NTM Research Consortium Meeting Agenda
Friday, November 4th, 2016
Newberg OR

Attendees: see attached *list*

NTMRC Site Updates

OHSU (Kevin Winthrop/Emily Henkle/Dave Lewinsohn)

Oregon NTM Cohort

- Results presented for mortality/clinical outcomes; papers in submission

NW NTM Biobank

- 350 enrolled, funded through June 2017
    - 300 pulmonary NTM
    - Rest extrapulmonary, pulmonary controls, healthy controls
- Aims to establish cohort, pilot immunology (MAITs/cytokine profiles)
- Clinical data, blood, QOL-B/NTM module, GAD7/PHQ-8
- Utilizes REDCap database

PCORI Non-CF Bronchiectasis Comparative Effectiveness and Safety

- Non-CF bronchiectasis cohort (full Medicare, 2006-2014)
- Safety and effectiveness of inhaled corticosteroids, macrolides, inhaled antibiotics
- Primary outcomes hospitalized pneumonia, NTM infection
- Ongoing, beginning descriptive analysis

Animal model

- Successful infection of 3 macaques

Pilot immunology

- Focus on mucosal-associated invariant T (MAIT) cells
- Peripheral MAIT cells missing in those with TB
- Pilot results: MAITs reduced in males and individuals with COPD

National Jewish (Chuck Daley)

Adult day unit

- Now incorporating QOL-B/NTM module and AE monitoring via Redcap electronic entry tool
- Looking at gene expression in sputum, capture blood at baseline/6m to look for biomarkers of injury/assoc. with AEs optic neuritis
- 500 patients with specimens/NTM with electronic medical record data

Colorado Cystic Fibrosis Research and Development Program

- Three research cores
    - NTM Culture, Biorepository, and Coordinating Core
    - Clinical Research Core
    - Molecular Core
- Pilot innovation funding: free whole genome sequencing on all isolates from CF patients
    - 393 isolates collected
    - Goal to identify patient-to-patient transmission
    - Working on linking samples to CF registry (complicated)
- PREDICT: Pre-treatment natural history protocol, quarterly visits after isolating NTM
- PATIENCE: Optimal treatment
- Planning to expand PREDICT/PATIENCE to other sites

Biorepository

- Enrolling patients in genetic biobank
- Save samples of any sample collected for clinical use (blood, urine, tissue, sputum, etc.)

NIH (Ken Olivier)

NHLBI clinic

- Most patients enrolled on a protocol- types of data collected are standard, though the frequency is not (sicker patients have more follow up)
- Most relevant protocols
    - Idiopathic bronchiectasis (stratified by sex, NTM)
    - CF registry started in 2010
        - Increasing NTM capture

NIAID Epi unit (*Becky Prevots*)

- Access to large national datasets
    - 5% Medicare sample, AHRQ utilization,
    - CF Foundation Registry
    - Hospital, HMO databases
    - Linkage to other Federal databases: NOAA, FAA, USGS
- Recent study
    - Hawaii- epi of NTM in state with highest rate of NTM.
    - Kaiser EHR data
    - Explore host/environmental factors

UT (David Griffith)

Clinical cohort

- Excel database with 1000 patients going back to 1970s.
- Biorepository: Save one isolate per patient (all patients)

Animal models

- Marmosets, pig (CF)

Invited Presentations

Bronchiectasis and NTM Research Registry (Tim Aksamit)

- Publication describing baseline data accepted at Chest
- Moving forward:
    - PPRN
    - Linkage to CMS, electronic health records

Ontario surveillance (Ted Marras)

- Laboratory based studies-
- Recent studies
    - Obstructive lung disease and NTM risk
    - Population-based, matched cohort study of survival after pulmonary NTM (by species, case or isolate)

Clinical Trials- lessons from TB experience (Chuck Daley)

- Timeline is long for new drugs (keep working on these)
- In interim, work on improving regimens
- Adaptive design allows for efficient study
- Think about pragmatic trials

NTM Module development (Alexandra Quittner)

- NTM Module developed according to FDA guidance on PROs (2009)
- Preliminary psychometric analyses complete
- Next steps: completing final psychometric analysis, determining MID

NTM Patient-centered research priorities from November 2015 meeting (Emily Henkle)

- Workshop report published: Ann Am Thorac Soc. 2016 Sep;13(9):S379-84.
- Summarized 13 patient-centered priorities
    - Working on person-to-person transmission, NTM symptom module, anxiety/depression impacts, correlation of HRQoL and clinical outcomes
    - Several still need to be addressed
        - Role of GERD
        - Validate molecular diagnostics
        - Comparative effectiveness of exercises/lung clearance devices
        - Understand who needs/benefits from therapy
        - New antibiotics, shorter courses of therapy duration
        - Disease severity index
        - Biomarkers

Discussion: Next steps for consortium

- No approved treatment for NTM
- Need for large, pragmatic trials balancing concerns for capacity
    - Pursue adaptive design, comparing regimens
- Need to organize sites- cultures, follow-up
    - Identify quality labs for diagnosis/culture
    - Agree on initial evalution/standard of care at "centers of excellence"? Work with NTMir?
    - Then expand to additional sites/physicians
- Common measures (include above standard of care, plus additional relevant to specific research questions)
- Explore common data models
    - PCORnet, Mini-sentinal, HMORN, etc
- Need for biomarkers
- NIH grants feasible, need to be hypothesis driven
- Models for consortium formation/growth
    - PCD rare disease network
    - CF Clinical Centers networks/Registry