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The Vasculitis Foundation supports and empowers
our community through education, awareness,
and research.

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

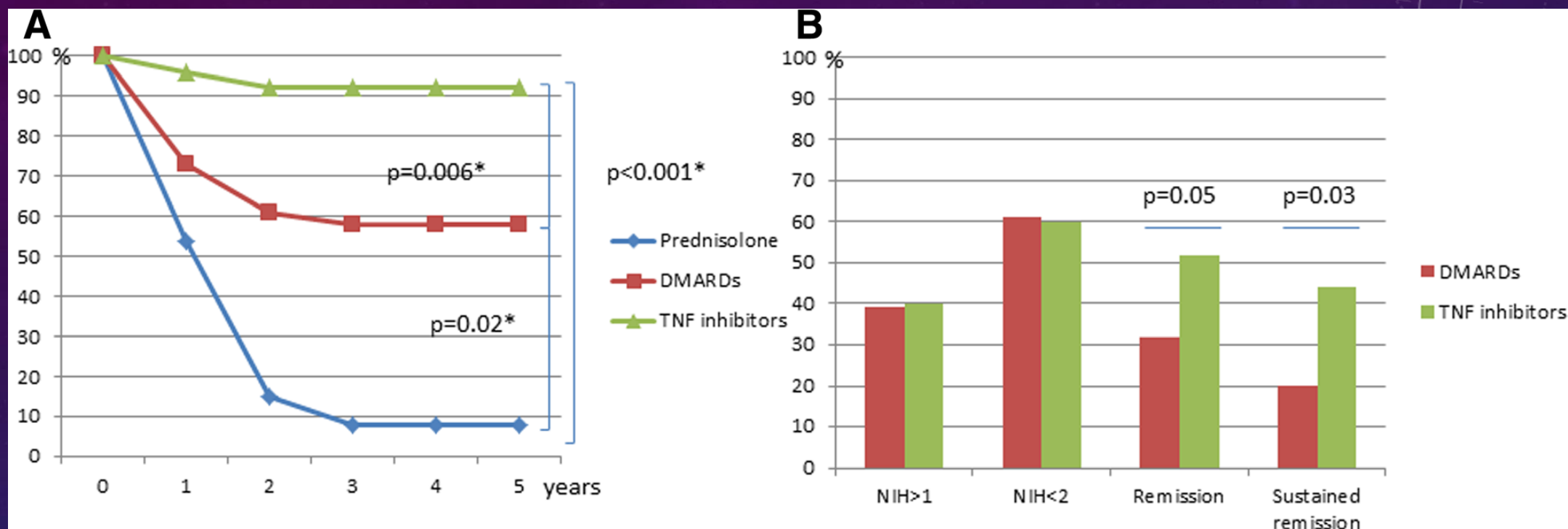
TREATMENT: PRE-BIOLOGIC ERA

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)

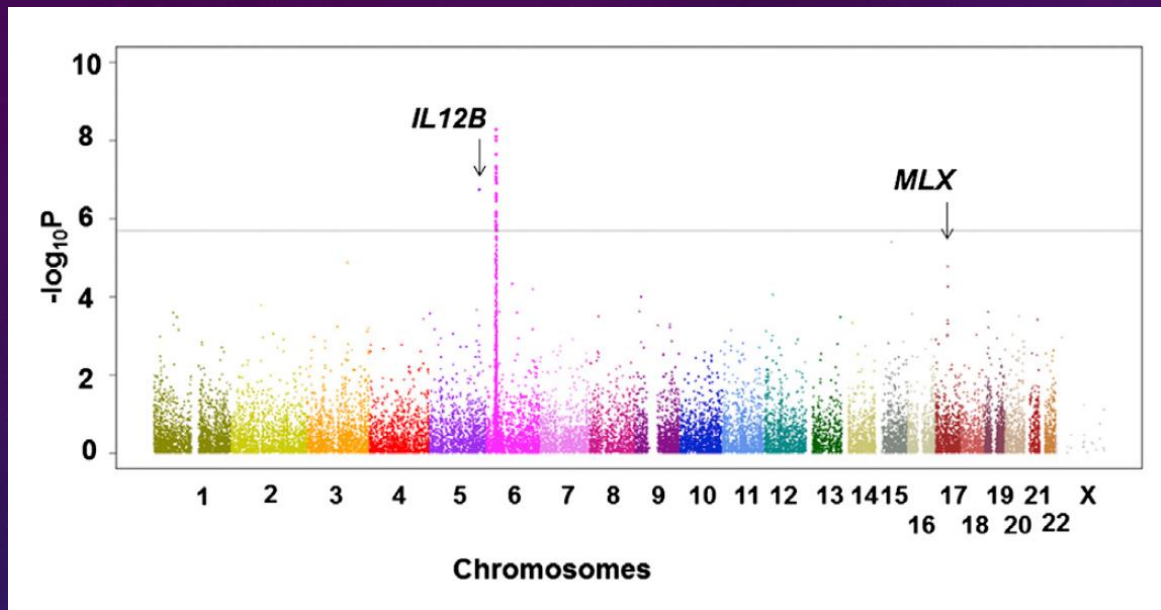
Seoul National University Hospital, Republic of Korea

Phase 2 study

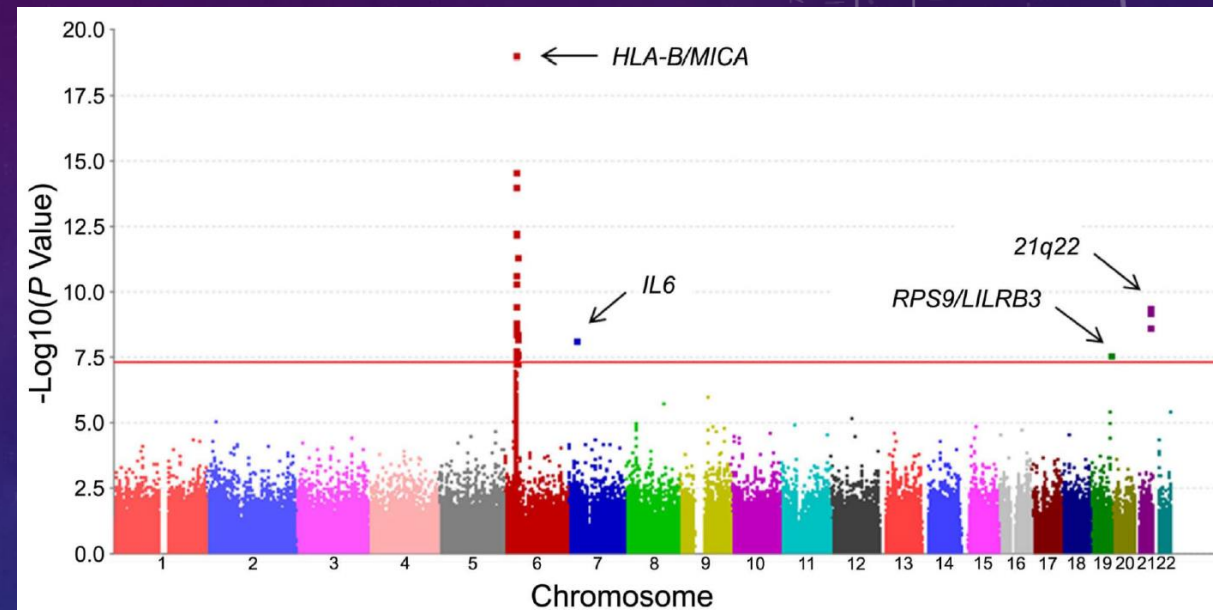
- Single arm (i.e. all will get Infliximab 5mg/kg)
- Planned enrollment of 11 subjects
- Primary outcome: Remission induction at 30 weeks

Recruiting with planned completion by August 2017

GENETIC RESEARCH SUPPORTING TREATMENT OPTIONS



Terao C et al. *Am J Hum Genet.* 2013;93:289-97.



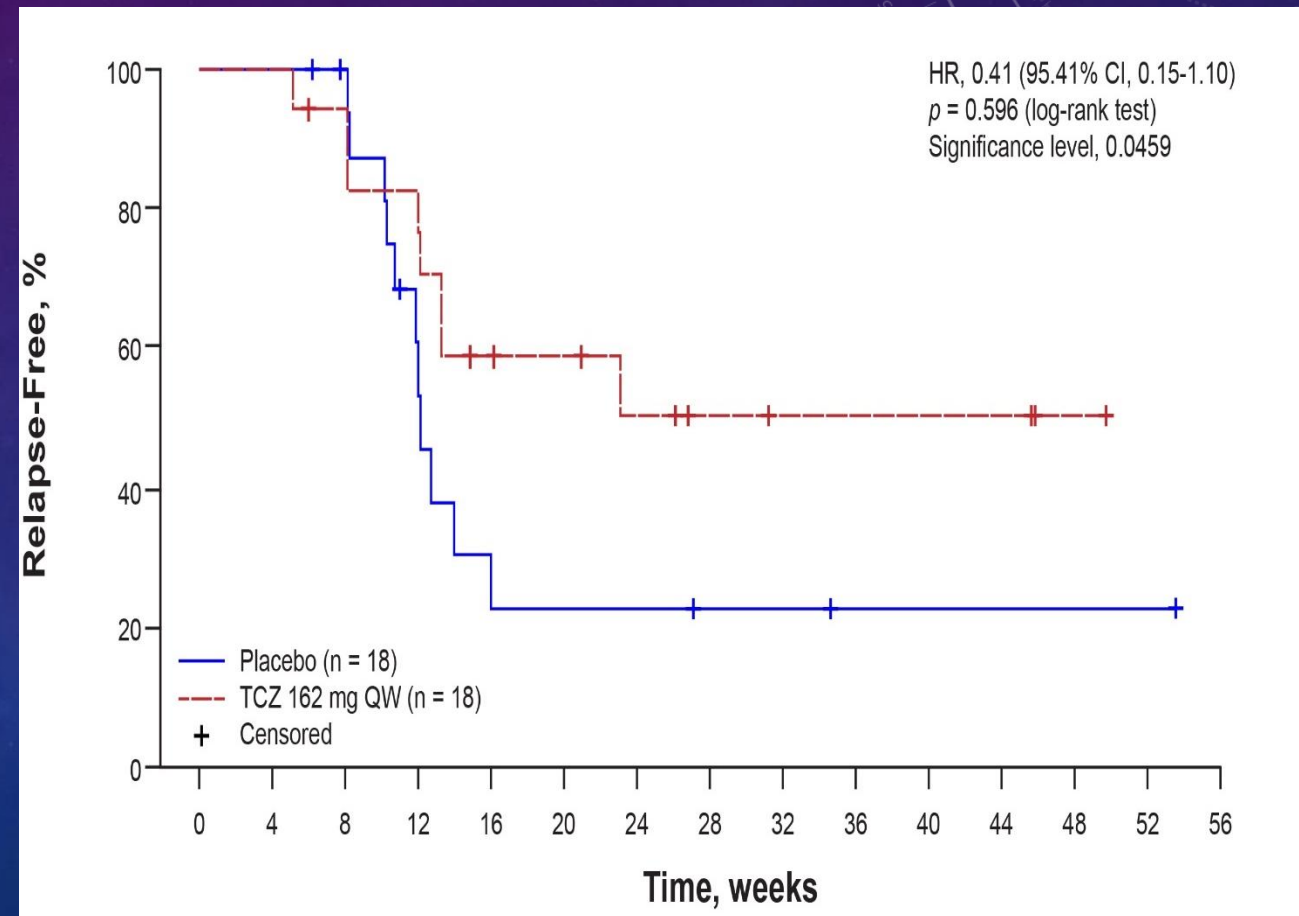
Sawalha A et al. *Arthritis Rheumatol* 2015;67(5):1361-8.

We can target some of these:

- Ustekinumab → targets IL-12
- Tocilizumab → targets IL-6

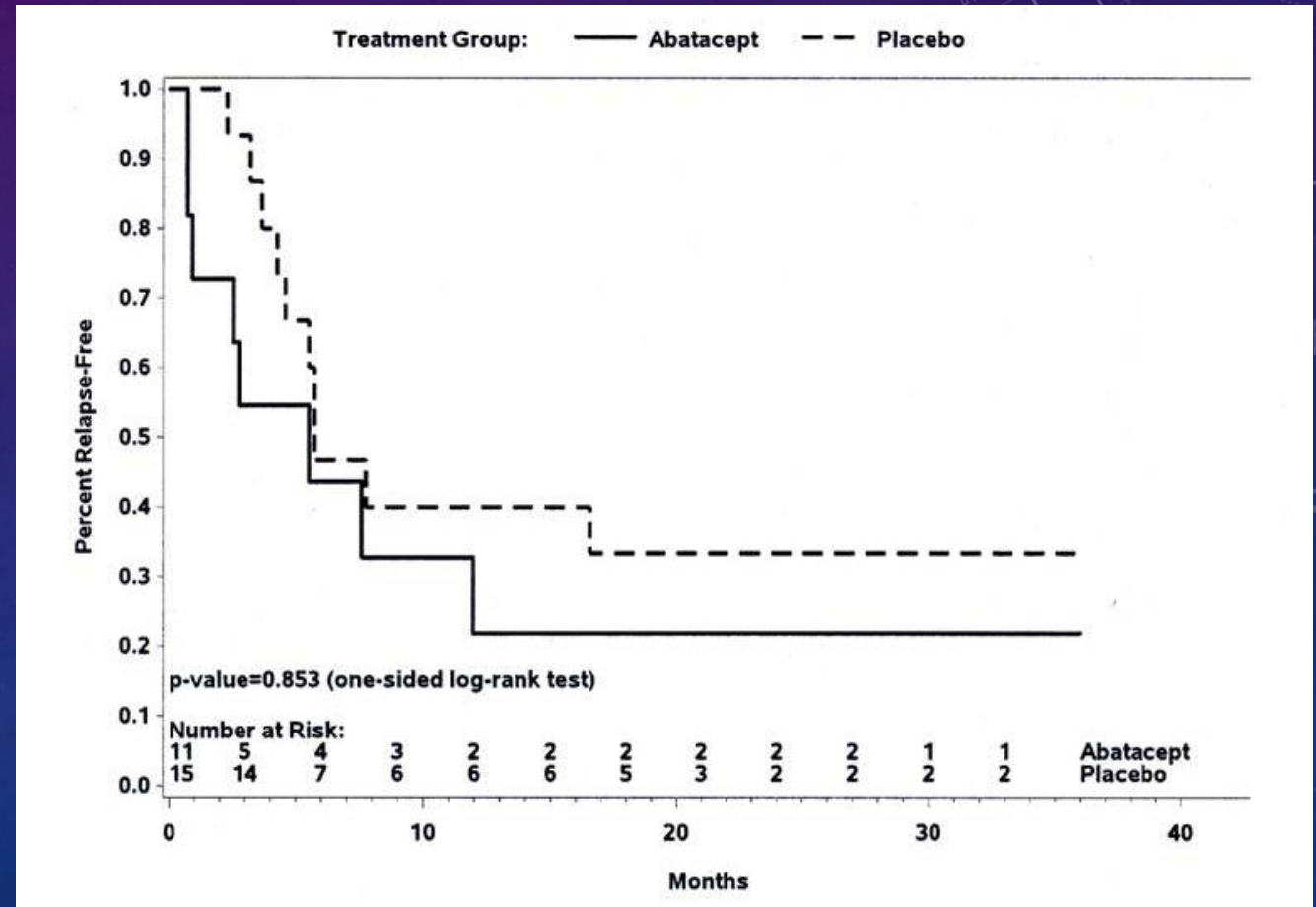
RANDOMIZED, DOUBLE-BLIND PHASE 3 STUDY OF TOCILIZUMAB IN TAKAYASU'S

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



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

