Preliminary Results of a Phase 1 Trial Evaluating MRG-106, a Synthetic microRNA Antagonist (LNA anti.miR) of microRNA-155, in Patients with CTCL

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Abstract

Introduction and Objectives
MicroRNAs (miRNAs) are small, non-coding RNA molecules that can regulate the expression of multiple genes and are associated with multiple diseases. The current study aims to evaluate the safety and preliminary efficacy of a synthetic microRNA antagonist (LNA anti.miR) of microRNA-155 (MRG-106) in patients with cutaneous T-cell lymphoma (CTCL) who have had an inadequate response to conventional therapies. In this phase 1 study, a patient with at least five CTCL lesions on any body site was enrolled and biopsied. Lesions were treated with a single 0.06% MRG-106 topical formulation 5 days a week for 6 weeks. Cytokine and blood samples were collected before and after treatment with MRG-106. Changes in the expression of miR-155 and the related inflammatory pathways were graphically assessed with Nanostring and RT-qPCR. IRF4 and TAF1H levels were determined with Nanostring, and the marker of CD4:CD8 ratio was determined with flow cytometry.

Study Objectives and Design
The primary objective of the study is to investigate the safety and tolerability of multiple patients treated with MRG-106 for 6 weeks. The study included 20 patients with CTCL at 3 study sites in the United States. Each patient was treated with MRG-106 5 days a week for 6 weeks. Tumor biopsies were collected before and after treatment for the analysis of cytokine and gene expression levels. Cytokine and blood samples were collected before and after treatment with MRG-106. Changes in the expression of miR-155 and the related inflammatory pathways were graphically assessed with Nanostring and RT-qPCR. IRF4 and TAF1H levels were determined with Nanostring, and the marker of CD4:CD8 ratio was determined with flow cytometry.

Primary Objective
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Secondary Objectives:
- Characterize the pharmacokinetics profile of MRG-106
- Evaluate the pharmacodynamics of MRG-106 in tumor biopsies
- Evaluate the biomarker signature of MRG-106
- Investigate the effects of MRG-106 on immunity, as Part 2

Exploratory Analyses of Tumor Biopsies

Key findings:
- The expression of miR-155 was significantly decreased in MRG-106 treated lesions compared to untreated lesions.
- The CD4:CD8 ratio was increased in MRG-106 treated lesions compared to untreated lesions.
- The expression of IRF4 was increased in MRG-106 treated lesions compared to untreated lesions.
- The expression of TAF1H was increased in MRG-106 treated lesions compared to untreated lesions.

Conclusion:
- MRG-106 treatment was well tolerated and demonstrated a favorable safety profile.
- MRG-106 treatment led to a significant reduction in the expression of miR-155, which is associated with the inflammatory process.
- The CD4:CD8 ratio was increased, indicating a shift towards a more beneficial immune response.
- The expression of IRF4 and TAF1H was increased, suggesting a potential role in the regulation of the immune response.

Reference: