Bioinformatics platform to study the genetics of biologic DMARD non-responders: design and protocol of the RA Non-responders to Treatment (RANT) study

Gregory McDermott[1,2], Mary Jeffway[1], Thany Seyok[1], Harrison Zhang[1], Megan Macvicar[1], Kumar Dahal[1], Dana Weisenfeld[1], Margaret Vella[2], Tracy Johansson[3], Gabriela Schmajuk[4], Kaleb Michaud[5], Cassandra Perry[2], Susanne Churchill[2], Katherine P Liao[1,2]

[1]Division of Rheumatology, Inflammation, and Immunity, Brigham and Women's Hospital, Boston, MA; [2]Harvard Medical School, Boston, MA; [3]American College of Rheumatology, Atlanta, GA; [4]Division of Rheumatology, University of California, San Francisco, San Francisco, CA; [5]Division of Rheumatology, University of Nebraska, Omaha, NE

Background/Aim

- RA treatment armamentarium has expanded in the last 30 years
  - –Some patients still inadequately respond to multiple lines of treatment
  - –Research of "difficult to treat" (D2T) and "extreme treatment nonresponders" limited by small numbers
  - –"Crowdsourced" studies of extreme phenotypes used in oncology
- **Aim**: Adapt a "crowdsourced" bioinformatics research platform to recruit RA patients with inadequate response to multiple biologic and targeted synthetic DMARDs (b/tsDMARDs)

Methods

- "Crowdsourced" cohort study (target n=200)
- Uses bioinformatics platform to investigate genetic and clinical predictors of b/tsDMARD nonresponders
- **Eligibility Criteria**
  - –RA patients with inadequate response to 2+ b/tsDMARDs (including 1+ TNFi)
- **Decentralized Study Process (Figure 1)**
  - –Uses self-directed online consent
    - •Allows access to electronic health records through third-party vendor
  - –RA treatment and disease status questionnaries
  - –Study staff confirms eligibility
  - –Sample kit sent/returned by mail for whole genome sequencing

Funding

NIH R21 AR078339
Harold and DuVal Bowen Fund
NIAMS National Institute of Arthritis and Musculoskeletal and Skin Diseases
Rheumatology Research Foundation Award Recipient

Results

Figure 1: Study design of RANT

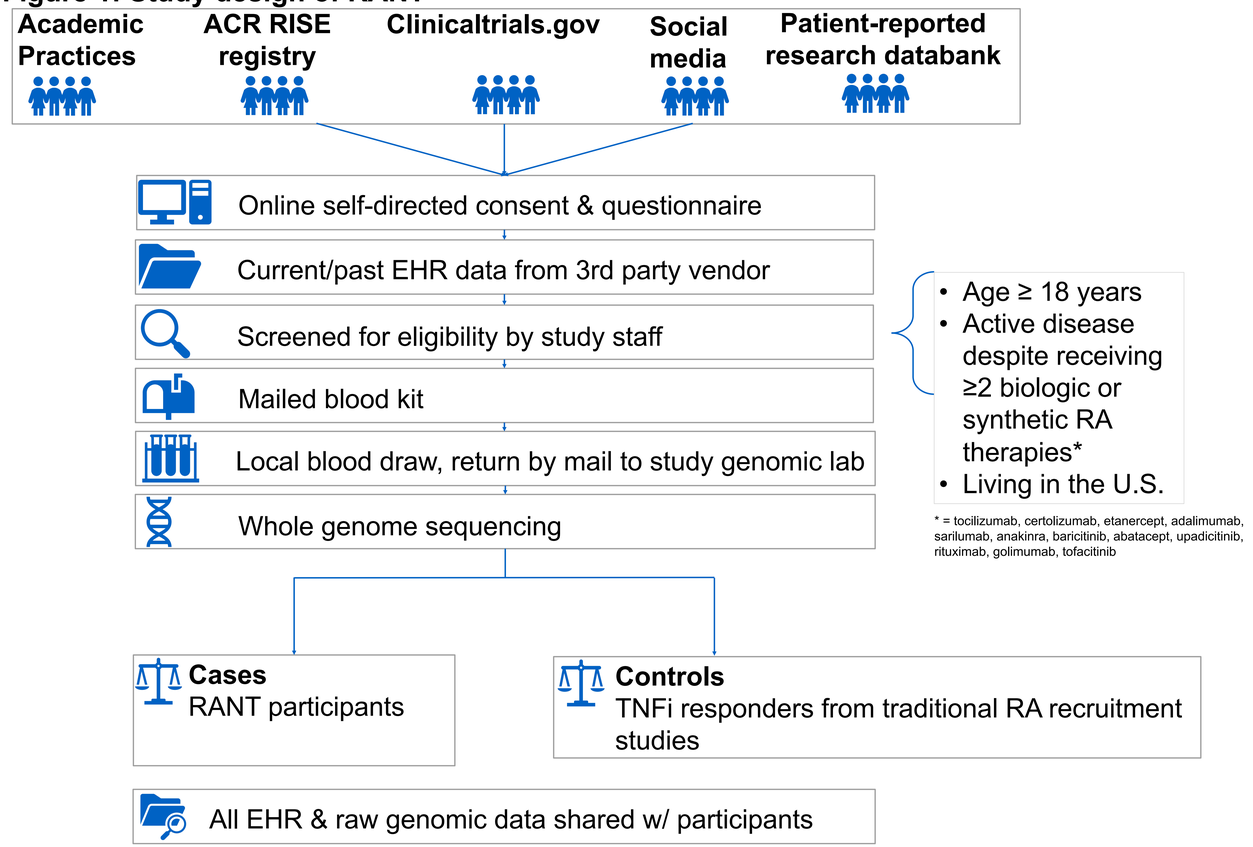

Table 1: Characteristics of RANT study participants and recruitment methods (n=162)

Characteristic	
Age at enrollment (years, mean, SD)	60.9 (12.1)
RA duration (years, mean, SD)	21.5 (10.9)
Female (n, %)	147 (90.7%)
Number of prior b/tsDMARDs (mean, SD)	5.2 (2.2)
Recruitment Method (n, %)	
FORWARD (Patient-reported research databank)	98 (60.5%)
Direct in-person clinic recruitment at academic practices	46 (28.4%)
Internet search/study website	9 (5.5%)
ACR RISE	7 (4.3%)
Clinicaltrials.gov	2 (1.2%)

Conclusion

"Crowdsourced" recruitment methods with "decentralized" online consent/enrollment are a feasible alternative design for certain rheumatology studies

Results Summary

- ***Baseline characteristics for the first 162 patients (Table 1)***
  - Majority female (91%); mean age 61y
  - Mean number of b/tsDMARDs prescribed was 5.2 (SD 2.2)
  - Most effective methods for recruitment targeting patients pre-screened for multiple b/tsDMARD prescriptions from: 1) established RA patient-reported research database; 2) In person clinic recruitment

Future Directions

- **Genetic Analysis/Comparison with RA Treatment Responders**
  - Compare demographics, RA clinical factors, and genetics in "extreme treatment nonresponders" vs. treatment responders from established cohorts

Additional Study Information

PEOPLE-POWERED MEDICINE

SCAN ME