

In Vitro Activity of Manogepix and Comparators against 610 Infrequently Encountered Yeast and Mould Isolates from the SENTRY Surveillance Program (2017–2022)

Michael Huband, Michael Pfaller, Abby Klauer, Beth Hatch, Paul Bien, Mariana Castanheira

JMI Laboratories, North Liberty, Iowa, USA; Pfizer, Inc., New York, NY, USA

Introduction

- Manogepix is a potent new antifungal agent targeting the fungal Gwt1 enzyme. The prodrug of manogepix (fosmanogepix) is entering Phase 3 clinical development for treatment of candidemia/invasive candidiasis (NCT05421858).
- Manogepix has previously demonstrated potent *in vitro* activity against *Candida* spp., except *C. krusei* (renamed *Pichia kudriavzevii*), *Aspergillus* spp., and rare mould isolates.
- This study determined the *in vitro* activity of manogepix and comparators against a large collection of infrequently encountered yeast and mould isolates from the SENTRY Surveillance Program.

Materials and Methods

- Overall, 610 infrequently encountered fungal pathogens were selected from the 8,869 isolates included in the SENTRY Surveillance Program for manogepix (2017–2022).
- The fungal isolates were collected from patients in medical centres located in North America (2 countries, 32 medical centres; 43.3% overall), Europe (14 countries, 26 medical centres; 33.7% overall), Latin America (6 countries, 7 medical centres; 6.0% overall), and the Asia-Pacific region (7 countries, 12 medical centres; 17.0% overall).
- Identifications were confirmed via MALDI-TOF and sequencing based methods, as required.
- Susceptibility testing was conducted according to CLSI M27 (2017), M27M44S (2022), M38 (2017), and M38M51S (2022) guidelines.

Results

- Manogepix demonstrated potent *in vitro* activity against infrequently encountered yeasts exhibiting elevated MIC values to other drug classes:
 - Candida fermentati* (MIC_{50/90}, 0.008/0.06 mg/L), *C. guilliermondii* (MIC_{50/90}, 0.008/0.016 mg/L), *C. quercitrusa* (MIC, 0.016 mg/L), *Saprochaete clavate* (formerly *Geotrichum clavatum*; MIC_{50/90}, 0.03/0.06 mg/L), *Magnusiomyces capitatus* (MIC range, 0.016-0.06 mg/L), *Rhodotorula minuta* (MIC, 0.016 mg/L), and *R. mucilaginosa* (MIC_{50/90}, 0.03/0.12 mg/L) (Table 1).
- Manogepix was active against infrequently encountered mould isolates exhibiting elevated MIC/MEC values to azoles, echinocandins, and/or amphotericin B:
 - Coprinopsis cinerea* (MEC, 0.004 mg/L), *Fusarium solani* species complex (MEC_{50/90}, 0.016/0.03 mg/L), *Gibberella fujikuroi* species complex (MEC_{50/90}, ≤0.008/0.03 mg/L), *Lomentospora prolificans* (MEC_{50/90}, 0.03/0.06 mg/L), *Microascus cirrosus* (MEC, 0.008 mg/L), *Paecilomyces* spp. (MEC_{50/90}, ≤0.008/0.016 mg/L), *Pleurostomophora richardsiae* (MEC, 0.06 mg/L), *Sarocladium kiliense* (MEC range, 0.016-0.12 mg/L), and *Scedosporium apiospermum* / *S. boydii* (MEC_{50/90}, 0.03/0.06 mg/L) (Table 2).

Conclusions

- Manogepix demonstrated potent *in vitro* activity against a majority of the infrequently encountered yeast and mould isolates tested, including strains with elevated MIC/MEC values to other drug classes.
- Additional clinical development of fosmanogepix in difficult-to-treat, resistant fungal infections is warranted.

Acknowledgements

JMI Laboratories received compensation for services in relation to preparing the poster, which was funded by Pfizer Inc (New York, NY).

References

- CLSI. M27Ed4. Reference method for broth dilution antifungal susceptibility testing of yeasts. Wayne, PA, Clinical and Laboratory Standards Institute, 2017.
- CLSI. M27M44Ed3. Performance standards for antifungal susceptibility testing of yeasts. Wayne, PA, Clinical and Laboratory Standards Institute, 2022.
- CLSI. M38Ed3. Reference method for broth dilution antifungal susceptibility testing of filamentous fungi. Wayne, PA, Clinical and Laboratory Standards Institute, 2017.
- CLSI. M38M51Ed3. Performance standards for antifungal susceptibility testing of filamentous fungi. Wayne, PA, Clinical and Laboratory Standards Institute, 2022.

Table 1. Activity of manogepix and comparators against 318 infrequently encountered yeast isolates

Organism (no. of isolates)	MIC range or (MIC _{50/90}) mg/L				
	MGX	AND	CAS	VOR	AMB
<i>Apiotrichum mycotoxinivorans</i> (5)	0.5->2	>4	>4	0.016-1	1-2
<i>Blastobotrys adenivorans</i> (1)	0.004	0.25	0.03	1	1
<i>Candida bracarensis</i> (5) (<i>Nakaseomyces bracarensis</i>)	0.002-0.03	0.03-2	0.03-0.25	0.004-0.06	0.5-1
<i>C. digboiensis</i> (1)	0.001	1	0.12	0.06	0.5
<i>C. duobushaemulonii</i> (4)	≤0.002-0.004	0.12-0.5	0.03-0.06	0.03-0.5	2
<i>C. fabianii</i> (11) (<i>Cyberlindnera fabianii</i>)	(0.004/0.004)	(0.06/0.06)	(0.03/0.03)	(0.03/0.06)	(0.5/1)
<i>C. fermentati</i> (34)	(0.008/0.06)	(1/2)	(0.25/0.5)	(0.12/0.5)	(0.5/1)
<i>C. guilliermondii</i> (29) (<i>Meyeromyces guilliermondii</i>)	(0.008/0.016)	(2/4)	(0.25/0.5)	(0.06/4)	(0.5/0.5)
<i>C. haemulonii</i> (6)	≤0.002-0.004	0.06-0.5	0.016-0.12	0.008-0.12	0.5-1
<i>C. inconspicua</i> (6)	0.5-2	0.008-0.06	0.03-0.06	0.12-0.25	0.25-0.5
<i>C. intermedia</i> (2)	0.004-0.03	0.016-0.12	0.016-0.12	0.016	0.25
<i>C. lipolytica</i> (7) (<i>Yarrowia lipolytica</i>)	0.008-0.06	0.03-1	0.06-0.5	0.016-0.06	0.5-1
<i>C. metapsilosis</i> (39)	(0.008/0.016)	(0.25/0.5)	(0.06/0.25)	(0.016/0.03)	(0.5-1)
<i>C. nivariensis</i> (6) (<i>Nakaseomyces nivariensis</i>)	≤0.002-0.008	0.03-0.12	0.016-0.03	0.016-1	0.5-1
<i>C. norvegensis</i> (7) (<i>Pichia norvegensis</i>)	0.12-1	0.016-0.06	0.03	0.03-0.5	0.5-1
<i>C. pararugosa</i> (5) (<i>Ditina pararugosa</i>)	≤0.002	0.06-0.25	0.06	0.06-0.12	0.25-1
<i>C. pelliculosa</i> (13) (<i>Wickerhamomyces anomalus</i>)	(≤0.002/≤0.002)	(0.016/0.03)	(0.016/0.03)	(0.12/0.25)	(0.5/1)
<i>C. pseudomaemulonii</i> (2)	0.004	0.03-0.06	0.008-0.016	0.016-0.5	0.5-2
<i>C. quercitrusa</i> (1)	0.016	2	1	0.016	0.25
<i>C. rugosa</i> (<i>Ditina rugosa</i>) (5)	0.004-0.03	0.06-0.5	0.12-0.5	≤0.008-0.06	0.5-1
<i>C. spencermartinsiae</i> (1)	0.008	0.5	0.12	0.06	0.5
<i>C. sphaerica</i> (3)	0.06-0.25	0.03-0.06	0.016	0.004-0.016	0.5-1
<i>C. theae</i> (2)	0.004	0.5-1	0.25-1	0.008-0.016	0.25
<i>C. utilis</i> (7)	≤0.002-0.008	0.016-0.03	≤0.008-0.03	0.03-0.12	0.12-1
<i>Kodamaea ohmeri</i> (4)	0.008-0.016	0.12->4	0.06->4	0.03-0.25	0.25-0.5
<i>Lodderomyces elongisporus</i> (1)	0.004	0.016	0.03	0.016	0.25
<i>Magnusiomyces capitatus</i> (5)	0.016-0.06	1-4	4->4	0.06-0.25	1
<i>Ogataea siamensis</i> (1)	0.03	0.03	0.03	≤0.008	0.25
<i>Pichia cactophila</i> (5)	0.5-4	0.016-0.03	0.03-0.06	0.03-0.12	0.25-0.5
<i>P. kluyveri</i> (3)	0.06-0.12	0.008-0.016	0.03	0.06-0.25	0.12-0.5
<i>Rhodotorula minuta</i> (1)	0.016	>4	2	1	1
<i>R. mucilaginosa</i> (18)	(0.03/0.12)	(>4/>4)	(>4/>4)	(0.5/2)	(0.5/0.5)
<i>Saccharomyces cerevisiae</i> (27)	(0.016/0.03)	(0.12/0.5)	(0.12/0.25)	(0.06/0.25)	(0.5/1)
<i>Magnusiomyces clavatus</i> (14) (formerly <i>Geotrichum clavatum</i>)	(0.03/0.06)	(4/4)	(>4/>4)	(0.12/0.25)	(1/1)
<i>Trichomonascus ciferrii</i> complex (formerly <i>Candida ciferrii</i>) (1)	0.001	0.016	0.016	0.12	0.5
<i>Trichosporon asahii</i> (30)	(>2/>2)	(>4/>4)	(>4/>4)	(0.06/1)	(1/1)
<i>T. capitatum</i> (1)	0.03	2	4	0.25	1
<i>T. inkin</i> (2)	1-2	>4	>4	0.008-0.016	0.5
<i>T. loubieri</i> (1) (<i>Apiotrichum loubieri</i>)	0.5	4	4	0.008	1
<i>T. mucoides</i> (2) (<i>Cutaneotrichosporon mucoides</i>)	>2	>4	>4	0.06->8	0.5

Abbreviations: MGX, manogepix; AND, anidulafungin; CAS, caspofungin; VOR, voriconazole; AMB, amphotericin B.

Table 2. Activity of manogepix and comparators against 292 infrequently encountered mould isolates

Organism (no. of isolates tested)	MIC/MEC range or (MIC/MEC _{50/90}) mg/L				
	MGX	AND	CAS	VOR	AMB
<i>Alternaria alternata</i> (1)	1	0.12	0.06	2	1
<i>Aspergillus alabamensis</i> (1)	0.008	0.03	0.06	0.5	1
<i>A. hortai</i> (1)	0.008	0.06	0.016	0.12	4
<i>A. lentulus</i> (7)	0.008-0.016	0.016-0.12	0.016-0.06	2	2->4
<i>A. nomius</i> (1)	0.008	0.004	0.004	0.5	2
<i>A. parasiticus</i> (3)	0.008-0.016	0.008	0.004-0.016	0.25-1	2
<i>A. sclerotiorum</i> (3)	0.016-0.03	0.03-0.5	0.016-0.5	0.12-1	1->4
<i>A. sydowii</i> (1)	0.016	No data	No data	0.5	2
<i>A. tamarii</i> (3)	0.03-0.06	0.004-0.016	0.008-0.03	0.25-0.5	1-2
<i>A. thermomutatus</i> (2)	0.06-0.25	0.016-0.03	0.016-0.03	4-8	0.5-1
<i>A. tubingenensis</i> (6)	≤0.008-0.03	≤0.008-0.016	0.004-0.06	1-4	0.5-1
<i>A. udagawae</i> (1)	0.016	0.06	0.03	2	2
<i>A. unguis</i> (2)	0.03	≤0.002-0.016	0.008-0.03	0.06-0.25	2-4
<i>A. ustus</i> species complex (11)	(≤0.008/0.016)	(0.03/0.12)	(1/2)	(4/8)	(1/4)
<i>A. versicolor</i> (7)	≤0.002-0.03	0.016-0.06	0.008-0.03	0.25-1	1-2
<i>Aureobasidium pullulans</i> (2)	0.008	0.25-1	0.03-0.25	0.03	0.25-0.5
<i>Coprinopsis cinerea</i> (1)	0.004	>4	>4	0.25	1
<i>Exophiala attenuata</i> (2)	0.008-0.016	0.5-2	0.25-2	0.03-0.12	2
<i>E. dermatitidis</i> (8)	≤0.008	0.12->4	0.06->4	0.06-0.25	0.25-1
<i>Fusarium dimerum</i> species complex (1)	0.06	>4	>4	8	2
<i>F. incarnatum-equiseti</i> species complex (4)	≤0.002->8	4->8	1->8	2-4	1
<i>F. oxysporum</i> species complex (8)	0.008-4	>4	>4	2->8	1-4
<i>F. solani</i> species complex (23)	(0.016/0.03)	(>4/>4)	(>4/>4)	(8/>8)	(2/2)
<i>Gibberella fujikuroi</i> species complex (16)	(≤0.008/0.03)	(>4/>4)	(>4/>4)	(4/>8)	(2/>2)
<i>Lichtheimia corymbifera</i> (7)	4->8	4-4	>4	>8	0.5-1
<i>Lomentospora prolificans</i> (17)	(0.03/0.06)	(>4/>4)	(>4/>4)	(>8/>8)	(>2/>2)
<i>Medicopsis romeroi</i> (1)	0.03	0.016	0.12	0.25	0.5
<i>Microascus cirrosus</i> (1)	0.008	>4	>4	>8	>4
<i>Monascus ruber</i> (1)	0.03	0.06	0.03	>8	0.12
<i>Mucor</i> spp. (14) ^a	(2/>8)	(>4/>4)	(>4/>4)	(>8/>8)	(0.25/0.5)
<i>Paecilomyces</i> spp. (22) ^b	(≤0.008/0.016)	(≤0.008/0.06)	(0.03/1)	(4/>8)	(0.5/>2)
<i>Penicillium citrinum</i> (1)	0.008	0.016	0.008	>8	1
<i>P. nobense</i> (1)	0.008	0.008	0.016	0.5	1
<i>Pleurostomophora richardsiae</i> (1)	0.06	>4	>4	0.5	1
<i>Rasamsonia argillacea</i> species complex (11)	(≤0.008/0.016)	(≤0.008/0.016)	(0.016/0.016)	(>8/>8)	(1/2)
<i>Rhizomucor pusillus</i> (5)	1->8	4->4	>4	>8	0.25-1
<i>Rhizopus</i> spp. (29) ^c	(8/>8)	(>4/>4)	(>4/>4)	(8/>8)	(1/1)
<i>Sarocladium kiliense</i> (4)	0.016-0.12	4->4	0.06->4	2-4	2->4
<i>Scedosporium apiospermum</i> / <i>S. boydii</i> (46)	(0.03/0.06)	(4/>4)	(4/>4)	(1/1)	(>2/>2)
<i>S. aurantiacum</i> (7)	0.03-0.06	4->4	4->4	0.25-1	>4
<i>S. dehoogii</i> (2)	0.03-0.06	8	>8	1-2	>2
<i>S. minutisporum</i> (2)	0.008-0.016	1-2	0.5-1	0.25	4
<i>Scopulariopsis brevicaulis</i> / <i>S. brumptii</i> (3)	≤0.002-0.008	0.5->4	0.06-1	1->8	4->4
<i>Trichoderma longibrachiatum</i> (1)	0.06	0.008	0.008	1	4
<i>Verruconis gallopava</i> (1)	0.5	0.12	0.06	0.25	0.5

Abbreviations: MGX, manogepix; AND, anidulafungin; CAS, caspofungin; VOR, voriconazole; AMB, amphotericin B.

^a Organisms include: *Mucor circinelloides* (6), *M. circinelloides/Mucor ramosissimus* (2), *M. indicus* (1), and unsp. *Mucor* (5).

^b Organisms include: *Paecilomyces lilacinus* (7), *P. variotii* (10), and unsp. *Paecilomyces* (5).

^c Organisms include: *Rhizopus microsporus* group (16), *R. oryzae* (12), and unsp. *Rhizopus* (1).

Contact

Michael Huband
JMI Laboratories
345 Beaver Creek Centre, Suite A
North Liberty, IA 52317
Phone: (319) 665-3370 x203
Fax: (319) 665-3371
Email: michael-huband@jmilabs.com



To obtain a PDF of this poster:
Scan the QR code or visit https://www.jmi-labs.com/data/posters/ECCMID2023_Manogepix.pdf