**ABSTRACT**

Background: Non-tuberculous mycobacteria (NTM) are increasingly associated with a variety of pulmonary and skin infections. Current treatment can be lengthy and variably effective, often leading to the emergence of resistance. Novel therapies are needed. This study evaluated activity of SPR719 against clinical isolates of 3 different species of NTM. SPR719 is an aminoimidazole carboxamide ribonucleotide (AMC) inhibitor with broad-spectrum activity against Mycobacterium. A panel of 20 strains is being used to evaluate SPR719 activity against NTM infections.

Methods: A panel of 20 multi-drug resistant bacterial isolates of diverse geographic origin were used. 10 strains of M. ulcerans, 5 strains of M. marinum and 5 strains of M. chimaera. Bacteria were grown on Brown and Buckle slopes and colonies were suspended in distilled water at ~ 4x10^8 CFU/mL. Suspensions were diluted and approximately 4x10^5 or 4x10^6 bacteria were plated onto duplicate 7H10 agar plates + 10% OADC supplement containing SPR719, rifampin, or clarithromycin. Plates were incubated for 2 weeks at 37°C for M. marinum, 5 weeks at 37°C for M. chimaera. MIC was defined as the lowest concentration of antibiotic that inhibited visible bacterial growth compared to the negative control. In addition, M. ulcerans grown in mycobacterial growth indicator tubes (MGIT), each tube was inoculated with 4x10^6 bacteria. Tubes were incubated for 3 weeks at 37°C before reading fluorescence by manual read. The MIC was defined as the lowest concentration of antibiotic that did not give detectable fluorescence.

Results: Concentration ranges at which SPR719 and comparator agents inhibited each species are summarized below. Table 1 shows the MIC range for SPR719 and comparator agents. SPR719 inhibited all isolates tested with MICs of 0.125-1 mg/L. SPR719 is an orally bioavailable phosphodiester prodrug of SPR719, a novel aminoimidazole carboxamide (AMC) inhibitor with broad-spectrum activity against Mycobacterium. A panel of 20 strains is being used to evaluate SPR719 activity against NTM infections. SPR719 was assessed for activity against rare NTM species Mycobacterium ulcerans, Mycobacterium marinum, and Mycobacterium chimaera utilizing MGIT and agar methods.

**METHODS**

**RESULTS**

**CONCLUSIONS**

In Vitro Activity of SPR719 against Non-Tuberculous Mycobacterium Strains of Mycobacterium ulcerans, Mycobacterium marinum, and Mycobacterium chimaera

S. Pidot, 1 T. Stinear, 1 T. Lister, 2* and A. Rubio 2

1Peter Doherty Institute for Infection and Immunity, University of Melbourne, VIC, Australia; 2Spero Therapeutics, Cambridge, MA, USA

Figure 1. Structure of SPR720 (left) and SPR719 (right)

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Table 1 shows the MIC range and MIC<sub>50</sub> of SPR719 and comparator agents, rifampin and clarithromycin, against a collection of isolates from the NTM species M. ulcerans, M. marinum, and M. chimaera. SPR719 exhibits potent, broad-spectrum MICs against all species and isolates tested. Additionally, SPR719 comparing favorably to rifampin and clarithromycin across the isolates examined.

**RESULTS**

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SPR719 exhibited potent activity against all species and strains of NTM assessed. Importantly, SPR719 demonstrated similar potency compared to clarithromycin and rifampin, indicating the potential for SPR719 to be utilized as a novel, potentially better tolerated oral treatment option for infections resulting from such Mycobacteria.