NEW DISEASE SPECIFIC THERAPIES AND RESEARCH IN TAKAYASU’S ARTERITIS

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CLINICAL TRIALS IN TAKAYASU’S

Challenges:

• Rare disease
• Difficult to assess disease activity
• Differences in definition worldwide

However,

• Multi-center collaboration (VCRC, others)
• Exciting time with many ongoing trials
DIAGNOSIS AND DISEASE ACTIVITY IN TAKAYASU’S ARTERITIS
DEVELOPMENT OF NEW CRITERIA

American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) Diagnostic and Classification Criteria for Primary Systemic Vasculitis (DCVAS)

Aim #1: Update Classification Criteria
  • Research purposes
  • Last Classification Criteria done in 1990’s

Aim #2: Develop Diagnostic Criteria
  • Assist with diagnosis of disease in clinical setting
  • First ever!

Estimated to enroll 260 Takayasu’s patients (and controls)

Estimated completion in December 2018
CONTRAST ENHANCED CAROTID ULTRASOUND

Ultrasound
• Noninvasive, less expensive
• Requires experience

Aim #1: Determine if contrast enhanced carotid ultrasound is an indicator of disease activity
Aim #2: Determine if there is arterial thickening compared to age/sex matched controls

Estimated enrollment: 15 Takayasu’s subjects, 5 controls
Enrollment completed but results pending

Cleveland Clinic
POSITRON EMISSION TOMOGRAPHY (PET)/CT FOR ASSESSING DISEASE ACTIVITY

Problem: Current modalities for assessing for active disease are limited

2 studies:

#1: Purpose: Compare PET/CT to clinical scoring in combination with laboratory values *(completed)*
   • Done through Instituto Nacional de Cardiologia, Mexico

#2: Purpose: Compare PET/CT to MR angiography *(recruiting)*
   • Done through Vasculitis Clinical Research Consortium
   • Active disease within 2 weeks of enrollment
   • Not pregnant or lactating
TREATMENT STUDIES

I. DMARDS/CYTOTOXIC AGENTS

II. BIOLOGICS
TREATMENT: PRE-BIOLOGIC ERA

Frequent relapses with Glucocorticoids alone

Cytotoxic agents (aka DMARDs)

• Cyclophosphamide, Methotrexate, azathioprine, mycophenolate (+ GCS)
• NIH cohort: 1/3 able to sustain remission
• CCF cohort: 63% relapses during therapy
TNF INHIBITORS COMPARED TO DMARDS

Specific TNF inhibitors
- Infliximab
- Adalimumab
- Etanercept

A: Percentage of patients without new vasculitis lesions over time (years since diagnosis)
B: Percentage of patients at certain disease activity levels

TUMOR NECROSIS FACTOR INHIBITOR (INFLIXIMAB)

Seoul National University Hospital, Republic of Korea
Phase 2 study

• Single arm (i.e. all will get Infliximab 5mg/kg)
• Planned enrollment of 11 subjects
• Primary outcome: Remission induction at 30 weeks

Recruiting with planned completion by August 2017
We can target some of these:

- **Ustekinumab** → targets IL-12
- **Tocilizumab** → targets IL-6
RANDOMIZED, DOUBLE-BLIND PHASE 3 STUDY OF TOCILIZUMAB IN TAKAYASU’S

- Encouraging results from small case series
- Blocks interleukin-6 (inflammatory cytokine)
- Refractory patients
- Randomized
  - 18 in tocilizumab group (+ steroids)
  - 18 patients with steroids alone

Nakaoka Y et al. ACR 2016 abstract # 976
RANDOMIZED, DOUBLE BLIND STUDY OF ABATACEPT FOR TAKAYASU’S

- Newly diagnosed or relapsing
- 34 patients started abatacept + steroids
- 26 randomized at 12 weeks
  - 11 in abatacept group
  - 15 in placebo group
USTEKINUMAB PILOT STUDY

3 refractory TAK patients

Improvements

• ESR
• CRP
• VAS

No demonstration of improvement

• By imaging