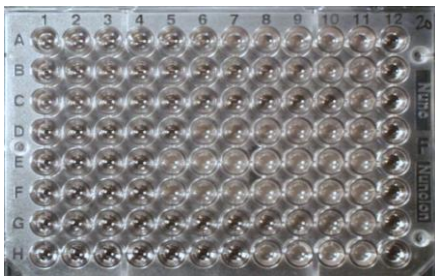


# EUCAST Susceptibility Testing of Rezafungin (CD101): Activity against *Candida auris*

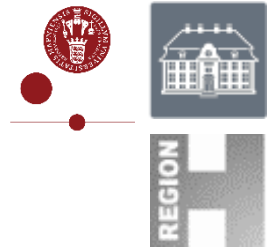
Karin Meinike Jørgensen, Anuradha Chowdhary, Jacques F. Meis, **Maiken Cavling Arendrup\***

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\*Disclosures: Research grants/contract work (Paid to SSI): Amplyx, Basilea, Cidara, F2G, Gilead, Pfizer & T2Candida. Speaker honoraria: Astellas, Basilea, Gilead, MSD, Novartis, Pfizer & T2Candida, Chair(wo)man for EUCAST-AFST, Past advisory board ( $\leq$  2014): MSD, Pcovery, Pfizer

# Background and Aim



## ❖ Rezafungin (CD101)

- new echinocandin; long-acting → weekly dosing

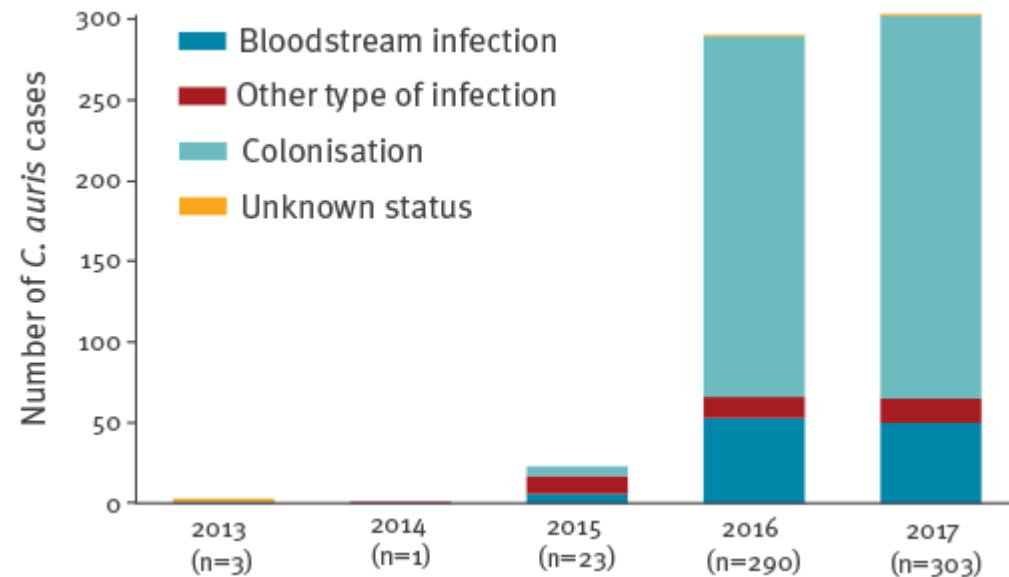
## ❖ *Candida auris*

- rapidly emerging as a significant cause of nosocomial infections
- often azole or multidrug resistant
- no EUCAST rezafungin MIC data published so far for *C. auris*

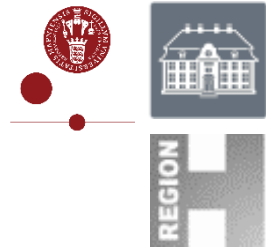
## ❖ Aim:

- investigate *in vitro* susceptibility of *C. auris* using EUCAST E.Def 7.3.1

2013-17: 620 *C. auris* cases in Europe\*



# Materials and Methods



❖ 122 Indian clinical *C. auris* isolates

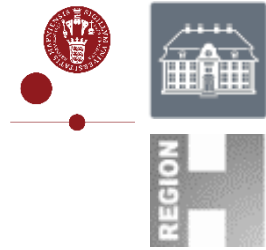
❖ *C. auris* reference strains

- KCTC17809
- KCTC17810
- JCM15448

❖ EUCAST E.Def 7.3.1<sup>1</sup>

- Cell-culture treated microtitre plates (Nunc, ThermoFisher Scientific, cat. no. 167008)
- Rezafungin and comparators
  - anidulafungin, micafungin, amphotericin B, fluconazole, isavuconazole, itraconazole, posaconazole and voriconazole
- Generating 1125 MICs in total

# Results: Overview EUCAST Rezafungin MICs

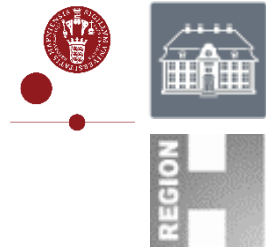


## • MICs (mg/L) against *C. auris*

	0.016	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	Range	Modal MIC	MIC <sub>50</sub>	MIC <sub>90</sub>
Clinical isolates			3	22	<b>63</b>	16	7	3		6	2	0.06-16	0.25	0.25	1
Ref strains															
CBS12372			1												
CBS12373			1												
CBS10913			1												

MIC<sub>50</sub> is highlighted in bold; Modal MIC underscored

# Results: Overview EUCAST Rezafungin MICs



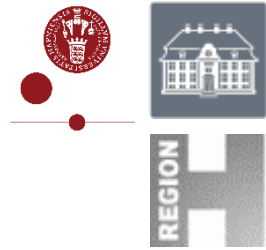
## • MICs (mg/L) against *C. auris*

	0.016	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	Range	Modal MIC	MIC <sub>50</sub>	MIC <sub>90</sub>
Clin isolates			3	22	<u>63</u>	16	7	3		6	2	0.06-16	<u>0.25</u>	<b>0.25</b>	1
Ref strains															
CBS12372			1												
CBS12373			1												
CBS10913			1												

For comparison\*:  
 Modal MIC for 179 DK *C. glabrata* blood stream isolates is similar:  
**0.125 mg/L**

MIC<sub>50</sub> is highlighted in bold; Modal MIC underscored; Tested concentration range indicated in white

# Results: Overview EUCAST MICs

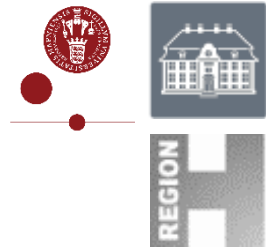


## • Rezafungin and comparators against *C. auris*

	0.004/ <0.008	0.008	0.016	0.03	0.06	0.125	0.25	0.5	1	2	>2/4	8	16	32	64	128	256	>256
Rzf					3	22	<u>63</u>	16	7	3		6	2					
AMB								14	<u>108</u>									
Anf			1	12	<u>34</u>	<b>30</b>	12	12	11	2	8							
Mfg				5	30	<u>69</u>	9				8							
Flu									1				4	10	6	14	<b>33</b>	<u>54</u>
Isa	20	1	1	19	9	<b>19</b>	<u>21</u>	<u>21</u>	6	5								
Itr	2	2	9	5	14	<b>34</b>	<u>36</u>	19	1									
Psc	17	5	19	<u>34</u>	32	11	3	1										
Vor	1			1	1	16	13	<b>34</b>	<u>38</u>	13	5							

MIC<sub>50</sub> is highlighted in bold; Modal MIC underscored; Tested concentration range indicated in white

# Results Overview EUCAST MICs Rezafungin and comparators

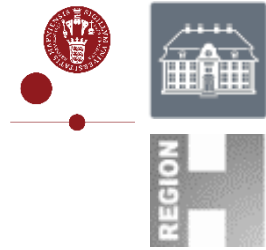


Against *C. auris* – *C. glabrata* ECOFFs applied\*

	0.004/ <0.008	0.008	0.016	0.03	0.06	0.125	0.25	0.5	1	2	>2/4	8	16	32	64	128	256	>256
Rzf					3	22	<u>63</u>	16	7	3		6	2					
AMB								14	<u>108</u>									
Anf			1	12	<u>34</u>	<b>30</b>	12	12	11	2	8							
Mfg				5	30	<u>69</u>	9				8							
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Isa	20	1	1	19	9	<b>19</b>	<u>21</u>	<u>21</u>	6	5								
Itr	2	2	9	5	14	<b>34</b>	<u>36</u>	19	1									
Psc	17	5	19	<u>34</u>	32	11	3	1										
Vor	1			1	1	16	13	<b>34</b>	<u>38</u>	13	5							

Colours indicate classification using ECOFFs for *C. glabrata*: Blue: wt; \**C. auris* and *C. glabrata* are phylogenetically closely related

# Results – High Rezafungin MIC



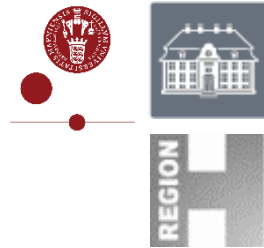
❖ 8 (6.6%) isolates with high rezafungin MICs

- all pan-candin cross resistant
- all fluconazole resistant
- but susceptible to amphotericin B

CD101 (mg/L)	ANF (mg/L)	MFG (mg/L)	FLC (mg/L)	AMB (mg/L)
8	>32	>32	>256	1
8	>32	>32	>256	1
8	>32	>32	>256	1
8	>32	>32	>256	1
8	>32	>32	>256	1
8	>32	>32	>256	1
16	4	>32	>256	1
16	>32	>32	>256	1



# In conclusion



- ❖ Rezafungin showed promising activity against the clinical *C. auris* isolates
- ❖ On a mg/L basis rezafungin was more or equally active (within 1 dilution) than
  - anidulafungin, micafungin, amphotericin B, fluconazole and voriconazole
- ❖ Modal MIC and MIC<sub>50</sub> was similar to that against *C. glabrata* (within 1 dilution)
- ❖ 6.6% presented elevated MICs showing cross-resistance to the included echinocandins and to fluconazole
- ❖ Rezafungin may be an attractive alternative to currently available echinocandins, allowing patients to be discharged if clinically possible.

# Acknowledgements:

## Co-authors

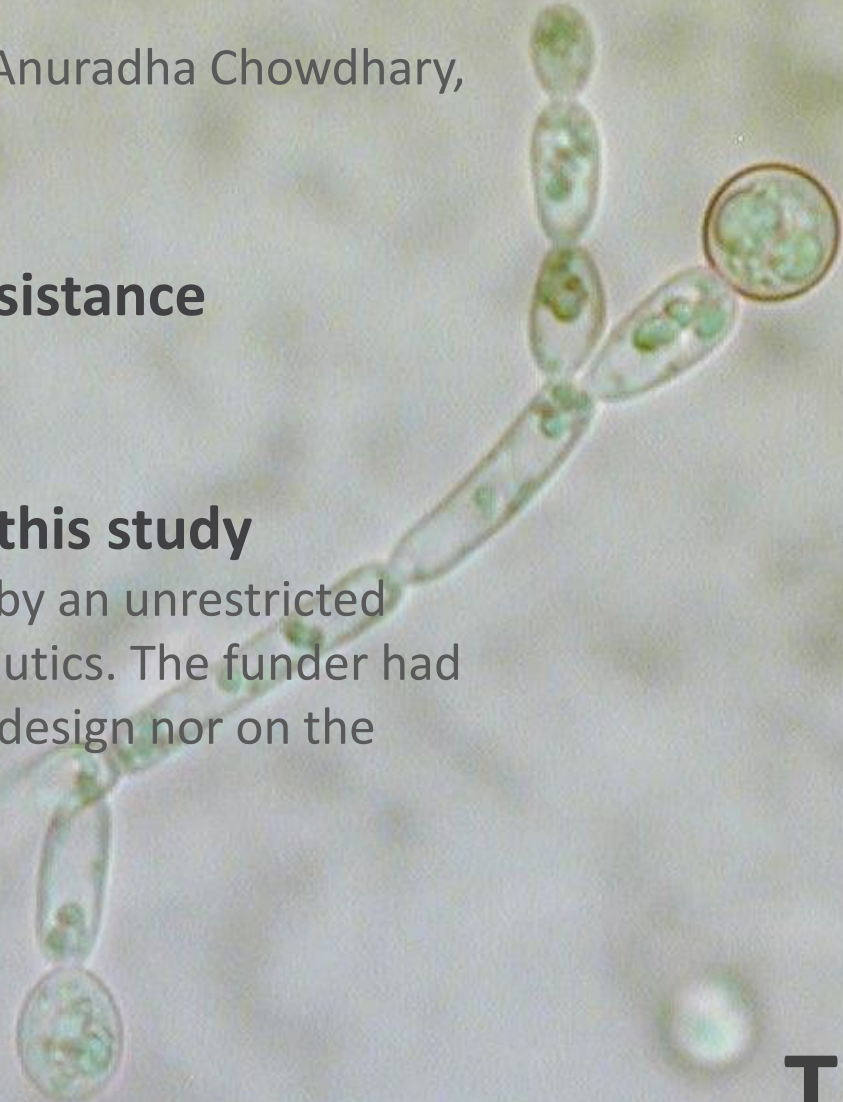
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Jacques F. Meis

## Excellent technical assistance

Birgit Brandt

## Financial support for this study

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**Thank you for  
your attention**