Streamlining HABP/VABP Trials Project

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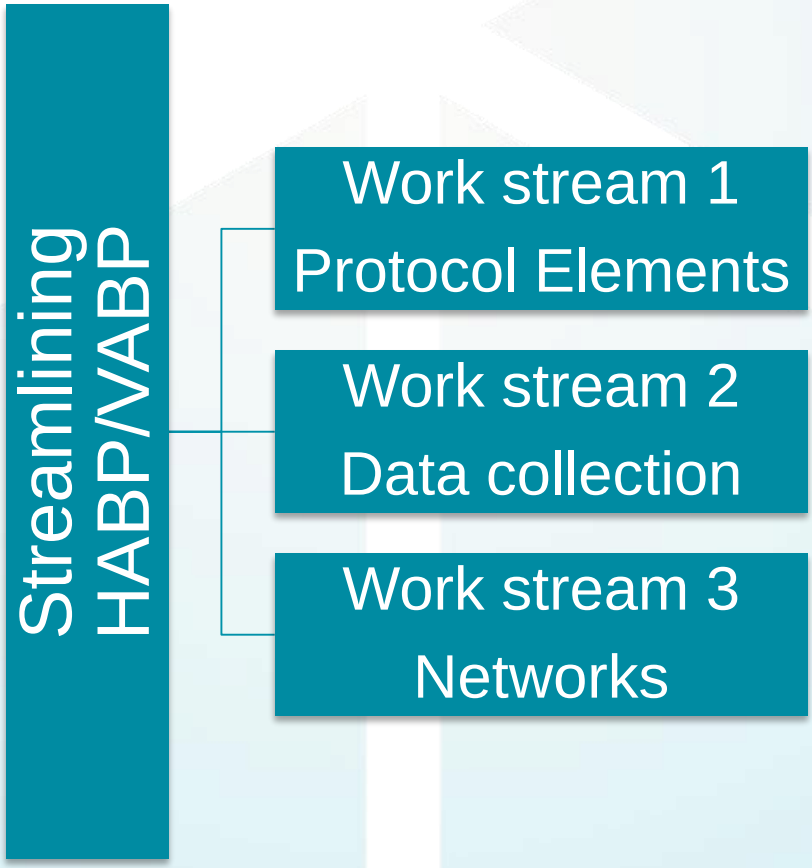
Streamlining HABP/VABP Trials



Workstream 1: Protocol Elements

- Objectives

  Identify barriers and seek solutions for the successful conduct of HABP/VABP studies

- Deliverables:

  Recommendations on alternate study design elements to overcome barriers in HABP/VABP studies

Protocol Elements: Activities

18 APR 2013

- Understanding issues in antibacterial drug development
- Webinar in advance of Workshop

22-23 APR 2013

- Applying Quality by Design (QbD) principles to HABP/VABP protocols

29 AUG 2013

- Developing streamlined elements for HABP/VABP studies
- Webinar

Current

- Recommendations and Publication
- Finalized Q2

CTTI

Issues and Barriers Identified

- Obtaining informed consent
- Inclusion criteria
  - Prior Antibacterial Therapy (PAT)
  - Concern that inclusion criteria may be too restrictive regarding underlying disease and co-morbidities
- Combining HABP and VABP patients
- Need for diagnostics and biomarkers
- Choice of active comparator
- Use of rescue/other non-study antimicrobial drug therapy
- Primary Endpoint Rationale for All-Cause Mortality vs Clinical Response

Public Discussion/Data Review led to Change

See revised FDA HABP/VABP Guidance May 2014:

- Single HABP/VABP trial with supportive evidence
- Allow 24 hrs PAT; sensitivity analysis
- Use of Gram stain as part of enrollment criteria and ITT as primary analysis population; sensitivity analysis in the microbiological ITT
- Approved active comparators not labeled for HABP/VABP
- Risk difference acceptable if control mortality rates are low; use of odds ratio from primary analysis is not required

Direction of Protocol Elements Recommendations

- Informed Consent
  - More training for staff obtaining informed consent
  - Approach patient/ legally authorized representative (LAR) earlier, Research Advanced Directives (RAD)
- Use of Centralized IRB
- Expand Inclusion Criteria: include patients who may have been traditionally excluded from HABP/VABP trials
- Enrich: Rapid Diagnostics and Severity of Illness Score
- Primary efficacy endpoint using All Cause Mortality
  - Explore clinical response endpoint

Workstream 2: Data Collection

- Objectives

  Simplify and reduce the amount of (safety) data collected in HABP/VABP studies

- Deliverables

  Recommendations on critical data to be collected to simplify data collection

Data Collection

12 NOV 2013

- Optimizing operational efficiencies for data collection in HABP/VABP trials
  - Challenges in data collection for HABP/VABP trials
  - Regulatory requirements for AE data collection in registration trials
  - Strategies to simplify data collection using a QbD approach

5 SEP 2014

- F2F team meeting
- Draft manuscript review

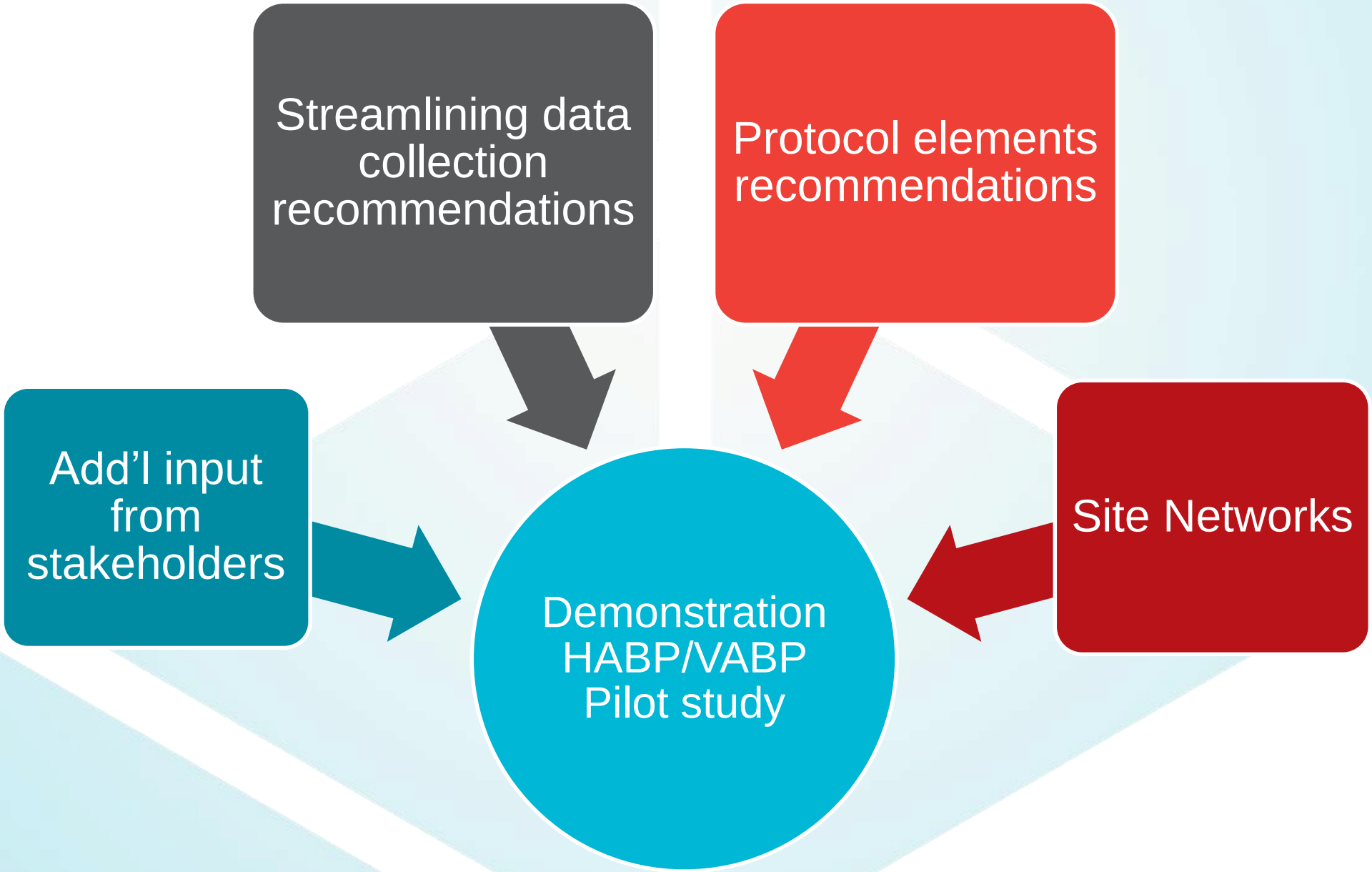
Current

- Recommendations and Publication
- Q2

CTTI

Direction of Data Collection Recommendations

- Regulatory framework already exists to support streamlining
  - Report SAEs consistent with FDA/EMA regulations
  - Discuss proposed streamlined approach with regulators
- See CTTI Recommendations:
  - http://www.ctti-clinicaltrials.org/briefing-room/official-recommendations#IND_Safety
- Data collection should be pre-specified in protocol
- Consider less frequent/abbreviated data collection:
  - Vital signs, arterial blood gas, electrolytes
  - Non-serious AEs not associated with drug discontinuation
  - Concomitant medications
    - Sedatives/analgesics e.g. for patients on sedation drips with mechanical ventilation where doses are frequently titrated and changed....consider capturing this info as “days on/off”


Streamlining data collection recommendations
Protocol elements recommendations
Add'l input from stakeholders
Site Networks
Demonstration HABP/VABP Pilot study

Thank you.

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