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A case of *Lomentospora prolificans* (LoPro) treated with the novel antifungal olorofim

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Abstract third-party references: F2G Ltd

Background: LoPro is difficult to treat with currently approved antifungals. Only voriconazole is approved for the treatment of LoPro and mortality remains high despite combination therapy and prolonged therapy is common. Olorofim is a novel antifungal agent of the orotomide class, acting via inhibition of the enzyme dihydroorotate dehydrogenase. Olorofim has shown strong in vitro and in vivo inhibition of LoPro.

Materials/methods: Case summary: Following bilateral breast enhancement in August 2018, an otherwise healthy 49-year-old woman from rural Western Australia developed infection of her right implant with *L. prolificans* that spread to adjacent soft tissues, rib and sternum. Implant removal (October 2018), repeated debridement, hyperbaric oxygen, voriconazole, terbinafine, miltefosine, posaconazole, and anidulafungin were employed serially, and in combination; with no control of the infection. She was transferred to Sydney and enrolled in an open-label study of the novel antifungal olorofim in November 2018 (ClinicalTrials.gov Identifier: NCT03583164), with continuing surgical debridement as needed.

Results: She was treated from 29 Nov 2018 to 16 Oct 2019 (322 days) with olorofim, initially at a dose of 60 mg twice daily. Gradual healing of the surgical site occurred with wound closure in July 2019. Wound cultures were intermittently positive for LoPro prior to wound closure, but olorofim MICs of these isolates remained at 0.25 ug/ml throughout. Because of blood trough levels at the lower end of the target range, the dose was increased to first 90 mg, and then 120 mg twice daily. Olorofim was well tolerated throughout.

Conclusions: In this case, a progressive, disfiguring, and potentially life-threatening chest wall infection due to LoPro that was unresponsive to all available therapies, however improved steadily on olorofim. In addition, olorofim was well tolerated during the extended duration required to control this complex infection.

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