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Olorofim for a case of severe disseminated Lomentospora prolificans infection

Shio Yen Tio*[1;2], Karin Thursky[1;2], Gwyneth Ng[2], John H. Rex[3], Dennis Carney[1;2], Monica Slavin[1;2]

[1]*The Royal Melbourne Hospital, Parkville, Australia*, [2]*Peter MacCallum Cancer Centre, Melbourne, Australia*, [3]*F2G Ltd, Eccles, United Kingdom*

Abstract third-party references: F2G, Ltd.

Background: Though rare, invasive *Lomentospora prolificans* infection causes significant morbidity and mortality particularly in immunocompromised patients. Mortality rate is least 65%, and near 100% if infection becomes disseminated. We describe a case of disseminated *Lomentospora prolificans* infection in an immunosuppressed patient who failed to respond to conventional therapy, and was commenced on Olorofim under clinical trial (NCT03583164).

Case report: A 56-year-old lady developed disseminated *Lomentospora prolificans* infection following HyperCVAD cycle-1b for T-cell acute lymphoblastic leukemia (T-ALL), including fungaemia, endophthalmitis, lumbar spine (L4/5 vertebrae) and presumed pulmonary involvement [avid pulmonary nodule on Positron Emission Tomography (PET)]. Voriconazole and terbinafine were immediately started. She was unable to achieve therapeutic voriconazole levels despite measures to augment levels, and had worsening PET uptake in the lumbar spine. *Lomentospora prolificans* was again isolated from lumbar vertebral biopsy after 3 months of combination regime. Failure of medical therapy prompted surgical debulking and spine stabilisation surgery.

Patient then developed new PET uptake at aortic root and aortic valve five months after spinal surgery. Serial echocardiography showed progressive moderate to severe aortic regurgitation. Eleven months into management of the infection, Olorofim was started at loading dose 180mg followed by 60mg twice daily (BD), and later increased to 90mg BD as guided by drug levels. Serial PET scan over six months demonstrated improvement in uptake at aortic root and lumbar spine, despite needing radiotherapy and Pralatrexate to control relapsed T-ALL (Figure 1). As of November 2019 patient has been on Olorofim for a year without adverse effects. Regular therapeutic drug monitoring confirmed stable drug levels. She is well, active and has gained weight since on Olorofim. Her vision is stable and reports of no further back pain.

Conclusions: *Lomentospora prolificans* is routinely intrinsically resistant to all antifungals, hence poses a therapeutic challenge. An open-label single-arm phase IIb study of F901318 is currently underway. Olorofim monotherapy has successfully controlled a case of osteomyelitis due to this pathogen, demonstrating its potential use in treatment of resistant invasive mould infections in patients lacking suitable alternative treatment options.

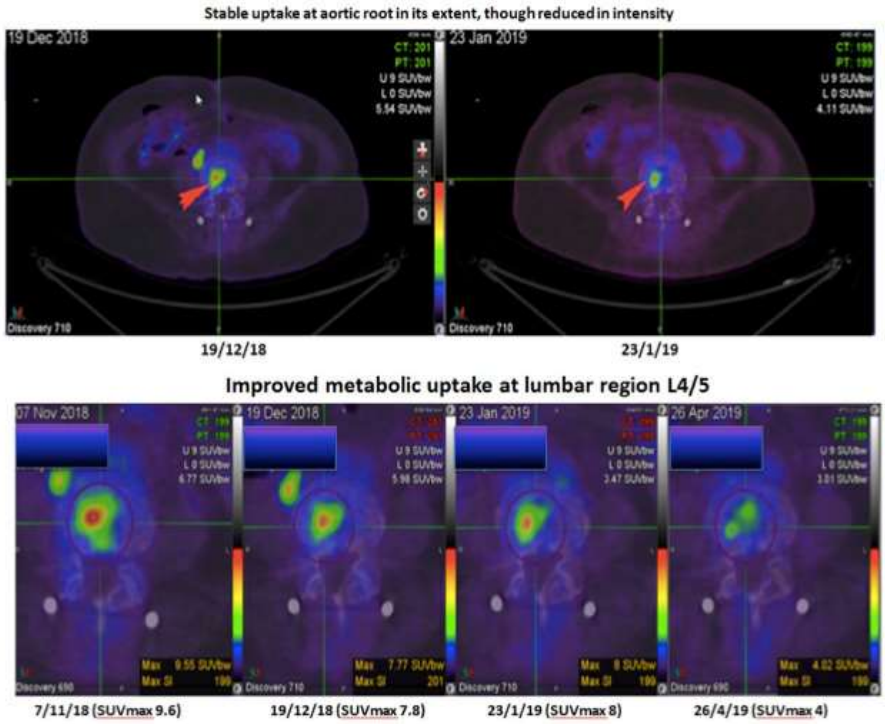

Figure 1. Serial PET showing improvement in metabolic uptake at aortic root and lumbar spine.

Presenter email address: shioyen.tio@petermac.org