Introduction

• Cutaneous T-Cell Lymphomas are rare, life altering forms of Non-Hodgkin’s Lymphoma presenting in the skin; the most common form, Mycosis Fungoides type Cutaneous Lymphoma (MF-CTCL) affects approximately 20,000 people in the U.S. Early stage MF-CTCL is confined to the skin, chronic and slowly progressing
• For many patients with MF-CTCL, pruritus is a major concern, significantly affecting quality of life
• Histone deacetylase (HDAC) enzymes catalyze removal of acetyl groups from lysine side chains in histones and other proteins
• MF-CTCL is sensitive to HDACis, which causes cell cycle arrest and cell death
• Synoptic histone deacetylase inhibitors (HDACi) can be efficacious, but toxicity is problematic for MF-CTCL patients
• Remetinostat is a unique topical HDACi, stable in skin with rapid breakdown by esterases in human blood (~5 – 4 min)
• A confirmed CAILS ORR of 40% was observed in the 1% BID treatment arm in a PH2 open-label study of 6-12 months duration
• Phase 2 data indicate a potential benefit of remetinostat, in addition to promising CAILS ORR, of a dose-dependent clinically meaningful reduction (CMRP) in pruritus for MF-CTCL without the typical systemic adverse effects of oral or intravenous HDACi

Hypothesis

Remetinostat will have an anti-pruritic effect, in addition to a significant anti-tumour effect, when applied topically to MF-CTCL lesions, without the systemic adverse effects of oral or intravenous HDAC inhibitors

Methods

A phase 2 open-label, multi-centre, randomized, 3 arm study to evaluate the efficacy and safety of remetinostat gel applied topically to specific skin lesions in patients with stage IA-IIA MF-CTCL (ClinicalTrials.gov NCT02213861) was completed.

60 patients were randomised to one of 3 treatment arms in a 1:1:1 ratio
• Remetinostat gel 1% QD
• Remetinostat gel 0.5% BID
• Remetinostat gel 1% BID

Standard inclusion/exclusion criteria were applied. Concomitant medications which may affect the assessment of pruritus, such as corticosteroids and antihistamines, were prohibited.

The primary endpoint was to assess the effect of remetinostat on CAILS ORR after 6 and 12 months’ dosing. Secondary endpoints included assessment of mSWAT, ORR, time to & duration of responses, safety & tolerability.

Results

Patients with clinically significant pruritus at baseline (≥30 mm) in the 1% BID treatment arm, n=10

Conclusions

• PH2 data indicate a dose-dependent response for pruritus for remetinostat in MF-CTCL patients with clinically significant pruritus at baseline
• Mean time to effect on pruritus (any response) was <80 days
• There was a high degree of maintained pruritus response with a median duration of response for all treatment arms of 5 months, plus a trend to longer duration of response in the highest dose arm
• A dose dependent response was observed for CAILS ORR reaching 40% in the 1% BID arm
• Remetinostat demonstrated a favourable safety and tolerability profile with no treatment related SAEs or systemic AEs

Safety results

Table 3 Safety and Tolerability. Treatment related adverse events seen in ≥ 2 patients, per treatment arm

Table 1 Baseline demographics by treatment arm

Table 2 Change in pruritus severity from baseline

Table 3 Summary of treatment related adverse events seen in ≥ 2 patients, per treatment arm

References