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**

March 2008 Statement of FDA Principles

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.

DAPT Study Objectives

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

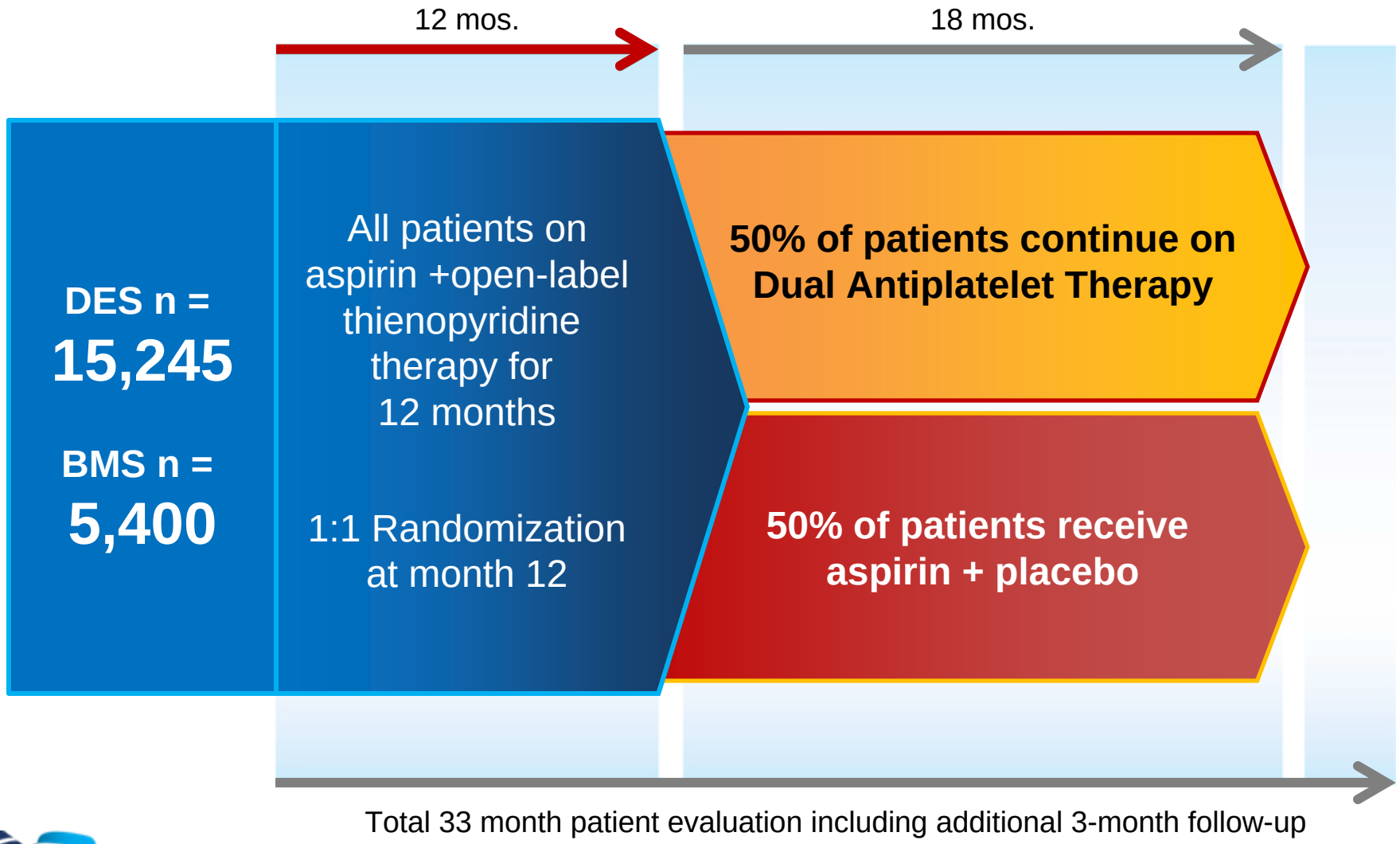
- Unique public-private collaboration
  - 8 manufacturers of stent and antiplatelet medications,
  - CDRH, CDER, and FDA Office of Critical Path Projects
- RCT with sufficient size and power to determine:
  - duration for dual antiplatelet therapy to protect patients from stent thrombosis and/or major 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

Dual Antiplatelet Therapy (DAPT) Study



DAPT STUDY

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 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