patients from stent thrombosis and/or major adverse cardiovascular and cerebrovascular events following the implantation of drug-eluting coronary stents.
DAPT Study

• Unique public-private collaboration
  – 8 manufacturers of stent and antiplatelet medications,
  – CDRH, CDER, and FDA Office of Critical Path Projects

• RCT with sufficient size and power to determine:
  – duration for dual antiplatelet therapy to protect patients from stent thrombosis and/or major adverse cardiovascular and cerebrovascular events
DAPT Study

Key Design Features

- Randomized trial 12 months vs 30 months of dual antiplatelet therapy
- Operator selection of stent and thienopyridine from FDA-approved stents and drugs (clopidogrel or prasugrel)
- 2 co-primary endpoints
  - Stent thrombosis
  - MACCE
- Powered safety endpoint
  - Major bleeding
50% of patients continue on Dual Antiplatelet Therapy

50% of patients receive aspirin + placebo

Total 33 month patient evaluation including additional 3-month follow-up

DES n = 15,245

BMS n = 5,400

1:1 Randomization at month 12

All patients on aspirin + open-label thienopyridine therapy for 12 months
DAPT Study Co-Primary Endpoints

• Two potential mechanisms of benefit of 30m of DAPT:
  – Device oriented (reduction in ST)
  – Patient oriented (disease progression/non-target lesion events)

• Significance on either endpoint will influence clinical practice
Poolability across stent and drug types

- DAPT Study not designed to compare stents or drugs
- Objective is a real world assessment of the impact of dual antiplatelet therapy duration beyond 12m
- Given known information about stents and drugs, the differences are expected to be small, particularly in the time frame beyond 12m
- If there is an important difference, DSMB will be empowered to detect it, and then share it with the FDA should a safety signal arise
Major Challenges for this Study

• Developing appropriate study design
• Defining a workable mechanism for industry cooperation so that the principal questions are answered
• Delineation of pathway by which each stent manufacturer will contribute patients to the trial
• Ensuring that stent specific results are not made public for the purpose of stent versus stent comparisons
Dual Antiplatelet Therapy (DAPT) Study Additional Information

www.clinicaltrials.gov – NCT00977938
www.daptstudy.org
www.hcri.harvard.edu