

TECHNICAL REPORT

July 9, 2019

Microbiologic Properties of Voriconazole intravenous solution against selected pathogens was assessed and the results are conveyed here.

Disclosure: This study was funded by Richie’s Specialty Pharmacy (“RSP”) pursuant to its research agreement with the UH College of Pharmacy (“UHCOP”). RSP is owned solely by Richie Ray, R.Ph. and he serves as its Pharmacist-In-Charge. He is a 1996 graduate of the UHCOP and RSP has had a research agreement with UHCOP since May 2012. RSP promotes appropriate pharmacy practices and is an advocate for infection treatments based upon supporting clinical data such as that provided by this report.

Executive Summary: Voriconazole Intravenous Solution (“DRUG”) was tested against the identified pathogens and the results of these tests are reported as follows. Should there be only a “blue-line” reported that means the DRUG was so effective against the pathogen that the detection limit was below the assay of the experiment.

Methods overview: Methods for this laboratory study were adapted from Bearden *et al* and from FDA Docket No. FDA-1975-N-0012.^{1,2} All experiments were performed using the commercially available formulations. Reductions in bacterial counts between agents were determined using analysis of variance.

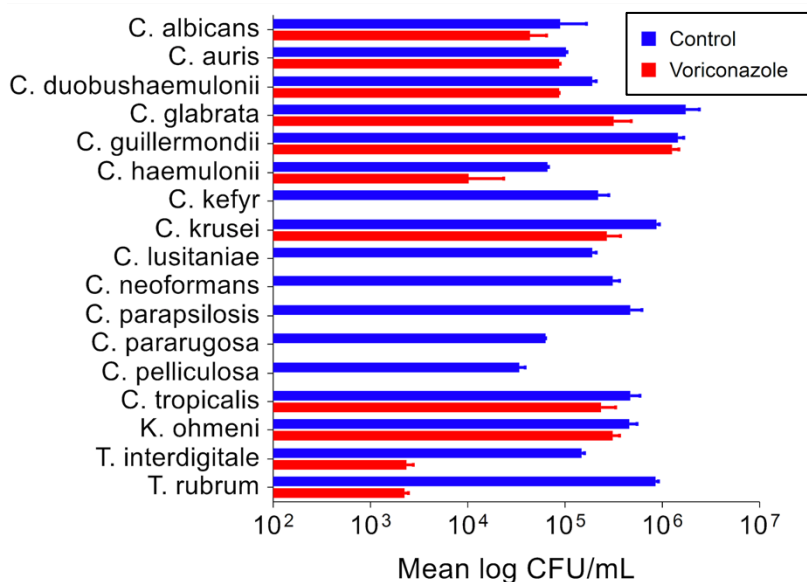
Methods and Results

Bacterial strains: Pathogens selected are defined in ATCC or CDC AR strains (Table 1, page 2).

Antimicrobial agents: Voriconazole 200mg vial (ALVOGEN NDC 47781-0466-71)

Experiment: Pre-sterilized gauze was inoculated with $1 \times 10^{7-8}$ CFU/mL of bacterial culture, allowed to incubate for 24 hours to mimic *ex vivo* infection, exposed to drug or negative control (phosphate buffer saline, PBS), and then incubated aerobically at 37°C for 48 hours. After this time, samples were cultured onto blood agar plates for colony forming unit (CFU/gauze) counts using serial dilution spread plate technique. The results are reported below. As stated above in the executive summary, should there be only a “blue-line” reported that means the DRUG was so effective against the pathogen that the detection limit was below the assay of the experiment.

Figure 1. Voriconazole was effective against multiple strains of *Candida* and non-*Candida* yeast, including killing below the level of detection* for several *Candida* species and *Cryptococcus*



Interpretation: Voriconazole was tested in two models mimicking a bandaged wound (experiment = gauze) or a non-bandaged wound (experiment = PBS). Voriconazole was effective against multiple strains of *Candida* and non-*Candida* yeast, including killing below the level of detection for several *Candida* species and *Cryptococcus*.

Table 1. Organisms Included in Testing

Organism	ATCC number
<i>Candida albicans</i>	ATCC 90028
<i>Candida auris</i>	BAA-41
<i>Candida duobushaemulonii</i>	AR 0391
<i>Candida guilliermondii</i>	AR 0590
<i>Candida glabrata</i>	ATCC 2001
<i>Candida haemulonii</i>	AR 0393
<i>Candida kefyr</i>	AR 0588
<i>Candida krusei</i>	ATCC 2159
<i>Candida lusitaniae</i>	AR 0398
<i>Candida parapsilosis</i>	ATCC 22019
<i>Candida pararugosa</i>	AR 0587
<i>Candida pelliculosa</i>	AR 0586
<i>Candida tropicalis</i>	AR 0345
<i>Cryptococcus neoformans</i>	ATCC 14116
<i>Kodameae ohmenii</i>	AR 0396
<i>Trichophyton interdigitale</i>	ATCC 9533
<i>Trichophyton rubrum</i>	ATCC 28188

References

1. Bearden DT, Allen GP, Christensen JM. Comparative in vitro activities of topical wound care products against community-associated methicillin-resistant *Staphylococcus aureus*. *J Antimicrob Chemother* 2008;62:769-72.
2. Huang DB, Okhuysen PC, Jiang ZD, DuPont HL. Enteroaggregative *Escherichia coli*: an emerging enteric pathogen. *Am J Gastroenterol* 2004;99:383-9.