Poster# 297

DNTH103, a potentially safer and more convenient novel, investigational therapy for generalized Myasthenia Gravis

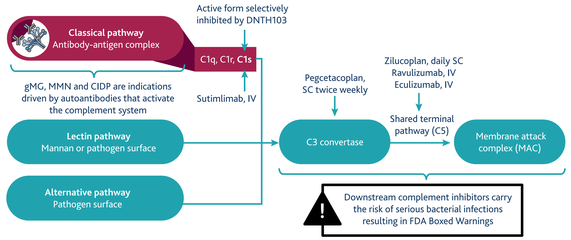
H John Vissing[1], Stojan Peric[2], Lisa A. Lewis[3], Jeffrey Stavenhagen[4], Sankalp Gokhale[4]

[1]Copenhagen Neuromuscular Center, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark; [2]University of Belgrade, Belgrade, Serbia; [3]Division of Infectious Diseases and Immunology, Department of Medicine, University of Massachusetts Chan Medical School, Worcester, MA, USA; [4]Dianthus Therapeutics, New York City, USA

BACKGROUND

Complement inhibitors are well established in gMG and other severe autoimmune disorders

Targeting C1s preserves immune activity of the lectin and alternative pathways, with the aim to provide a safe therapeutic option

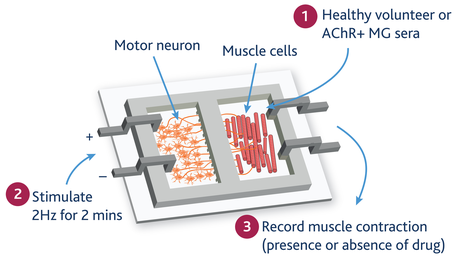


DNTH103 – a picomolar-potent monoclonal antibody selectively targeting active C1s

- DNTH103 is a fully human immunoglobulin G (IgG4) monoclonal antibody binding to active C1s, allowing low-volume SC self-administration
- Alternative and lectin pathways are left intact
- In a Phase 1 clinical trial in healthy volunteers, DNTH103 demonstrated an extended half-life of 60 days and potent complement inhibition, supporting potential for infrequent, low-volume SC dosing

Global Phase 2 studies in generalized Myasthenia Gravis (gMG) and Multifocal Motor Neuropathy (MMN) are ongoing, and a global Phase 2 trial in Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) is planned to start in 2024

Preclinical evaluation of DNTH103 in an established *in vitro* model of MG



- Serum from three acetylcholine receptor-positive (AChR+) MG patients used in a validated commercially available humanized *in vitro* MG model[1,2,3]
- Endpoint: Fatigue index in response to anti-C5 antibody* or DNTH103
  - A reduction in fatigue index indicates improvement in neurotransmission and muscle contraction

*Engineered using the ravulizumab patent sequence
gMG, generalized Myasthenia Gravis; MMN, Multifocal; Motor Neuropathy; CIDP, Chronic Inflammatory Demyelinating Polyneuropathy; IV, intravenous; SC, subcutaneous; FDA, Food and Drug Administration; MG, Myasthenia Gravis; AChR+, acetylcholine receptor-positive

CONCLUSIONS

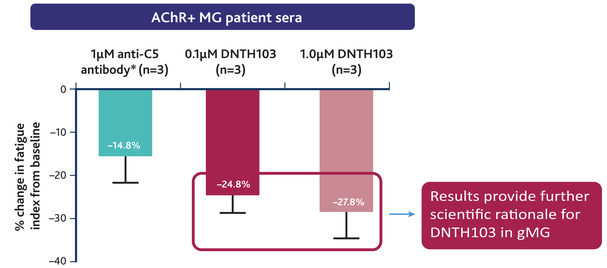
DNTH103 is a highly potent picomolar inhibitor of active C1s that is as effective in improving neurotransmission and muscle contraction as an anti-C5 antibody in a preclinical model of Myasthenia Gravis

DNTH103 selectively inhibits the classical pathway with the potential to be safer than complement therapies that also block the lectin and/or alternative pathways

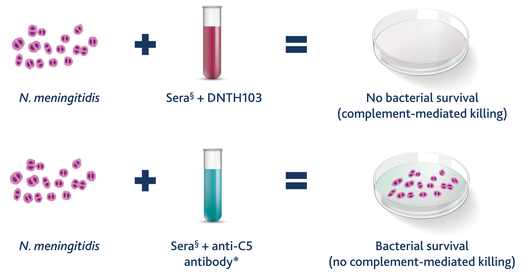
DIANTHUS THERAPEUTICS

RESULTS

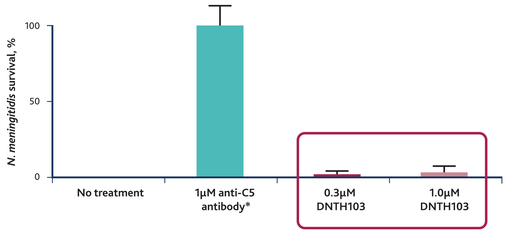
DNTH103 improves neurotransmission and muscle contraction in an AChR+ MG model† (change from baseline)



DNTH103 *in vitro* study demonstrates lower risk of *Neisseria meningitidis* infections



N. meningitidis bacterial killing is unaffected despite inhibition of the classical pathway



In this assay, DNTH103 maintained bacterial killing, potentially leading to a decreased risk of infection vs. anti-C5 antibody*

Dianthus Therapeutics data on file
†Validated in healthy volunteer sera; *engineered using the ravulizumab patent sequence; §Normal human sera
AChR+ MG, acetylcholine receptor-positive Myasthenia Gravis; MG, Myasthenia Gravis; gMG, generalized Myasthenia Gravis

References

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