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# THE IMPACT OF LOW AFFINITY IMMUNOGLOBULIN GAMMA FC REGION RECEPTOR III-A GENE POLYMORPHISMS IN NEUROMYELITIS OPTICA SPECTRUM DISORDER AND IMPLICATION FOR TREATMENT OUTCOMES: RESULTS FROM THE N-MOMENTUM STUDY

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Introduction: Neuromyelitis optica spectrum disorder (NMOSD) is an autoantibody-mediated CNS disease. The rs396991 F176V polymorphism of the low-affinity IgG Fc region receptor III-A (FCGR3A) gene affects IgG binding affinity and is associated with reduced efficacy of anti-CD20 therapies for NMOSD. We characterized the relationship between rs396991 polymorphism, NMOSD disease activity, and treatment response in N-MOmentum trial participants.

Materials and Methods: N-MOmentum (ClinicalTrials.gov identifier: NCT02200770) had a randomized controlled period (RCP; inebilizumab 300 mg or placebo on days 1 and 15) of up to 28 weeks, followed by an open-label period (OLP). A total of 142 participants (inebilizumab, n=104; placebo, n=38) consented for genotyping via TaqMan qPCR assay.

Results: Historical annualized attack rates (AARs) and change in Expanded Disability Status Scale (EDSS) scores from NMOSD onset to enrolment were nominally higher in rs396991 V-allele carriers (V-allele genotype [V/V or V/F], n=74) than in F/F–allele homozygotes (n=68). In the placebo group, AAR, new/enlarged T2 MRI lesions, and NMOSD-related hospitalizations were nominally higher in V-allele carriers than in F/F–allele homozygotes. At the RCP end, V-allele carriers receiving inebilizumab had greater median (IQR) B-cell, plasma-cell, and Ig depletion than F/F–allele homozygotes, as well as nominally lower AAR and new/enlarged T2 lesions. By dose 4 in the OLP, there was little difference between the subgroups in clinical metrics or B-cell depletion.

Conclusions: V-allele carriers may have increased NMOSD disease activity and response to inebilizumab was not reduced compared with F/F–allele homozygotes.