Serum glial fibrillary acidic protein is elevated in a subset of neuromyelitis optica patients and associated with increased risk of attacks

Hans-Peter Hartung, M.D.,1 Orhan Aktas, M.D.,1 Michael A. Smith,2 William Rees, Ph.D.,2 Kazuo Fujihara, M.D.,3 Friedemann Paul, M.D.,4 Romain Marignier, M.D.,5 Jeffrey L. Bennett, M.D., Ph.D.,6 Ho Jin Kim, M.D.,7 Brian Weinshenker, M.D.,4 Sean J. Pittcock, M.D.,9 Dean Wingerchuk, M.D.,9 Gary Cutter, Ph.D.,10 Ari Green, M.D.,11 Maureen A. Mealy, Ph.D.,2 Jorn Drappa, M.D., Ph.D.,2 Gerard Barron, BSc.,2 Soraya Madani, Ph.D.,2 Liangwei Wang,2 Dewei She, Ph.D.,2 Daniel Cimbora, Ph.D.,2 John N. Ratchford, M.D.,2 Eliezer Katz, M.D.,2 and Bruce A.C. Cree, M.D., Ph.D., M.A.S.,12 on behalf of the N-MOmentum study investigators

1Medical Faculty, Heinrich-Heine-University, Düsseldorf, Germany; 2Viela Bio, Gaithersburg, MD, United States; 3Department of Multiple Sclerosis Therapeutics, Fukushima Medical University and Multiple Sclerosis and Neuromyelitis Optica Center, Southern Tohoku Research Institute for Neuroscience, Koriyama, Japan; 4Experimental and Clinical Research Center, Max Delbrueck Center for Molecular Medicine and Charité – Universitätsmedizin Berlin, Berlin, Germany; 5Lyon University Hospital, Lyon, France; 6University of Colorado, School of Medicine, Anschutz Medical Campus, Aurora, CO, United States; 7Research Institute and Hospital of National Cancer Center, Seoul, South Korea; 8Mayo Clinic, Rochester, MN, United States; 9Mayo Clinic, Scottsdale, AZ, United States; 10University of Alabama at Birmingham, Birmingham, AL, United States; 11UCSF Weill Institute for Neurosciences, Department of Neurology and Department of Ophthalmology, University of California San Francisco, San Francisco, CA, United States; 12UCSF Weill Institute for Neurosciences, University of California San Francisco, San Francisco, CA, United States.
Disclosures

- **HP Hartung** reports ……

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sGFAP concentration in N-MOmentum: a biomarker of disease activity

- In NMOSD, autoantibodies target the AQP4 water channel predominantly expressed on astrocytes
- Destruction of astrocytes leads to increased levels of GFAP in the serum (sGFAP)
- In N-MOmentum, the anti-CD19 antibody, inebilizumab, reduced the risk of attacks by 73% compared with placebo
- In this study, we investigated the relationship between sGFAP concentration and attacks adjudicated by an independent committee
Cross-sectional NMOSD study: increased [GFAP] in serum
Single Molecule Array (SIMOA): digital ELISA → detection of single CNS proteins in the circulation

→ Compare volume of an erythrocyte: ~90 fl

→ Usual size of wells in ELISA:
  200 µl = 200 000 nl
  200 000 000 pl
  200 000 000 000 fl

Rissin et al.; Nat Technology 2010
N-MOmentum: a global, pivotal study

Efficacy and safety of inebilizumab in adults with NMOSD¹

- Double-masked, placebo controlled study at 99 medical centers in 25 countries
- **Monotherapy (no background immunotherapy permitted)**
- Time-to-event design²

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¹Study end defined as 67 NMOSD attacks, or when 252 patients had been randomized and received study drug.

Pre-defined, clinically significant attack diagnosis criteria enabling association of biomarkers and clinical activity

- **Optic neuritis**
- **Myelitis**
- **Brain/brainstem**

**The Expanded Disability Status Scale (EDSS)**

10 criteria representing overt clinical change

8 criteria representing moderate clinical change & New MRI lesion

Adjudication committee confirmation

**NMOSD ATTACK**
Elevated concentration of sGFAP is associated with adjudicated attack risk

- At baseline, 29% of patients with NMOSD had an sGFAP concentration above the level in healthy donors.
- NMOSD patients with elevated sGFAP at baseline were three times more likely to have an adjudicated attack.
- Compared with placebo, inebilzumab-treated patients with elevated sGFAP at baseline were 61% less likely to have an adjudicated attack, and those who did not have elevated baseline sGFAP concentration were 79% less likely to have an attack.
- sGFAP increases during adjudicated NMOSD attacks.
  - sGFAP concentration is correlated with attack severity.

HD, healthy donors; HR, hazard ratio; NMOSD, neuromyelitis optica spectrum disorder; RRMS, relapsing-remitting multiple sclerosis; sGFAP, serum glial fibrillary acidic protein.
Inebilizumab (anti-CD19) reduces elevated sGFAP concentration

- During attacks, inebilizumab-treated patients had a 1-fold change in sGFAP concentration compared with a 20-fold change in patients who received placebo.
- In patients who did not have an adjudicated attack, sGFAP concentration in patients treated with inebilizumab decreased by 12.9% and fewer patients had elevated sGFAP compared with patients receiving placebo.
- In conclusion, these observations suggest that sGFAP is a biomarker of NMOSD disease activity and attack risk.
  - Treatment with inebilizumab reduces the risk of an adjudicated attack in patients with or without elevated sGFAP concentration at baseline and reduces sGFAP concentration irrespective of attack status.

Placebo group: clear upregulation of sGFAP during attacks
Inebilizumab group: non-significant sGFAP changes during attack
Patients without adjudicated NMOSD attacks: sGFAP decrease during inebilizumab treatment

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FC, fold change; HD, healthy donors; NMOSD, neuromyelitis optica spectrum disorder; RCP, randomized controlled periods; sGFAP, serum glial fibrillary acidic protein.
Conclusions

• In the N-MOmentum study, participants with NMOSD had increased sGFAP concentration compared with participants in the HD and the RRMS reference cohorts.
• For NMOSD, increased baseline sGFAP concentrations were three times more likely to have an adjudicated attack.
• sGFAP concentration increased significantly within 1 week of an adjudicated attack and correlated with adjudicated NMOSD attack severity.
• sGFAP concentrations during adjudicated NMOSD attacks were lower in inebilizumab-treated patients than in participants receiving placebo.
  – This is consistent with the observation that adjudicated attacks in inebilizumab-treated participants had a lower optico-spinal impairment score (OSIS) than those receiving placebo.
• sGFAP concentrations decreased in inebilizumab-treated patients who did not experience an adjudicated NMOSD attack.
• These observations suggest that sGFAP could be a clinically useful biomarker of disease activity and increased attack risk in NMOSD.