performed before and after drug administration. Results: A novel signature was observed, with reduced serum interleukin 8 (IL-8) levels and reduced CD11b integrin expression on monocytes associated with increased CXCR1 expression. Conclusions: This set of linked phenotypes suggests that blockade of the IL-1β pathway results in reduced monocyte CD11b integrin expression which may be related to an alteration in IL-8 signaling and is consistent with a model of reduced ability of mononuclear cells to traffic to sites of inflammation. This may have important implications for ongoing clinical trials using IL-1β blockade in type 1 diabetes.

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F.104. A Phase 2, Open-label, Investigator-initiated Study to Evaluate the Safety and Efficacy of Apremilast in Subjects with Recalcitrant Contact or Atopic Dermatitis

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Introduction: Atopic dermatitis (AD) and allergic contact dermatitis (ACD) are chronic inflammatory diseases characterized by pruritis. Current systemic treatments are associated with numerous end-organ toxicities. Apremilast is a novel phosphodiesterase type-IV inhibitor that has demonstrated efficacy in phase 2 trials in patients with psoriasis or psoriatic arthritis. This therapy may offer improved control over AD and ACD. Objective: Evaluate the efficacy and safety of Apremilast in patients with recalcitrant moderate to severe atopic or contact dermatitis. Research Design and Methods: Proof-of-concept, phase 2, open-label, single institution trial to evaluate the efficacy and safety of Apremilast, 20 mg capsule twice daily for 12 weeks, in ten subjects. Clinical efficacy was determined by the Eczema Assessment Severity Index (EASI) and the Investigator Global Assessment (IGA). Results: Preliminary results show that four out of nine patients experienced a 30% or greater improvement in EASI scores during the treatment phase. These patients also demonstrated a one point improvement in IGA from baseline. Overall, there was a 5% worsening in mean EASI scores in all nine subjects. All patients tolerated Apremilast well with no serious adverse events. Common side effects included headache, dermatitis flare, nausea, dyspepsia, and soft stool. Limitations: Small, single-arm, open-label study with no control. Discussion: Early results of this ongoing trial demonstrate that Apremilast is well-tolerated with four out of nine subjects showing mild improvement in their dermatitis during the 12-week treatment course. However, the efficacy was modest and not as good as that seen in patients with moderate to severe psoriasis.

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F.108. Early Evaluation of Immunogenicity to a Biotherapeutic by Assessing Antigen-specific T Cells from Whole Blood Derived Peripheral Blood Mononuclear Cells from Cynomolgus Monkeys

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Preclinical pharmacokinetic (PK) and toxicokinetic (TK) studies involve the administration of a bio-therapeutic to non human primates. Dosing of cynomolgus monkeys with a fully human monoclonal antibody-based therapeutic drug leads to an immune response which can impact PK profiles. Based on the nature of the immune response generated, anti-drug antibodies (ADA) can have binding or neutralizing activities. The former can contribute to abnormal PK by clearing or enabling the persistence of the drug in circulation in the form of immune complexes, while the latter can bind to idiotype and impact efficacy. In order to characterize the immune responses to the drug, we have assessed ADA and T helper-cell functional responses following dosing of 8 cynomolgus monkeys. Six of the 8 dosed animals were positive for binding antibodies to the F(ab)'2; reactivity towards the Fc was positive in 5 of the 6 animals. Animals that were reactive to the F(ab)'2 demonstrated an enhanced clearance of the drug (CL). The functional T helper cell responses to the idiotypic region of the antibody, irrelevant Fc region and the whole antibody was evaluated in an IFN-γ ELISPOT assay. Three animals showed an effector T cell response in the form of IFN-γ secreting memory T cells to the idiotypic region of the biotherapeutic. A strong humoral response was also observed. Hence, monitoring of the ADA and T helper cell responses can provide additional insight into the mechanism of induction of immune responses to therapeutic proteins in preclinical studies.

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