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Oral Ibrexafungerp (SCY-078) in Refractory Fungal Diseases
Interim Analysis by Pathogen of a Phase 3 Open-label Study (FURI)

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Transparency Declaration

Research grants	Actelion, Amplyx, Astellas, Basilea, Cidara, Da Volterra, F2G, Gilead, Janssen Pharmaceuticals, Medicines Company, MedPace, Melinta Therapeutics, Merck/MSD, Pfizer, Scynexis
Advice on study design or DRC or DSMB	Actelion, Allecra Therapeutics, Amplyx, Astellas, Basilea, Biosys UK Limited, Cidara, Da Volterra, Entasis, F2G, Gilead, IQVIA, Matinas, MedPace, Menarini Ricerche, Merck/MSD, Octapharma, Paratek Pharmaceuticals, Pfizer, PSI, Rempex, Scynexis, Seres Therapeutics, Tetraphase, Vical
Speaker honoraria	Astellas, Basilea, Gilead, Merck/MSD, Pfizer
Shareholder	CoRe Consulting

Innovative Medicines Initiative

ND4BB COMBACTE

National Institutes of Health

DFG

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SEVENTH FRAMEWORK PROGRAMME

European Commission

HORIZON 2020

UNIVERSITY OF LEEDS

ARLG Antibacterial Resistance Leadership Group

DZIF

Federal Ministry of Education and Research

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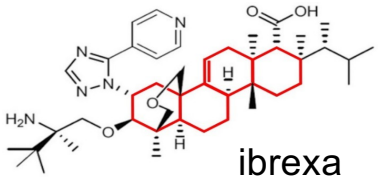
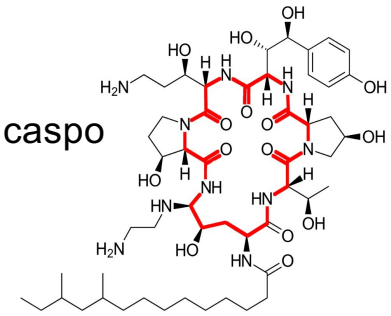
Ibrexafungerp: A Novel Triterpenoid Antifungal

Novel Glucan Synthase Inhibitor (GSI)



ibrexa

caspo



- Structurally distinct from other glucan synthesis inhibitors, e.g. echinocandins
- Different enzyme-drug interaction → lower impact of common FKS mutations
- Oral bioavailability

Key Attributes

- Activity against
  - *Candida* spp.
  - *Aspergillus* spp.
  - *Pneumocystis* spp.
- Active against azole- and most echinocandin-resistant strains
- > 500 subjects exposed
- Low risk of drug-drug interactions
- Extensive tissue distribution (V_{dss} > 8 L/kg)

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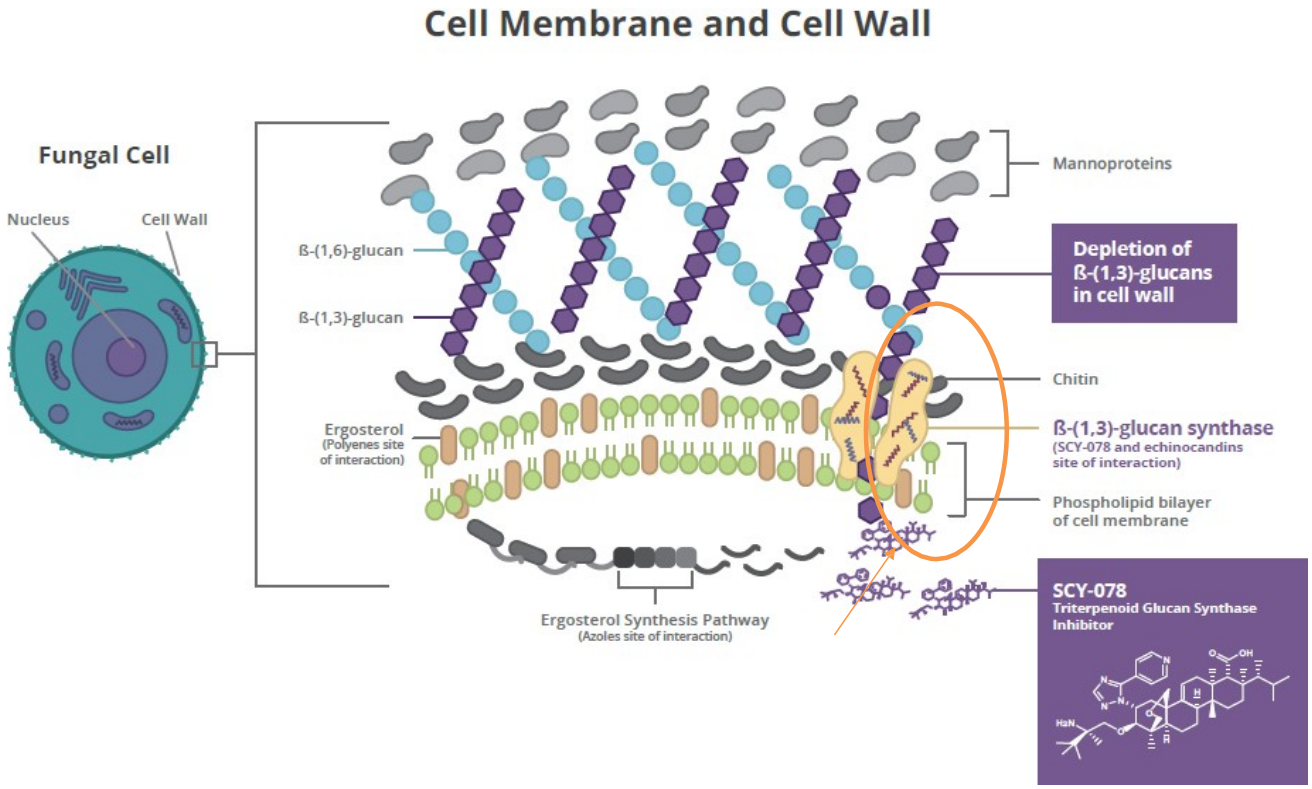
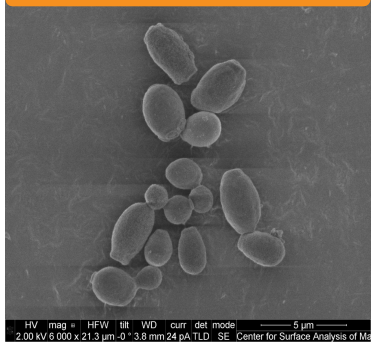
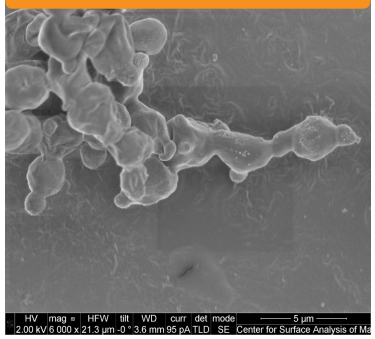
Ibrexafungerp MoA: Glucan Synthase Inhibitor



C. auris before SCY-078



C. auris after SCY-078



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FURI – Primary Objectives

- To evaluate the efficacy of oral ibrexafungerp as determined by a Data Review Committee (DRC) by assessing Global Success (composite assessment of clinical, microbiological, serological and/or radiological responses) at End of Treatment (EoT)
- To evaluate the safety of oral ibrexafungerp

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FURI – Primary Endpoints

- Efficacy measured by
  Percentage of subjects with Global Success (Complete or Partial Global Response) at the End of Treatment (EoT) visit as determined by the Data Review Committee
- Safety measured by
  Physical exam, vital signs, adverse events, electrocardiogram, and laboratory tests

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FURI – Eligible Fungal Diseases

- Acute or chronic invasive candidiasis including candidemia and/or acute or chronic severe mucocutaneous candidiasis that is
  - Refractory to or intolerant of, or has toxicities associated with at least one approved SoC antifungal treatment and/or
  - Long-term IV antifungal therapy is not feasible or desirable due to clinical or logistical circumstances or
  - If other oral antifungal alternatives are not appropriate.

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FURI – Exclusion Criteria (selected)

- CNS, heart or eye involvement
- Inappropriately controlled fungal infection source (e.g., persistent catheters, devices, identified abscess)
- AST or ALT >10 x ULN and/or total bilirubin >5 x ULN
- ANC < 500/µL at baseline
- Prohibited medications
- Known hypersensitivity to ibrexafungerp
- Pregnant or lactating

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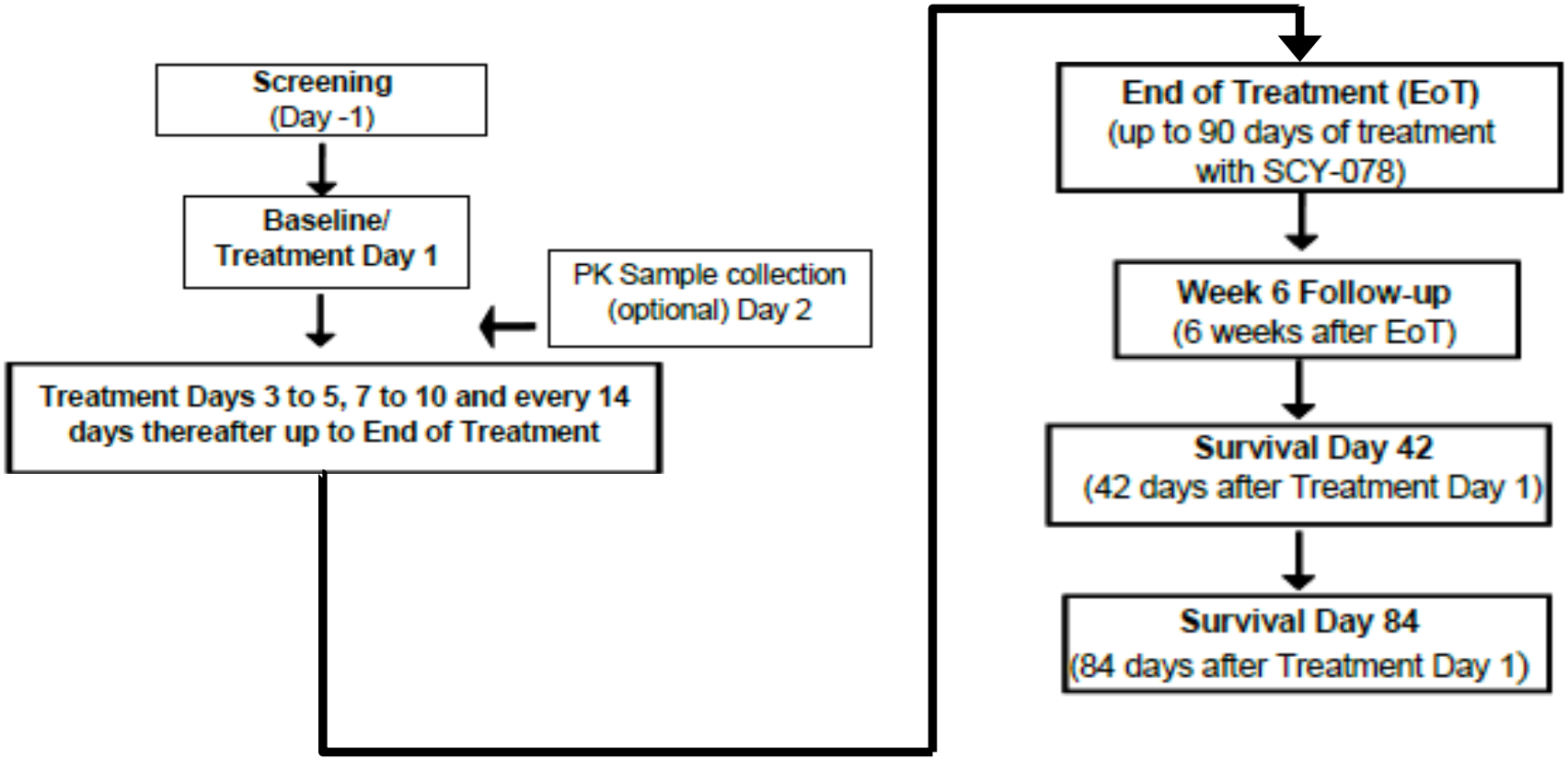
FURI – Patient Flow



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FURI – Dose Regimen

- Ibrexafungerp PO 750mg BID for 2 days

  followed by

- Ibrexafungerp PO 750 mg QD

- Duration of therapy is at investigators discretion
  - max. 90 days
  - if >90 days required → expanded access program

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FURI – DRC Review: Global Response by IFD

	Condition: # of subjects	Global Response
Mucocutaneous Candidiasis	Esophageal candidiasis: 6	CR/PR: 4 Stable: 2
	Oropharyngeal candidiasis: 2	CR/PR: 1 PD: 1
	Chronic mucocutaneous candidiasis (CMC): 1*	Stable: 1
Invasive Candidiasis	Intra-abdominal infections: 5	CR/PR: 2 Stable: 1 PD: 1 Indeterm.: 1
	Spondylodiscitis: 2*	Stable: 2
	Candidemia and endocardial infection: 1	CR/PR: 1
	Surgical wounds infection: 1	CR/PR: 1
	Mediastinitis: 1	CR/PR: 1

*One patient with CMC and one with spondylodiscitis continue therapy beyond Day-90, per investigator's request. The DRC efficacy assessment for these patients (Stable) was done based on their status at Day-90 (end of FURI participation), status and true EOT still pending

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FURI – DRC Review: Global Response by IFD

	Complete/Partial Response	Stable Disease	Progression of Disease	Indeterminate
All Patients n=20	11 (55%)	6 (30%)	2 (10%)	1 (5%)

Ibrexafungerp treatment duration:

Mean	36.4 days
Range	7-90
Median	30.5

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FURI: Global Outcome by Pathogen

Pathogen (n)	Complete/Partial Response	Stable Disease	Progressive Disease	Indeterminate
C. glabrata **(11)**	6	3	2*	0
C. krusei **(4)**	1	2	0	1
C. albicans **(3)**	2	1	0	0
C. parapsilosis **(1)**	1	0	0	0
unidentified (1)	1	0	0	0

* 1 intra-abdominal and 1 OPC in a HIV+ patient with persistent CD4<10

** One case “unable to determine”. The patient had an intra-abdominal infection that discontinued the study due to a non-drug related AE after 7 days of ibrexafungerp therapy.

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FURI – Interim Safety

- Oral ibrexafungerp was generally well-tolerated
- No deaths were reported due to progression of the fungal infection
- One death was reported due to bacterial liver abscess
- The most common drug related AEs were mild to moderate diarrhea, nausea and less frequently vomiting

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ClinicalTrials.gov Identifier: NCT030599902

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Ibrexafungerp at ECCMID 2019

Favourable Clinical Outcome of Two Patients with *Candida* spp Spondylodiscitis treated with Oral Ibrexafungerp (formerly SCY-078) from the FURI Study

- Presenter: Philipp Koehler, Oliver Cornely
- Date and Time: Saturday, April 13, from 15:30-16:30 CET
  Oral Presentation #: L0033
- Session: Other issues and diverse late breaker aspects

Use of ibrexafungerp (formerly SCY-078) to Treat Severe Azole-refractory Oesophageal Candidiasis: A Case Report from the FURI Study.

- Presenter: Jose Vazquez
- Date and Time: Saturday, April 13, from 15:30-16:30 CET
  Poster Presentation #: P0125
- Session: Clinical pharmacokinetics, treatment strategies and prescribing of antifungals

Successful Treatment of Two Patients with *Candida auris* Candidemia with the Investigational Agent, Oral Ibrexafungerp (formerly SCY-078) from the CARES Study

- Presenter: Deven Juneja, MD
- Date and Time: Saturday, April 13, from 15:30-16:30 CET
  Poster Presentation #: L0028
- Session: Other issues and diverse late breaker aspects