IDCases 33 (2023) e01843

Contents lists available at ScienceDirect

IDCases

journal homepage: www.elsevier.com/locate/idcases

Letter to the Editor

Safety and tolerability of long-term use of omadacycline in the treatment of *Mycobacterium abscessus* infections

ARTICLE INFO

Keywords
M. abscessus
Tetracycline
Tolerability

To,
The Editor,
IDCases.

We read the case report and review of literature by Siddiqa et al. [1] describing the therapeutic outcomes of omadacycline-containing combination regimens used to treat *Mycobacterium abscessus* infections in five patients, including one with pulmonary lung disease. All five patients were initially treated with regimens containing tigecycline that was later switched to omadacycline due to the adverse side effects. The dose of omadacycline ranged between 150 mg PO twice daily to 450 mg loading dose, followed by 300 mg PO daily. The omadacycline therapy ranged between three to six months. The authors report that one patient (20 %) encountered an adverse event while on omadacycline combination therapy; clinical success was reported in 5/5 (100 %) patients. However, we could not identify the number of patients with microbiological cure.

The study by Siddiqa et al. [1] is important in several aspects. The optimal treatment regimen and duration of therapy to treat *M. abscessus* infection are not defined [2]. Tigecycline is included in the regimen, as reported in these five cases, and is associated with severe side effects. Thus, omadacycline, a new tetracycline class of antibiotic, due to its potent *in vitro* and *in vivo* activity against *M. abscessus,* appears to be an attractive replacement for tigecycline [3–6]. Recently, several investigators reported clinical success in treating *M. abscessus* infection with omadacycline-containing regimens [1,7–9]. However, until recently, there was a lack of pharmacokinetics/pharmacodynamics evidence to determine the omadacycline clinical dose to treat *M. abscessus* infections, including pulmonary disease. A recent study [6] using the *in vitro* preclinical hollow fiber model of *M. abscessus* and computer-aided clinical simulations determined that a loading dose of 450 mg PO for two days followed by 300 mg PO daily was the optimal omadacycline dose. The authors also performed a retrospective study comparing the safety and efficacy of omadacycline *versus* other tetracyclines (including tigecycline). Microbiological cure and clinical improvement were observed in 8/10 (80 %) and 8/8 (100 %) patients, respectively, compared to the tigecycline-containing regimens with microbiological cure and clinical improvement in 1/9 (11 %) and 5/9 (55.5 %) patients, respectively [6]. In comparison, therapy discontinuation due to drug toxicity was observed in 3/9 (33.3 %) patients receiving a tigecycline combination *versus* no reported toxicity with an omadacycline combination regimen [6].

Regarding the prolonged, the omadacycline combination therapy in the study by Siddiqa et al. ranged between three to six months [1]. This is similar to the study by Singh et al. [6], where one patient was also prospectively enrolled, and microbiological cure and symptom improvement were reported after three months of the therapy. The patient remained relapse-free at 12-month receiving an omadacycline combination regimen, and no adverse event was reported with prolonged use.

In summary, the case series by Siddiqa et al. [6] adds to the growing body of evidence that omadacycline is tolerable and safe for long-term use to treat *M. abscessus* infection. More studies are required to identify the optimal combination, clinical dose, susceptibility breakpoint, and therapy duration. To this end, preclinical models, computer-aided clinical trial simulation studies, and mathematical models developed using the clinical data could be helpful in reducing time and resources as well as avoiding unnecessary risks to the patients.

Author contributions

All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work, and have given their approval for this version to be published. SS wrote the first draft of the manuscript. TG read, edited, and approved the final version for publication.

Funding

None.

Conflict of interest

TG founded and is president and CEO of Praedicare Inc., a preclinical and translational contract research organization, and founded Praedicare Africa Pvt. Ltd., a clinical contract research organization. SS has nothing to declare.

https://doi.org/10.1016/j.idcr.2023.e01843
Received 4 July 2023; Accepted 4 July 2023
Available online 5 July 2023

Acknowledgments

None.

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