Analysis of Efficacy from STRIVE Phase 2 Trial of Rezafungin Treatment of Candidemia and/or Invasive Candidiasis: Outcomes During Initial Days of Treatment

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Treatment of Candidemia 'Hit Early, Hit Hard'

- Hit Early
 - Delayed treatment predicts mortality (OR=1.42, p<0.05)¹
- Hit Hard
 - Guidelines recommend 1st-line treatment with echinocandins^{2,3}
 - Echinocandins significantly decrease mortality (27% vs 36% for azole- or polyene-based regimens; p<0.0001)⁴

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1. Ostrosky-Zeichner, et al. Med Mycology 2011;493. Cornely, et al. Clin Microbio Infect 2012;18.2. Pappas, et al. Clin Infect Dis 20164. Andes, et al. Clin Infect Dis 2012;54

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- Is This Enough?^{5,6}
 - Current doses defined before modern PK/PD era
 - Increasing echinocandin MICs (FKS mutations)
 - Evidence of inadequate drug exposure in critically ill, moderatesevere hepatic impairment, obesity, ECMO, burn

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Front-Loading and Exposure Shape for **Antifungal Efficacy**



Fungal burden in neutropenic mice following Candida albicans infection and 2 mg/kg rezafungin AND INFECTIOUS DISEASE

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Lakota, et al. Antimicrob Agents Chemother. 2017;61:e00758-17.

healthy mice, total dose 2 mg/kg

STRVE Trial Design and Subanalysis



mITT: microbiological intent-to-treat (all randomized subjects who receive any amount of study drug who had documented Candida infection Thompson et al. *Clin Infect Dis*. 2020, ciaa1380, https://doi.org/10.1093/cid/ciaa1380. Erratum *Clin Infect Dis*. doi:10.1093/cid/ciab402.

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STRVE Time to Negative Blood Culture

mITT: All randomized patients who received study drug and had documented Candida infection



Pooled rezafungin vs **Caspofungin** *p*=0.0016 posthoc log-rank test

 Rezafungin efficacy early in treatment course suggests clinical effect of high, front-loaded plasma drug exposure S

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 Rezafungin efficacy early in treatment course suggests clinical effect of high, front-loaded plasma drug exposure More pronounced effect in mITT2 suggests patients with infection at the time of treatment initiation may be more likely to benefit from potential clinical effect of front-loaded exposure

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STRVE Efficacy In Initial Days of Treatment

Patients with Candidemia Only



Online 9 – 12 July 2021

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mITT All randomized patients who received study drug and had documented Candida infection

mITT2

Patients in mITT with positive blood culture within 12h before and 72h after enrollment

Conclusions

- Rezafungin, a novel echinocandin in clinical development, demonstrates high plasma drug exposure following front-loaded, once-weekly dosing
- In the STRIVE Phase 2 trial, rezafungin demonstrated high rates of early treatment efficacy in patients with candidemia
- Rezafungin efficacy was more pronounced among patients with ongoing active infection
- Ongoing Phase 3 treatment trial (ReSTORE; NCT03667690) will provide further data regarding rezafungin efficacy and the potential clinical benefit and effect of front-loaded pharmacometrics

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