BRIGHAM AND WOMEN'S HOSPITAL RHEUMATOID ARTHRITIS SEQUENTIAL STUDY (BRASS)

A collaboration of scientific technology and clinical expertise

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For further information regarding BRASS, please visit our website at www.BRASSSTUDY.org

Project Goals

The BRASS registry began recruitment in March 2003 establishing a prospective observational cohort of 1,000 rheumatoid arthritis patients in order to:

• Determine and validate biomarkers that predict drug response and toxicity in rheumatoid arthritis.

• Determine and validate biomarkers that predict disease activity and prognosis in rheumatoid arthritis.

• Evaluate the natural history of treated rheumatoid arthritis by measuring clinical, functional and economic outcomes

Clinical Data

	Questionnaire Time Points (months)											
PATIENT DOMAINS	Baseline	6	12	18	24	30	36	42	48	54	60	66	72
Demographics													
Age	✔		✔		✔		✔		✔		✔		✔
Marital status	✔		✔		✔								
Education	✔												
# of children	✔		✔										
# of sibs	✔												
Patient birth order/birth weight													
Family history (RA, co-morbid)		✔					✔						✔
Ethnicity	✔												
Race	✔												
Psychosocial social support	✔		✔										
Smoking	✔		✔		✔		✔		✔		✔		✔
Beverages (alcohol, caffeine)	✔		✔		✔		✔		✔		✔		✔
Alcohol only													
General Health													
Symptoms		✔	✔		✔		✔		✔		✔		✔
List of co-morbidities	✔		✔	✔	✔		✔		✔		✔		✔
New conditions		✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
Surgeries	✔		✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
MRC Dyspnoea Scale	✔		✔										
Cognitive function	✔		✔										
Menopause		✔					✔						
Pregnancy		✔	✔		✔		✔		✔				
Oral Contraceptive Use		✔	✔		✔		✔		✔				
Menstruation history		✔											
Use of antibiotics (past 6 mos)		✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
Vaccinations		✔											
Daycare/Teacher/Healthcare		✔											
Teeth and Gums													
Morning Stiffness	✔		✔		✔		✔		✔		✔		✔
Current Meds													
Arthritis	✔		✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
Pain	✔		✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
Corticosteroid	✔		✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
CAM			✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
Vitamins			✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
Non-arthritis meds (heart, etc.)			✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
Alternative Providers			✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
Exercise			✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
Past Meds													
All Arthritis (past 6 months)			✔		✔		✔		✔		✔		✔
Methotrexate (past 6 months)			✔		✔		✔		✔		✔		✔
Miscellaneous													
MDHAQ	✔		✔	✔	✔		✔		✔		✔		✔
SF-12			✔		✔		✔		✔		✔		✔
MHI-5	✔		✔		✔		✔		✔		✔		✔
PHQ-9													
EuroQol			✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
RADAI & Joint Man	✔		✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
Arthritis Self-Efficacy	✔		✔		✔		✔		✔		✔		✔
Flare Question	✔		✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔

PHYSICIAN DOMAINS	Baseline	Annual
Inclusion Criteria	✔	
Health & Symptoms		
Morning Stiffness	✔	✔
VAS	✔	✔
Infection/Opportunistic Infections	✔	✔
Extra-Articular Manifestations	✔	✔
Co-morbidities/drug toxicities	✔	✔
28 Joint count	✔	✔
Medication Changes		
Start	✔	✔
Stop/reason	✔	✔
Change/reason	✔	✔

Blood Collection/X-Ray Schedule	Baseline	12	24	36	48	60	72
DNA	✔	✔					
Serum	✔	✔	✔	✔	✔	✔	✔
RNA	✔	✔		✔	✔	✔	✔
Hand Radiographs	✔		✔		✔		

Cohort Statistics

N=1092 Variable	Values
Female, N (%)	897 (82)
Age, mean (SD)	56.1 (14.05)
Disease Duration, mean (SD)	13.7 (12.32)
MDHAQ, median	0.6 (0.53)
DAS28-CRP, mean (SD)	3.97 (1.58)
RF positive, N (%)	568 (63)
CCP positive, N (%)	670 (61)
Modified RADAI	3.52 (2.27)
Total Swollen Joints (0-28)	7.63 (7.34)
Total Painful Joints (0-28)	8.55 (8.04)
Physician Global Assessment (0-10)	3.39 (2.15)
Patient Global Assessment (0-100)	32.85 (25.21)

Sharp Score Data

Erosion

Joint Space Narrowing

Erosion Scoring
1= discrete
2= larger, depends on surface area involved
3= large & extends over imaginary middle of bone
4= partial collapse of bone
5= complete collapse of bone

Joint Space Narrowing Scores
0= normal
1=focal or doubtful
2= generalized, >50% of the original joint space
3= <50% of the original space left or subluxation
4 = bony ankylosis or complete luxation

Results:

• 540 subjects with Sharp scores read at baseline and at follow-up
• 133 (24.6%) erosion free at baseline and follow-up
• Mean duration of time between radiographs was 26.4 (SD 7.6) months

Characteristic	Erosion Free (n=133)	Erosions (n=407)	P-Value
Mean age (SD)	**50.5 (13.6)**	**56.7 (11.6)**	**0.001**
Female (%)	**77.4**	**84.7**	**0.06**
Disease Duration, Yrs (SD)	**7.4 (8.2)**	**16.9 (12.2)**	**<0.0001**
Ever smoker, %	46.5	50.4	0.44
MDHAQ	5.1 (5.1)	5.9 (5.1)	0.09
DAS 28, mean (SD)	3.7 (1.6)	4.2 (1.5)	0.09
Mean SJC	**6.1 (7.0)**	**8.8 (7.2)**	**0.0003**
Mean TJC	**7.6 (7.6)**	**8.8 (7.2)**	**0.02**
JSN median/mean	**0 (1.2)**	**19 (27.9)**	**<0.0001**

GWAS

GWAS on Transformed CCP titer
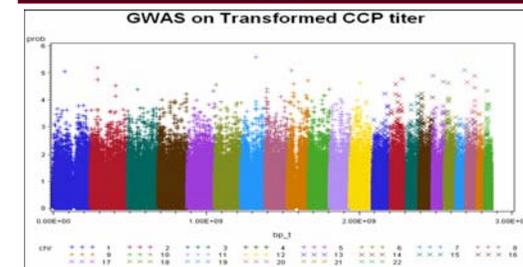
• GWAS conducted for transformed anti-CCP titer using 734,008 filtered SNPs, which passed quality control criteria, in 491 BRASS CCP+ samples.
• Each SNP is tested for additive association with Anti-CCP level.
• From 900K SNP analysis, there are 7470 SNPs that have a p value <0.01
• Will confirm any real associations among the NARAC, and EIRA datasets.

Abstracts/Publications

2009 BRASS POSTERS/PRESENTATIONS:

• Rheumatoid arthritis risk alleles as predictors to anti-TNF therapy in rheumatoid arthritis.
• Rheumatoid Arthritis Risk Alleles Predict Anti-CCP Level in RA patients.
• Genome Wide Predictors of Quantitative Anti-CCP in Rheumatoid Arthritis
• Clinical factors that predict erosion-free status in rheumatoid arthritis
• Prevalence of Alcohol Consumption among Rheumatoid Arthritis (RA) Patients on Methotrexate (MTX) and Impact on Liver Function Tests
• Stepwise Development of a Multi-Protein Biomarker Index of RA Disease Activity

PUBLICATIONS:

• **The relationship between focal erosions and generalized osteoporosis in postmenopausal women with rheumatoid arthritis.** Solomon DH, et al. Arthritis & Rheumatism. 2009
• **Investigation of candidate polymorphisms and disease activity in rheumatoid arthritis patients on methotrexate.** Lee YC, et al. Rheumatology. 2009
• **TNF alpha inhibitors may improve asthma symptoms: a case study of 12 patients with rheumatoid arthritis and asthma.** Stoll ML, et al. J Clin Rheumatol. 2009
• **Genome wide association study of determinants of anti-cyclic citrullinated peptide.** Cui J, et al. Molecular Medicine. 2009.
• **Common variants at CD40 and other loci confer risk of rheumatoid arthritis.** Raychaudhuri, S, et al. Nature Genetics. 2008.
• **Predictors of discontinuation of tumor necrosis factor inhibitors in patients with rheumatoid arthritis.** Argarwal SK, et al. J Rheumatol. 2008.
• **Two independent alleles at 6q23 associated with risk of rheumatoid arthritis,** Plenge, RM, et. al., Nature Genetics, 2007.

Collaborators

• Broad Institute, Cambridge, MA
• University of Alabama
• University of Arizona
• University of Toronto
• UCLA, School of Medicine
• National Institute of Environmental Health Sciences
• Bristol Myers Squibb Foundation