Utilizing the RAPID Core Data Set: Cook Medical Perspective

MDEpiNet
RAPID Working Group Meeting
April 13, 2016
Aaron Lottes, PhD
Cook Medical

Overview

- *Utilizing the RAPID Core Data Set*

  Case Study: Zilver® PTX® Drug-Eluting Peripheral Stent

  - *Near-label use*
  - *Potential for expanded indication*
  - *Post-approval safety and performance monitoring*
- *Challenges to full utilization*
- *RAPID: opportunities and impact*

Case Study for RAPID Core Data Set (CDS)

Zilver PTX Stent

Indicated for improving luminal diameter for treatment of *de novo* or restenotic symptomatic lesions in native vascular disease of the above-the-knee femoropoliteal arteries

Pre-market clinical program exceeded 1000 patients and 2000 Zilver PTX stents globally

- Randomized study (RCT)
  - 479 patients
  - 55 sites in US, Japan, and Germany
  - 5-year follow-up demonstrating superior results to both PTA and BMS
- Single-arm study (SAS) also conducted
  - 787 patients
  - 30 sites in Europe, Canada, and Korea
  - 2-year follow-up with comparable results to RCT

Extensive global pre-market clinical data collected

Utilization of RAPID CDS

Near-Label Use and Expanded Indication

- Industry has responsibility to understand device performance in near-label use
- Traditional PAS costly:
  - Little value with strict indication
  - Considerable overhead under IDE for near-label use
- Can RAPID CDS be used to collect data on actual post-market usage patterns and inform:
  - The need for pursuing additional indications
  - Development of future products to fill unmet needs

Near-Label Use and Expanded Indication

Zilver PTX Stent

- In the US, indication is limited to treatment of "native vessel"
  - Due to excellent performance and limited alternative treatment options, some physicians use for treatment of in-stent restenosis

CLINICAL RESEARCH

Treatment of Femoropopliteal In-Stent Restenosis With Paclitaxel-Eluting Stents

Zeller, et al.
JACC Card Int, 2013

Yokoi, et al.
VIVA, 2015

	RCT	SAS	Japan PMS
% of patients with in-stent restenosis enrolled in each study	0%	15%	19%

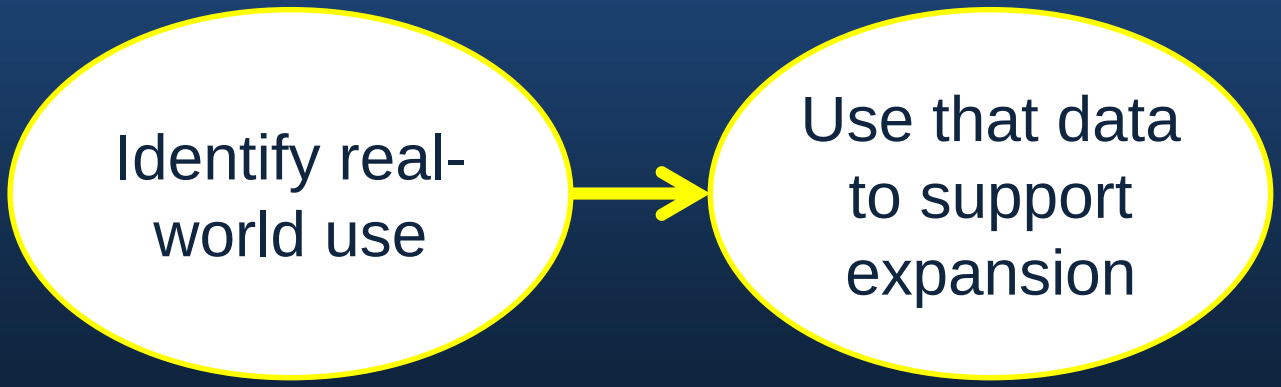
Is ISR treatment safe and effective?

Long time and high cost to run traditional clinical study in small population

Near-Label Use and Expanded Indication

Zilver PTX Stent

- How can the RAPID CDS assist near-label use?
  - Identify actual usage rate for treating in-stent restenosis and other near-label uses in clinical practice
- How can the RAPID CDS assist expanded indication?
  - Provide a pathway for collecting clinical data to support an expanded indication



Near-Label Use and Expanded Indication

Points/Questions to Consider

- Is there adequate incentive for industry to commit resources to traditional clinical trials for expanded indications?
  - ➢ Will use of RAPID CDS be more efficient?
- Will regulators accept RAPID CDS (i.e., EHR data source and limited data elements) as adequate clinical information to support approval for expanded indication?

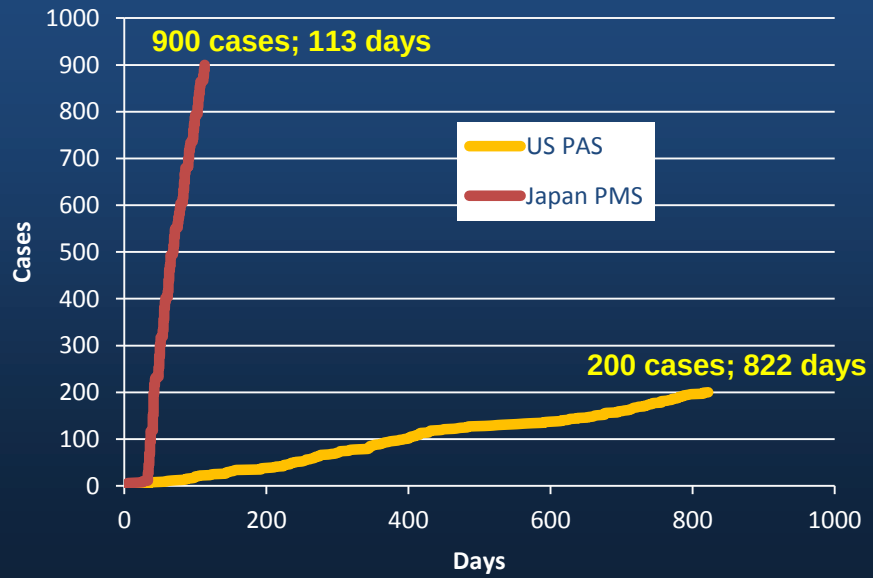
STAKEHOLDER	BENEFITS
Patients & Physicians	Knowledge of near-label outcomes, more treatment options
Regulators	Safety and performance data for near-label use
Payers	Evidence to support treatment options
Manufacturers	Labeling expansion with ability to promote additional use, reduced compliance risk

Using RAPID CDS could potentially benefit *ALL* stakeholders by reducing time to market and cost of healthcare

Utilization of RAPID CDS

Post-approval Safety & Performance Monitoring

- In addition to extensive pre-market data for the Zilver PTX stent, a PAS in US and a PMS in Japan were also required
  - Japan PMS – 900 all-comer patients encompassing near-label use enrolled in 113 days
  - US PAS – 200 on-label patients enrolled in 822 days
    - 1-year follow-up on 200 patients available 4 years after approval
    - << 0.5% of patients treated with device in the US



How can the US process be more efficient and reflective of actual device usage?

Is this a role for RAPID?

Utilization of RAPID CDS

Post-approval Safety & Performance Monitoring

Possible ways RAPID can help:

- Shift some of pre-market burden into post-market space
  - Decreased timeline for physician and patient access to new and improved technologies
- Eventual replacement of traditional post-approval studies
  - Data on more patients, broader (i.e., near-label) population, more quickly
  - More accurate evaluation of post-market performance
- Earlier notification/availability of emerging safety signals

Challenges to Full Utilization

How can RAPID's chance of success be maximized?

- Regulators agree that RAPID core data set can provide adequate clinical evidence to expand indication for use
- RAPID data replaces some or all traditional post-approval study requirements
- Manufacturers have access to data beyond core data set as needed (e.g., imaging, lab results) to accurately assess device safety, performance, and appropriate use, and fulfill legal responsibility to evaluate events potentially subject to regulatory reporting
  - Informed consenting issues?

Opportunities and Impact

Can RAPID core data set provide ***greater benefit*** at a ***lower cost*** to all stakeholders?