Poster #195

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

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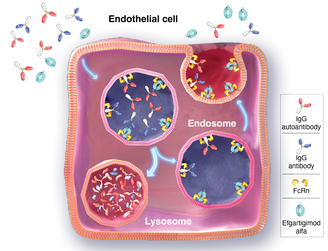
## INTRODUCTION

### 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 lysosomal degradation of IgG[2-6]
  - Targeted reduction of all IgG subclasses
  - No impact on immunoglobulins M or A
  - No reduction in albumin levels
  - No increase in cholesterol

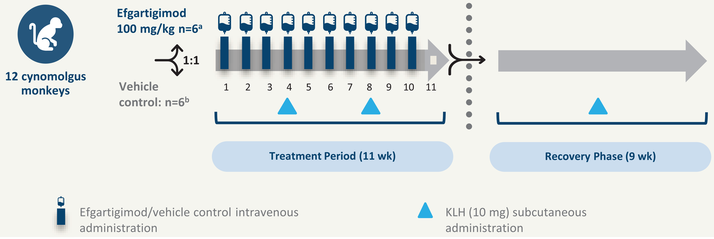
### Keyhole Limpet Hemocyanin (KLH): A Model Antigen for Testing T-Cell–Dependent Antibody Response (TDAR) and Simulating Conjugate Vaccines[7]

- Following KLH immunization, PBMCs secrete cytokines including IFN-γ as part of cell-mediated immune response[7]
- TDAR against KLH has been demonstrated in cynomolgus monkeys[8]
- Quantification of the antibody response to immunization with a T-cell–dependent antigen is a sensitive method for assessing immunocompetence[7]

## METHODS

**Outcomes reported include timing and magnitude of anti-KLH IgM and IgG responses[8] and elicited levels of interferon-gamma secretion of PMBCs 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 observed difference 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

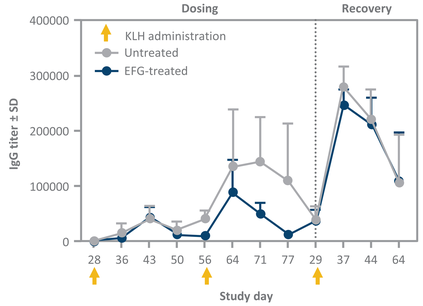
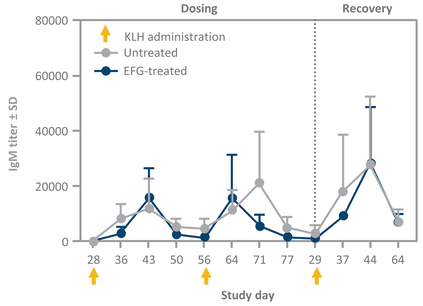



**Figure 2.** Anti-KLH IgM Titer – Average Male + Female

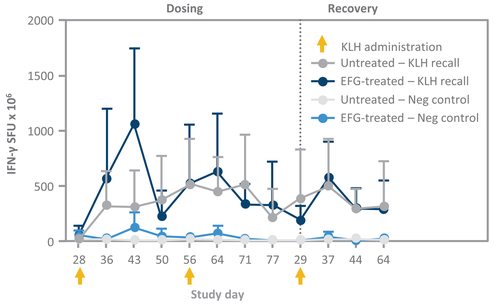
- Anti-KLH IgM: no statistical differences between groups




### Cellular Response: KLH Recall

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

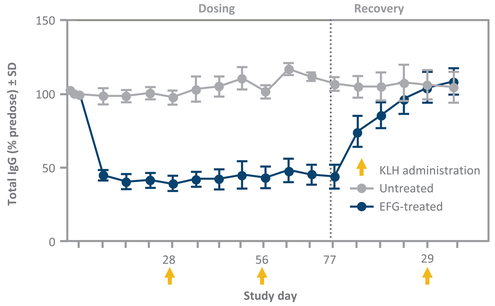
- Comparable KLH-specific cellular responses between treated vs untreated groups
- No differences between groups during treatment-free period (recovery)




### 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**
EFG, efgartigimod; ELISpot, enzyme-linked immunosorbent spot; FcRn, neonatal Fc receptor; IFN-γ, interferon-γ; IgG, immunoglobulin G; KLH, keyhole limpet hemocyanin; PBMC, peripheral blood mononuclear cell; SFU, spot-forming unit; TDAR, T-cell–dependent antibody response.

**REFERENCES**
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