ARQ-234: A High-Affinity CD200-Fc Fusion Protein for the Treatment of Atopic Dermatitis

Joseph Sheridan,1 Jonathan Heil,1 David R. Berk,2 Patrick Burnett,2 David J. Blackbourn,3,4 Philip Huxley,5 Rebecca Ashfield2,5

Clinical Development Pharmaceutical Co., BD-Oncology, Cambridge, MA; Merck Research Laboratories, Inc., Westlake Village, CA; UT Southwestern Medical Center, University of Surrey, Guildford, UK; Institute of Medical Sciences, University of Aberdeen, Aberdeen, Scotland, UK; Business Development, Ltd., Bristo, UK

INTRODUCTION

Checkpoints receptors are important for maintaining immune homeostasis, and dysregulation of these checkpoints can lead to the development of inflammatory diseases. ARQ-234, a high-affinity CD200-Fc fusion protein, is engineered to target the CD200R receptor expressed on many myeloid cells and lymphocyte populations, including CD4+ T and γδ T lymphocytes.

We engineered high-affinity CD200R agonists, including human CD200-Fc proteins with engineered CDR loops to express high levels of human CD200R.

Higher-affinity murine CD200-Fc (DS-227) was significantly more potent in reducing clinical score compared with wild type.

High-affinity human CD200-Fc significantly reduced cell infiltrate in bronchoalveolar lavage fluid.

In Vivo Proof of Concept for Inhibiting Inflammation With Higher-Affinity CD200-Fc

High-affinity human CD200-Fc complex (DS-227) showed activity in a model of contact hypersensitivity.

The highest-affinity huCD200-Fc (DS-118) showed activity in a model of Ascaris suum (roundworm)-induced lung inflammation in non-human primates.

The PK profiles of DS-118 and ARQ-234 were compared with that of the CD200R agonist antibody in non-human primates.

CONCLUSION

Targeted immunomodulation of the CD200-CO200R axis could modulate chronic inflammation and restore immune homeostasis.

ACKNOWLEDGMENTS

We thank the study volunteers, all investigators, study sites, and all study staff for their contributions. We thank Aragen, Syngene, WuXi, and Physiomics. We also thank Mark Edwards for providing the diagram of ARQ-234, and Dr. Diysong Liu for providing the data for Figure 5B.