High baseline disease activity and seropositivity are associated with RA treatment response at one year post synovial biopsy

K Murray[1], C Low[1], F Young[1], M Bienicka[1], E Mylod[1], U Fearon[2], DJ Veale[1]
1. The EULAR Centre for Arthritis and Rheumatic Disease, St Vincent's University Hospital, Elm Park and University College Dublin, Dublin 4
2. Molecular Rheumatology, Trinity Biomedical Sciences Institute, Pearse St, Dublin 2

BACKGROUND

- Despite therapeutic advances, our ability to predict prognosis and therapeutic response in RA remains imprecise
- Synovial biopsy has improved understanding of RA pathogenesis, identified potential therapeutic targets and assessed current and new therapies
- This study examines for biomarkers predictive of RA outcomes at 1 year post arthroscopy

METHODS

- RA patients underwent knee arthroscopy with synovial biopsy under local anaesthetic
- Patients were assessed on the day of arthroscopy and at 2 weeks, 3, 6 and 12 months
- Erosive disease was defined based on X-rays of hands and feet
- Patients were classified as responders (moderate/good response) and non-responders by EULAR response
- Clinical characteristics, synovial tissue cell profiles and immunohistochemistry were analysed for T Cells (CD3), B Cells (CD20, CD138), macrophages (CD68) and vascularity (Factor VIII) to establish predictors of treatment response
- The sub-lining (SL) of each biopsy section was independently scored by 2 observers using a well-validated semiquantitative scoring method, ranging from 0 to 4 (0=no staining, 1=<25%, 2=25–49%, 3=50–74%, and 4=75–100% staining)
- Factor 8 was scored by calculating the mean count of stained blood vessels per high-power field (at 20X magnification)

RESULTS

- Patient characteristics are presented in Table 1 and 1 year outcomes in Table 2
- Rates of RF and ACPA positivity, tender and swollen joint counts, DAS28 and DAS28CRP were all higher amongst treatment responders
- There were no significant differences in gender, age, disease duration, medications, erosive status, ESR, CRP or synovitis or vascularity at arthroscopy
- Immunohistochemistry was a poor predictor of treatment response with no significant differences between the two groups in CD3, CD20, CD138, CD68 or Factor 8 score

Table 1. Baseline characteristics

	Responder (n=30)	Non-responder (n=18)	p
Female	20 (66.7%)	14 (77.8%)	NS
Age	51.5 (11.2)	54.2 (10.9)	NS
Disease duration	0.5 (0-16)	0.5 (0-10)	NS
RF positive	**22 (73.3%)**	**5 (27.8%)**	**0.003**
ACPA positive	**22 (73.3%)**	**8 (44.4%)**	**0.045**
Erosions	8 (26.7%)	5 (27.8%)	NS
Medications			
No DMARD	23 (76.7%)	10 (55.6%)	NS
csDMARD only	4 (13.3%)	3 (16.7%)	NS
TNFi	2 (6.7%)	3 (16.7%)	NS
Other bDMARD	1 (3.3%)	2 (11.1%)	NS
PGH VAS*, (mm)	54.2 (10-100)	51.5 (0-90)	NS
SJC (28 Joints)	**4.5 (0-16)**	**1 (0-18)**	**0.001**
TJC (28 Joints)	**7 (1-25)**	**1 (0-15)**	**0.001**
ESR, mm/hr	23 (2-120)	24 (2-81)	NS
CRP, mg/L	5 (1-95)	6.5 (1-64)	NS
DAS28	**5.01 (1.95-7.36)**	**3.93 (1.40-6.62)**	**0.003**
DAS28CRP	**4.78 (2.82-7.13)**	**3.39 (1.21-6.26)**	**0.002**
Synovitis, VAS	65 (10-100)	70 (30-100)	NS
Vascularity, VAS	60 (10-90)	70 (30-100)	NS

Data presented as n (%) or median (range)
*Patient Global Health Visual Analogue Score

Table 2. 1 year outcomes

	Responder (n=30)	Non-responder (n=18)	p
Medications			
No DMARD	3 (10%)	1 (5.6%)	NS
csDMARD only	14 (47.6%)	8 (44.4%)	NS
TNFi	12 (40%)	5 (27.8%)	NS
Other bDMARD	1 (3.3%)	4 (22.2%)	NS
PGH VAS*, (mm)	**30 (0-100)**	**60 (0-100)**	**0.015**
SJC (28 Joints)	0.6 (0-4)	1 (0-4)	NS
TJC (28 Joints)	**0 (0-14)**	**2 (0-28)**	**0.048**
ESR, mm/hr	11.5 (2-95)	19 (7-61)	NS
CRP, mg/L	3 (1-66)	7.5 (1-110)	NS
DAS28	**2.87 (0.49-5.81)**	**4.13 (1.78-6.54)**	**0.002**
DAS28CRP	**2.47 (1.35-4.92)**	**3.92 (1.36-5.34)**	**0.006**
ΔDAS28	**-1.84 (-4.4 to -0.72)**	**0.24 (-0.55 to 1.93)**	**<0.001**
ΔDAS28CRP	**-1.78 (-3.7 to -0.64)**	**0.21 (-0.93 to 3.02)**	**<0.001**

Data presented as n (%) or median (range)
*Patient Global Health Visual Analogue Score

CONCLUSIONS

- In this small study, seropositivity and disease activity were higher in responders
- Baseline immunohistochemical staining was not a good discriminator of treatment response.