

Background

Nipocalimab binds to FcRn with high affinity which prevents IgG recycling, leading to reduced serum levels of total IgGs, including pathogenic IgG autoantibodies. Rapid, sustained lowering of IgG was observed in the phase 2 VIVACITY study in generalized myasthenia gravis (gMG) and in phase 1 healthy volunteers. In gMG patients, nipocalimab induced rapid and sustained lowering of anti-AChR autoantibodies and MG-ADL scores, but no serious adverse events including clinically significant infections.

Design/Methods

Nipocalimab was evaluated extensively in vitro and in nonhuman primate-based chronic toxicology studies to evaluate selectivity, tolerability, safety and immunopharmacology. Safety, tolerability and immune-focused assessments in clinical phase 1 and Phase 2 MG studies were also completed (NCT02828046, NCT03772587).

Results

Nipocalimab binds specifically in vitro to FcRn without activation of effector function or inhibition of antigen presentation. In nonhuman primates administered up to 300 mg/kg nipocalimab QW for up to 6 months, sustained lowering of IgG was observed without adverse effects. Immunotoxicology identified no effect on immune cell phenotypes; CD8 T cell, NK or innate cell functions; T-dependent neoantigen IgM responses. Neoantigen IgG production was observed, but with lowered peak IgG titers consistent with the anticipated increase in IgG clearance with nipocalimab. In clinical studies, nipocalimab demonstrated a reproducible selective decrease in total serum IgG, including all subclasses of IgG, with no effect on IgM, IgA, IgE, CH50, C3, C4, inflammatory cytokines or acute phase proteins including, C-reactive protein (CRP).

Conclusions

These data suggest that nipocalimab can selectively lower IgG and IgG autoantibodies while preserving cellular immunity, complete IgM response and IgG production after neoantigen challenge. Overall, nipocalimab's selective effect on IgG recycling provides a mechanistic rationale for potentially decreased infection risk despite substantial IgG lowering.

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Validation of MATCH Score: A Predictive Tool for Identification of Patients With Kelch-Like Protein-11 Autoantibodies

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Objective

To validate performance of the MATCH score using an independent paraneoplastic neurological syndrome (PNS) cohort.

Background

Kelch-like protein 11 (KLHL11)-IgG is a high-risk paraneoplastic antibody associated with rhombencephalitis. MATCH score is a composite clinical model recently developed to predict KLHL11-IgG positivity

Design/Methods

Retrospective review of cases with definite or probable PNS who underwent neural specific autoantibody evaluation at Mayo Clinic Neuroimmunology laboratory between January 2001 and December 2021 was performed. MATCH score was calculated for all patients to assess the score's discriminative ability

Results

186 patients who met the definite or probable PNS criteria were identified. The MATCH score was = 4 in 31/36 patients who were KLHL11-IgG positive and in 17/150 patients who were KLHL11-IgG negative but positive for other high-risk autoantibodies including CRMP5, ANNA1, PCA1 and amphiphysin, among others, or seronegative to all antibodies. MATCH Score's sensitivity, specificity, positive and negative predictive value were 86%, 89%, 65% and 96%, respectively. The score showed an excellent discriminative ability with an AUC of 0.924 [95% CI 0.885-0.962].

Conclusions

MATCH score is a sensitive and specific tool to identify patients likely to be KLHL11-IgG positive. Utilization of MATCH score can improve pre-test probability. However, some KLHL11-IgG cases with motor neuropathy or limbic encephalitis presentation or those without a detectable testicular cancer at the time of initial assessment may potentially be missed.

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Caveolae-Associated Protein (cavin)-4 Autoantibodies in Immune Mediated Rippling Muscle Disease

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