

In vitro susceptibility of olorofim against 1,682 clinical *Aspergillus* isolates

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Introduction

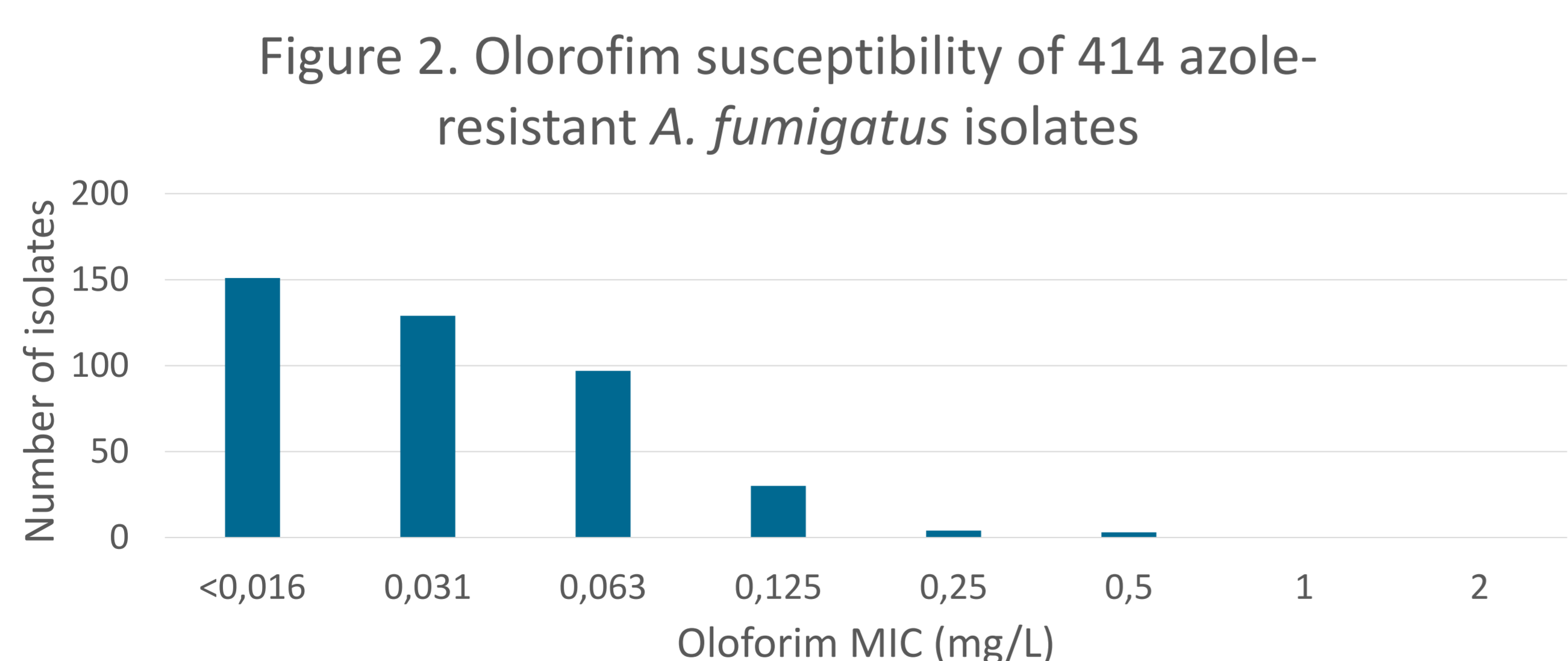
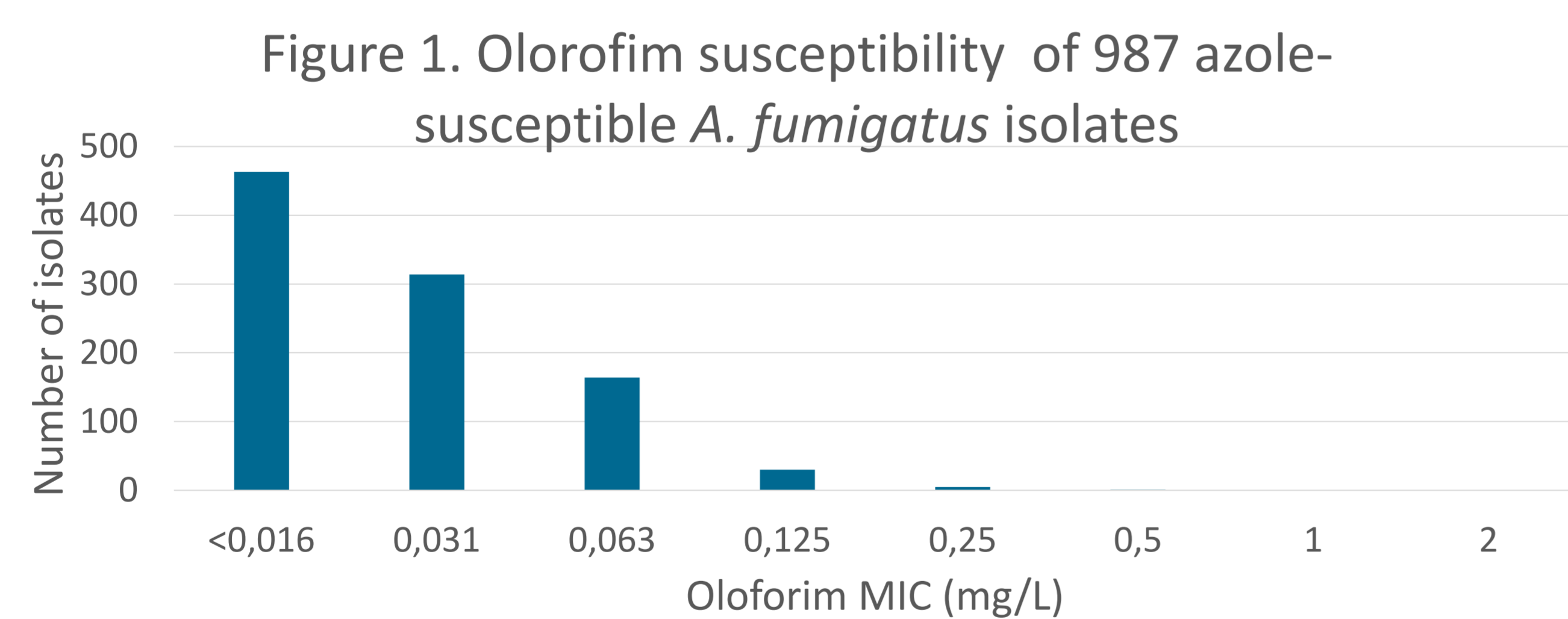
- Invasive aspergillosis is a life-threatening disease mainly affecting immunocompromised patients
- Management is complicated by the emergence of azole resistance
- Olorofim is a novel antifungal agent with potent activity against filamentous fungi such as *Aspergillus* spp., *Scedosporium* spp. and *Lomentospora prolificans*

Objective

We included olorofim in our routine MIC-panel for filamentous fungi and analysed the in vitro susceptibility of olorofim against clinical *Aspergillus* isolates received in our laboratory between May 2017 and March 2019

Results

- The in vitro MICs of clinical *A. fumigatus*, *A. flavus* species complex, *A. terreus* species complex, *A. niger* species complex, *A. versicolor* species complex were found to be uniformly <1mg/L.
- Figures 1 and 2 show the MIC distributions of azole susceptible and azole resistant *A. fumigatus* isolates. The MIC distributions, and Geometric mean MICs (See Table) are very similar for both groups
- A small number of Isolates belonging to the *Aspergillus aspergillus* species complex (*A. hollandicus*, *A. glaucus*, *A. chevalieri*) were found to have elevated MIC's: 1 isolate with a MIC of 1 mg/L and 5 with a MIC of >2 mg/L).



*Susceptibility of *A. fumigatus* isolates with MICs ≥ 0.25 mg/L was <0.25 mg/L in repeated testing

Material and Methods

The in vitro activity of olorofim was tested against 1,682 clinical *Aspergillus* isolates (987 azole-susceptible *A. fumigatus* isolates, 414 azole-resistant *A. fumigatus*, 72 *A. flavus* species complex (SC), 32 *A. nidulans* SC, 110 *A. niger* SC, 21 *A. terreus* SC, 7 *A. versicolor* SC, and 39 other species).

- Olorofim susceptibility was determined using broth microdilution based on EUCAST guidelines.
- Isolates were identified to the species complex level using microscopy and growth characteristics.

Discussion and Conclusion

- Olorofim was tested against a panel of 1682 recent clinical *Aspergillus* isolates
- Olorofim had potent in vitro activity against the commonly isolated species such as *A. fumigatus*, *A. flavus*, *A. niger*, *A. nidulans*, *A. terreus* and *A. versicolor*.
- Olorofim was equally potent against azole-susceptible and azole-resistant isolates of *A. fumigatus*.
- Olorofim was less potent against six isolates belonging to the *Aspergillus aspergillus* species complex (formerly *Eurotium*). Isolates from this species complex are rarely cultured from clinical specimens and the clinical significance of these species is highly questionable.

Species	Number of isolates	Geometric mean (GM)	MIC 50 (mg/L)	MIC 90 (mg/L)
Azole-susceptible <i>A. fumigatus</i>	987	0.027	0.031	0.063
Azole-resistant <i>A. fumigatus</i>	414	0.033	0.063	0.063
<i>A. flavus</i> SC	72	0.023	≤ 0.016	0.063
<i>A. terreus</i> SC	21	0.023	≤ 0.016	0.063
<i>A. niger</i> SC	110	0.034	0.031	0.063
<i>A. nidulans</i> SC	32	0.043	0.031	0.125

Table 1. Olorofim susceptibility of *Aspergillus* isolates