Poster M262

Effects of Efgartigimod Treatment on Humoral and Cellular Immune Responses: Analysis of T-Cell–Dependent Antibody Response in Cynomolgus Monkeys

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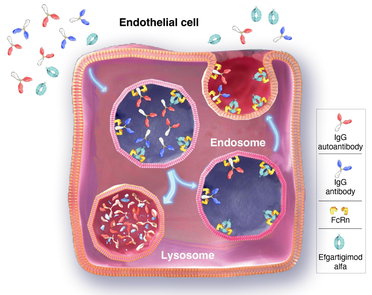
SCAN ME

INTRODUCTION

Efgartigimod Mechanism of Action: Blocking FcRn



- FcRn recycles IgG, extending its half-life and maintaining its serum concentration[1]
- Efgartigimod is a human IgG1 Fc fragment, a natural ligand of FcRn, engineered for increased affinity to FcRn[2,3]
- Efgartigimod was designed to outcompete endogenous IgG, preventing recycling and promoting IgG lysosomal degradation without directly impacting its production[2-6]
  - Targeted reduction of all IgG subtypes
  - No impact on IgM or IgA
  - No reduction in albumin levels
  - No increase in cholesterol

Immunosuppressive Therapies Used in Treatment of gMG May Increase Susceptibility to Infections and Impair Immune Response to Vaccines[7-8]

- Previous gMG treatments have the potential to[7,9-10]:
  - Increase risk of infection
  - Reduce therapeutic antibody response
  - Impair cellular immune responses to vaccination
- Glucocorticoids and B-cell–depleting therapies (including MMF) have been shown to substantially reduce immunogenicity of mRNA vaccines to SARS-CoV-2[8]

Evidence Suggests Efgartigimod Does Not Impair Humoral Response to COVID-19 Vaccination[11]

- Among ADAPT+ study patients with gMG who received COVID-19 vaccination prior to October 2021, COVID-19 immunization resulted in antigen-specific IgG responses in most patients receiving efgartigimod (12/15 patients)[11,12]
- Impact of concomitant immunosuppressive therapies (eg, glucocorticoids and B-cell–depleting therapies such as MMF) warrants additional investigations[11]

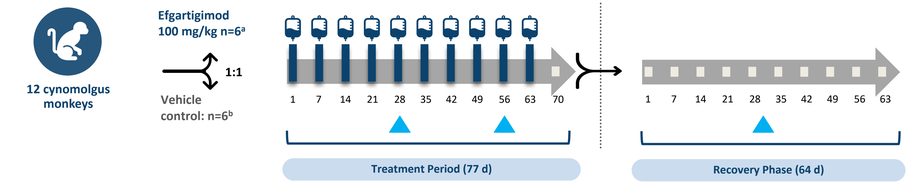
Keyhole Limpet Hemocyanin (KLH): A Model Antigen for Testing T-Cell–Dependent Antibody Response (TDAR) and Simulating Vaccines Responses[13]

- Following KLH immunization, PBMCs secrete cytokines including IFN-γ as part of cell-mediated immune response[13]
- TDAR against KLH has been demonstrated in cynomolgus monkeys[14]
- Quantification of the antibody response to immunization with a T-cell–dependent antigen is a sensitive method for assessing immunocompetence[14]

METHODS

Outcomes Reported Include Timing and Magnitude of Anti-KLH IgM and IgG Responses and Elicited Levels of IFN-γ Secretion of PBMCs in Response to KLH Challenges in an ELISpot Assay

Study Design: TDAR in Cynomolgus Monkeys



[a]The study group includes both male (n=3) and female (n=3) cynomolgus monkeys. [b]The vehicle control article was 20 mM histidine/histidine HCl, 60 mM sucrose, 100 mM sodium chloride, 10 mM L-methionine 0.04% w/v polysorbate 80, pH 6.0.

SUMMARY

- Lower anti-KLH IgG titers were observed after the second KLH challenge in efgartigimod-treated animals that normalized during the treatment-free period
- No difference was observed in IgM titers or KLH-elicited cellular response between efgartigimod- and vehicle control–treated animals
- T-cell–dependent antibody and cellular immune responses were mounted to a prototypical antigen under efgartigimod treatment
- Total IgG titers significantly decreased under efgartigimod treatment, consistent with the mechanism of action of the drug

RESULTS

Humoral Response: Anti-KLH IgM and IgG Antibodies Titers

Figure 1. Anti-KLH IgG Titer – Average Male + Female

- Anti-KLH IgG: lower IgG titers after 2nd KLH dose in efgartigimod-treated animals; however, no statistical difference between groups after washout

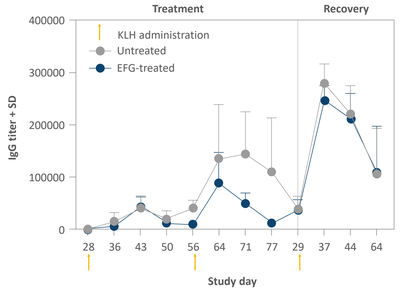
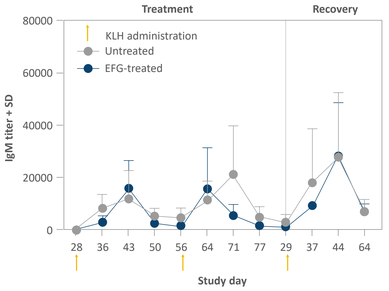


Figure 2. Anti-KLH IgM Titer – Average Male + Female

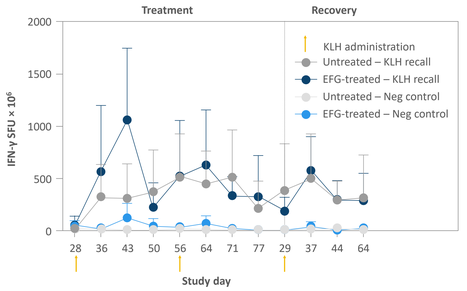
- Anti-KLH IgM: no statistical differences between groups



Cellular Response: KLH Recall

Figure 3. KLH Recall vs Negative Control – Average Male + Female

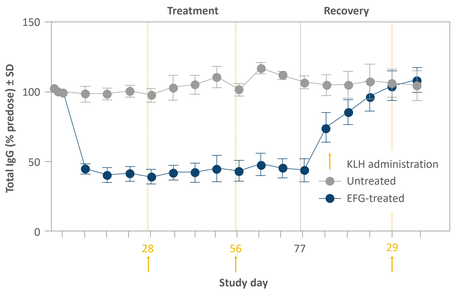
- Comparable KLH-specific cellular responses between treated vs untreated groups
- No differences between groups during treatment-free period (recovery)



Pharmacodynamics: Total IgG Marker

Figure 4. Total IgG (% predose)

- Total IgG titers decreased under efgartigimod treatment, consistent with efgartigimod's expected mechanism of action



ABBREVIATIONS

COVID-19, coronavirus 2019; EFG, efgartigimod; ELISpot, enzyme-linked immunosorbent spot; FcRn, neonatal Fc receptor; gMG, generalized myasthenia gravis; IFN-γ, interferon-γ; IgG, immunoglobulin G; KLH, keyhole limpet hemocyanin; MMF; mycophenolate mofetil; mRNA, messenger RNA; PBMC, peripheral blood mononuclear cell; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SFU, spot-forming unit; TDAR, T-cell–dependent antibody response.

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