Mauritian Cynomolgus Monkeys Are a Suitable Model for Assessing Biologic Immunogenicity

Confidential Collaborator: ANEWCRO Pilot NHP Study

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Background

Nonhuman primates (NHPs) are a critical model for evaluating the immunogenicity and pharmacokinetics (PK) of biologic therapeutics. A collaborator's prior immunogenicity data were generated in cynomolgus monkeys of Asian origin. This pilot study, conducted with ANEWCRO, evaluated whether Mauritian-origin cynomolgus monkeys reproduce the anti-drug antibody (ADA) and drug-exposure profiles of two known immunogenic biologics — Adalimumab and Afimkibart.

Study Objectives

- Characterize ADA responses to Adalimumab and Afimkibart in Mauritian cynomolgus monkeys
- Measure drug exposure (PK) across a three-dose regimen
- Benchmark results against historical Asian-NHP data

Study Design

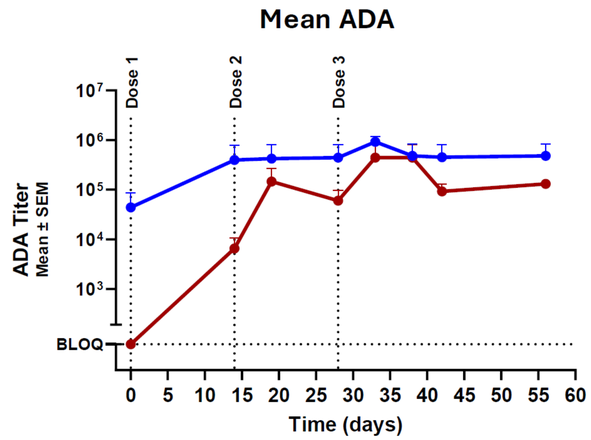
Test articles	Adalimumab Afimkibart
NHP origin	Mauritian cynomolgus (Naïve to human antibodies)
Dose / route	1.0 mg/kg, intravenous (IV)
Animals	3 per group
Dosing	3 doses, biweekly
ADA timepoints	Pre-dose; D14 (post-dose 1); D5, 14 (post-dose 2); D5, 14, 28 (post-dose 3)
Assays	MSD bridging assay (ADA); bridging ELISA (PK)

Immunoassays & Detection – Methods

Immunogenicity Assessment
Anti-drug antibodies were measured using validated MSD bridging immunogenicity assays employing biotinylated and Sulfo-Tag conjugated forms of Adalimumab and Afimkibart. Predose samples were evaluated for pre-existing ADA reactivity.

Pharmacokinetic Assessment
Serum concentrations of Adalimumab and Afimkibart were determined using bridging ELISA methodologies to evaluate exposure over time and monitor clearance following repeated administration.

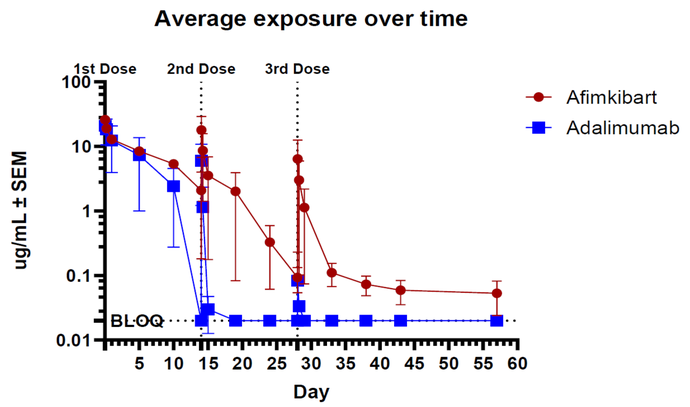
Results 1 — ADA Responses



ADA Responses - MSD bridging immunogenicity assay reagents: biotinylated and sulfo tag conjugates were generated for Adalimumab and Afimkibart.

- Both Adalimumab and Afimkibart elicited measurable ADA responses in Mauritian cynomolgus monkeys.
- ADA responses were observed by Day 14 following the first dose.
- ADA titers increased following subsequent administrations.
- One animal (BC2084) demonstrated pre-existing ADA reactivity to both assay bridging reagents prior to dosing.
- ADA responses were comparable to those previously observed the collaborator's prior study utilizing Asian-origin cynomolgus monkeys.

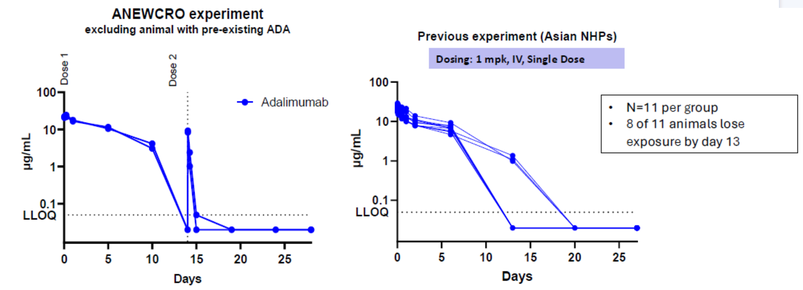
Results 2 — Loss of Drug Exposure



Pharmacokinetics - PK analysis performed by bridging ELISAs

- Both molecules exhibited progressive loss of exposure during the study.
- High ADA titers were associated with accelerated drug clearance.
- Rapid clearance was observed in nearly all animals after the second dose.
- One Afimkibart-treated animal demonstrated prolonged exposure relative to the remaining animals.
- Animal BC2084 showed markedly reduced Adalimumab exposure after the first dose due to pre-existing ADA.

Results 3 — Mauritian vs. Asian NHP



Comparison with prior studies conducted in Asian-origin cynomolgus monkeys demonstrated highly similar exposure profiles for Adalimumab.
Key observation:

- Mauritian and Asian-origin cynomolgus monkeys displayed comparable pharmacokinetic responses and immunogenicity profiles.

Discussion & Conclusions

Discussion

Both Adalimumab and Afimkibart were immunogenic in Mauritian cynomolgus monkeys, leading to the expected generation of anti-drug antibodies and corresponding reductions in systemic exposure. The observed ADA kinetics and PK profiles closely matched historical findings from Asian-origin cynomolgus monkeys. The detection of pre-existing ADA in one biologic-naïve animal is consistent with published reports and previous toxicology studies evaluating fully human monoclonal antibodies.

Conclusions

- Adalimumab and Afimkibart were immunogenic in Mauritian cynomolgus monkeys.
- ADA responses were detected after the first administration and increased following repeated dosing.
- Increased ADA responses resulted in reduced systemic drug exposure.
- Pre-existing ADA to human IgG-based therapeutics can occur in biologic-naïve animals.
- **Results were consistent with previous studies and published literature. Mauritian cynomolgus monkeys represent a suitable nonclinical model for evaluating immunogenic biologics.**

Key Takeaways

✓ Both antibodies generated robust ADA responses
✓ ADA development correlated with loss of exposure
✓ Results mirrored historical Asian NHP data

References & Notes

- Immunogenetics (2019) 71:605-615. Pre-existing anti-human IgG antibodies in cynomolgus monkeys

- ADA = anti-drug antibody; PK = pharmacokinetics; NHP = nonhuman primate; IV = intravenous; BLOQ = below limit of quantitation.