E41. INVESTIGATION OF GENETIC VARIANTS IN PREDICTING RESPONSE TO BIOLOGIC DRUGS USED TO TREAT RHEUMATOID ARTHRITIS

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Background: Etanercept, a soluble tumour necrosis factor (TNF) receptor fusion protein, is a biologic drug that can be used to treat RA, which is resistant to standard disease-modifying therapies. However, 30% of patients fail to respond and given the high cost of treatment and risk of side effects, there is a need to identify predictive factors of anti-TNF treatment response. Recently, a genome-wide association study (GWAS) identified a single nucleotide polymorphism (SNP), rs6427528, mapping to the CD84 gene locus to be associated with etanercept treatment response \( (n=733; \ P = 8 \times 10^{-8}) \). Our current study aimed to test association of the same SNP in an independent UK RA etanercept-treated population.

Methods: DAS for 28 joints (DAS28) was computed in 247 British RA patients at baseline and at 3/6 months after initiation of etanercept treatment. DNA samples were genotyped using either Illumina or Affymetrix genotyping arrays. Following quality control of the genotyping data, the SNP rs6427528 was tested for association with treatment response, defined as the change in DAS28 score between pre-treatment and 3/6 months post treatment (\( \Delta \)DAS28), using linear regression. Linear regression analysis was carried out using PLINK (version 1.07) software and statistical power for the current study was calculated using the software Quanto. A meta-analysis was performed using the METAL software tool, combining the current data with the original GWAS to determine the association of the CD84 SNP with etanercept treatment response.

Results: Our study had 68% power to detect the same effect size as reported in the original GWAS at the 5% significance threshold \( (P = 0.05) \). No evidence for association between the SNP rs6427528 and etanercept treatment response \( (\Delta \)DAS28) was detected in our patient group \( (P = 0.18; \text{Table 1}) \). However, the meta-analysis revealed a strong association between the SNP and etanercept treatment response \( (\Delta \)DAS28), albeit with less significance than the original study \( (P = 1.06 \times 10^{-7}) \).

Conclusion: In a replication study carried out within the UK RA population, we found no association between the CD84 SNP rs6427528 and etanercept treatment response. More replication studies will have to be carried out in larger sample sizes to confirm if this association is indeed a genuine one.
Disclosure statement: The authors have declared no conflicts of interest.

<table>
<thead>
<tr>
<th>SNP</th>
<th>Chromosome</th>
<th>$\beta$ (95% CI)</th>
<th>$P$-value</th>
<th>$P$-value</th>
<th>$P$-value</th>
</tr>
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<tbody>
<tr>
<td>rs6427528 A</td>
<td>1q23</td>
<td>0.29 (-0.13, 0.71)</td>
<td>0.18</td>
<td>0.71</td>
<td>$8 \times 10^{-8}$</td>
</tr>
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$\beta$: regression coefficient; Ref-allele: reference allele for the association test; SNP: single nucleotide polymorphism.