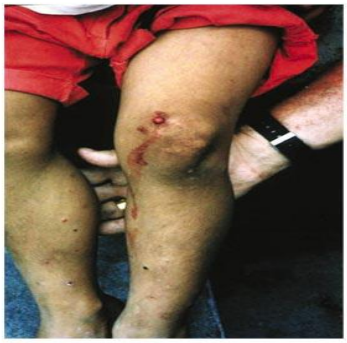
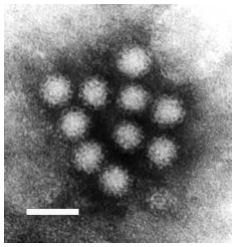
Was kommt auf uns Zu—Bakterien, Viren, Pilze und mögliche Therapien





Günter Weiss

Universitätsklinik für Innere Medizin II

Infektiologie, Immunologie, Rheumatologie, Pneumologie

Medizinische Universität-Landeskrankenhaus, Innsbruck

Reise nach Indien, dort 3 Tage im KH wegen eines Unfalls; zwei Wochen später Aufnahme in Innsbruck bei hohem Fieber, Urosepsis, multiple Abszesse in der Muskulatur

Kultureller Erregernachweis:

Aerobe Kultur — Wachstum nachgewiesen

Antibiotikaspiegel — nachgewiesen

1. ca. 10.000 Keime/ml **Klebsiella pneumoniae**
   Screening auf Hypervirulenz negativ
   4MRGN (laut Robert Koch-Institut): multiresistentes gramnegatives Stäbchen mit Resistenz gegen 4 von 4 definierten Antibiotikaklassen (Acylureidopenicilline, 3./4. Generations-Cephalosporine, Carbapeneme, Fluorochinolone)

Antibiotikum/Antimykotikum	1.
Amikacin	R
Aminopenicillin	R
Amoxicillin + Clavulansäure i.v.	R
Amoxicillin + Clavulansäure p.o.	R
Cefiderocol	R
Cefepim	R
Cefpodoxim	R
Ceftazidim	R
Ceftazidim-Avibactam	R
Ceftriaxon	R
Cefuroxim - Axetil	R
Ciprofloxacin	R
Colistin	R
Ertapenem	R
Fosfomycin	R
Mecillinam	R
Meropenem	R
Meropenem-Vaborbactam	R
Imipenem-Relebactam	R
Nitrofurantoin	R
Piperacillin-Tazobactam	R
Trimethoprim + Sulfonamid	R

S = sensibel, I = sensibel bei erhöhter Antibiotika-Exposition, R = resistent

Kuenzli *et al. BMC Infectious Diseases* 2014, **14**:528
http://www.biomedcentral.com/1471-2334/14/528

BMC Infectious Diseases

RESEARCH ARTICLE Open Access

High colonization rates of extended-spectrum β-lactamase (ESBL)-producing *Escherichia coli* in Swiss Travellers to South Asia– a prospective observational multicentre cohort study looking at epidemiology, microbiology and risk factors

Esther Kuenzli[1,2*], Veronika K Jaeger[2,3], Reno Frei[4], Andreas Neumayr[2], Susan DeCrom[5], Sabine Haller[5], Johannes Blum[2], Andreas F Widmer[1], Hansjakob Furrer[6], Manuel Battegay[1], Andrea Endimiani[7] and Christoph Hatz[2,5]

Abstract

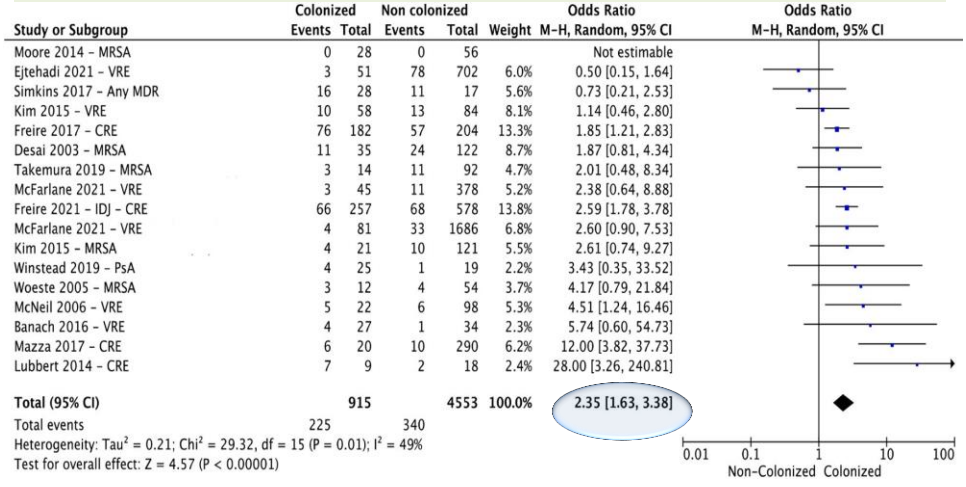
Background: International travel contributes to the worldwide spread of multidrug resistant Gram-negative bacteria. Rates of travel-related faecal colonization with extended-spectrum β-lactamase (ESBL)-producing *Enterobacteriaceae* vary for different destinations. Especially travellers returning from the Indian subcontinent show high colonization rates. So far, nothing is known about region-specific risk factors for becoming colonized.

Methods: An observational prospective multicentre cohort study investigated travellers to South Asia. Before and after travelling, rectal swabs were screened for third-generation cephalosporin- and carbapenem-resistant *Enterobacteriaceae*. Participants completed questionnaires to identify risk factors for becoming colonized. Covariates were assessed univariately, followed by a multivariate regression.

Results: Hundred and seventy persons were enrolled, the largest data set on travellers to the Indian subcontinent so far. The acquired colonization rate with ESBL-producing *Escherichia coli* overall was 69.4% (95% CI 62.1-75.9%), being highest in travellers returning from India (86.8%; 95% CI 78.5-95.0%) and lowest in travellers returning from Sri Lanka (34.7%; 95% CI 22.9-48.7%). Associated risk factors were travel destination, length of stay, visiting friends and relatives, and eating ice cream and pastry.

Conclusions: High colonization rates with ESBL-producing *Enterobacteriaceae* were found in travellers returning from South Asia. Though risk factors were identified, a more common source, i.e. environmental, appears to better explain the high colonization rates.

Death within one-year posttransplant among multidrug-resistant colonized solid organ transplant recipients.

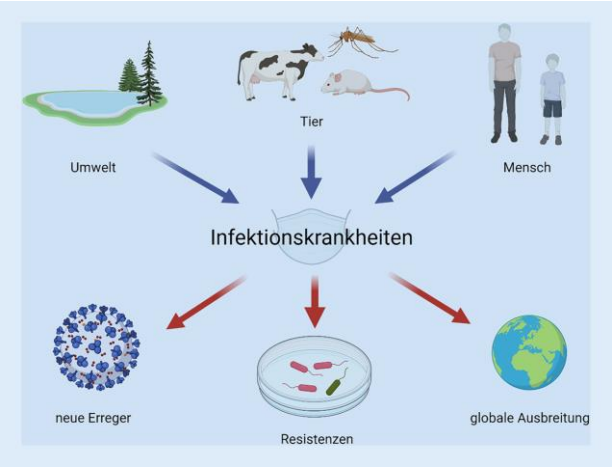


Universitätsklinik für Innere Medizin II Innsbruck
(Infektiologie, Immunologie, Tropenmedizin, Rheumatologie, Pneumologie)

Almohaya A et al. CMI 2024

Medizinische Universität Innsbruck

AB-Resistenz/Infektionen—One Health



Die Innere Medizin 3/2024

Table 1. Estimated incid… …nce and trend 2019–2023, as well as the percentage change 2019–2023, EU/EEA, 2023 [1,2]

Country	Estimated incidence[a] of *K. pneumoniae* isolates from bloodstream infections with carbapenem resistance (n per 100 000 population)			
	2019	2023	Trend[b] 2019-2023	Change (%)[c] 2019-2023
Austria	0.20	0.29	-	+45.0
Belgium	0.27#	0.47#	↑	+74.1
Bulgaria	2.24#	7.75#	↑	+246.0
Croatia	1.2#	4.53	↑	+277.5
Cyprus	2.61	9.80	↑	+275.5
Czechia	0.09^	0.26^	↑	+188.9
Denmark	0.07	0.08	-	+14.3
Estonia	0.00^	0.44^	↑	NA
Finland	0.06	0.02	↓	-66.7
France	0.22	0.13 (2022)*	NA*	NA*
Germany	0.20#	0.25#	-	+25.0
Greece	13.05#	21.44	↑	+64.3
…				4.4
…				…
…				.6
…				.2
…				…
…				.2
…				.5
…				.5
…				.0
…				.0
…				7.4
…				.0
…				1.2
…				5.8
…				:40
…				.3.3
Sweden	0.03	0.12	↑	+300.0
EU[d]	**2.52**	**3.97**	↑	**+57.5**

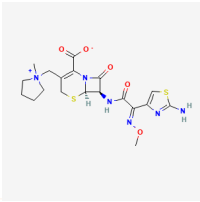
Table 2. Comparison of consumption of newly approved antimicrobials with activity against carbapenem-resistant Enterobacterales, polymyxins and carbapenems, EU/EEA, 2023

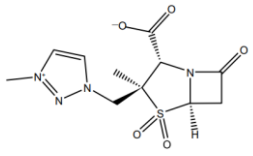
Name	EU/EEA consumption volume (number DDD)	EU/EEA consumption rate**** (DDD per 1 000 inhabitants per day)
Newly approved antimicrobials with activity against CRE*	652 808	0.00405
Polymyxins**	4 113 729	0.02576
Carbapenems***	11 317 105	0.07031

DDD – defined daily doses; EEA – European Economic Area; EU – European Union.
** Newly approved antimicrobials included in the calculation for this table are ceftazidime-avibactam, meropenem-vaborbactam…*

Universitätsklinik
für Innere Medizin II Innsbruck
(Infektiologie, Immunologie, Tropenmedizin, Rheumatologie, Pneumologie)
MEDIZINISCHE UNIVERSITÄT INNSBRUCK

Cefepime/Enmetazobactam (EXBLIFEP®)





Chemical structure of enmetazobactam

Pharmacodynamics

In vitro activity against MDR Enterobacterales in the presence of some β-lactamases and ESBL of the following groups: CTX-M, SHV, TEM, and VEB; no activity against bacteria producing KPC, metallo-β-lactamases or some oxacillinases

Good activity in animal models of cefepime-resistant, ESBL-producing Enterobacterales infection

Key clinical trials of cefepime/enmetazobactam (Allecra)

Drug(s)	Indication	Phase	Status	Location(s)	Identifier
Cefepime/enmetazobactam, piperacillin/tazobactam	Complex urinary tract infection (adults)	3	Completed	Global	NCT03687255; ALLIUM; EudraCT2017004868-35
Cefepime/enmetazobactam	Complex urinary tract infection (paediatric)	2	Recruiting	Europe	NCT05826990
Cefepime/enmetazobactam, cefepime	Complex urinary tract infection (adults)	2	Completed	Europe	NCT03680612; CACTUS

Universitätsklinik für Innere Medizin II Innsbruck
(Infektiologie, Immunologie, Tropenmedizin, Rheumatologie, Pneumologie)

Pubchem
Keam SJ, Drugs 2024

MEDIZINISCHE UNIVERSITÄT INNSBRUCK

JAMA | Original Investigation

Effect of Cefepime/Enmetazobactam vs Piperacillin/Tazobactam on Clinical Cure and Microbiological Eradication in Patients With Complicated Urinary Tract Infection or Acute Pyelonephritis
A Randomized Clinical Trial

Keith S. Kaye, MD; Adam Belley, PhD; Philip Barth, PhD; Omar Lahlou, PharmD; Philipp Knechtle, PhD; Paola Motta, PhD; Patrick Velicitat, MD

Table 1. Demographic and Baseline Characteristics of Patients Who Received at Least 1 Dose of Study Drug (continued)

	No. (%)	
	Cefepime/enmetazobactam (n = 516)	Piperacillin/tazobactam (n = 518)
Presence of concurrent bacteremia at baseline	41 (7.9)	30 (5.8)
Diabetes at baseline	79 (15.3)	78 (15.1)
Enterobacterales baseline pathogen, extended-spectrum β-lactamase producing	98 (19.0)	89 (17.2)

3x2,5g Cef/Enmet vs. 3x4.5 g Pip/Taz for 7 days

Table 2. Primary Outcome, Clinical Cure, and Microbial Eradication in the Primary Analysis Set

	No. (%)		
Response at visit	Cefepime/enmetazobactam (n = 345)	Piperacillin/tazobactam (n = 333)	Treatment difference, % (95% CI)[a]
Day 14[b]			
Overall success[c]	273 (79.1)	196 (58.9)	21.2 (14.3 to 27.9)
Clinical cure	319 (92.5)	296 (88.9)	3.5 (−1.0 to 8.0)
Microbiological eradication	286 (82.9)	216 (64.9)	19.0 (12.3 to 25.4)

Cefepime/Enmetazobactam (EXBLIFEP®): Key Points

An IV antibacterial fixed-dose combination of a cephalosporin and an ESBL inhibitor being developed by Allecra and ADVANZ for the treatment of infections caused by MDR Gram-negative bacteria.

Received its first approval on 22 February 2024 in the USA.

Approved in the USA for use in patients 18 years and older with cUTI including pyelonephritis and in the EU for use in patients 18 years and older with cUTI including pyelonephritis, HAP including VAP, and bacteraemia associated with any of these infections.

Universitätsklinik für Innere Medizin II Innsbruck
(Infektiologie, Immunologie, Tropenmedizin, Rheumatologie, Pneumologie)

Keam SJ, Drugs 2024
Kaye et al. JAMA 2022

MEDIZINISCHE UNIVERSITÄT INNSBRUCK

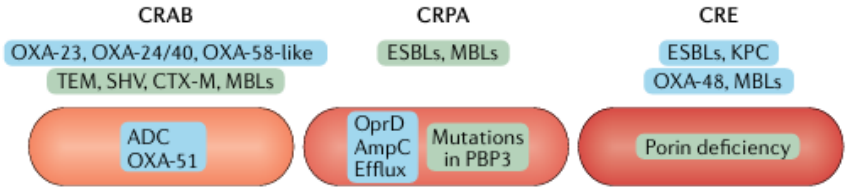


Fig. 1 | **Relevance of resistance determinants.** The resistance determinants in carbapenem-resistant *Acinetobacter baumannii* (CRAB), carbapenem-resistant *Pseudomonas aeruginosa* (CRPA) and carbapenem-resistant Enterobacterales (CRE)

Theuretzbacher et al. Nat Rev Microbiol 2020

Beta-laktamaseinhibitoren

Table 3 Activities of β-lactamase inhibitors against various β-lactamase enzymes

	β-lactamase inhibitor					
	Relebactam	Vaborbactam	Avibactam	Clavulanic acid	Sulbactam	Tazobactam
Class A						
TEM	+	+	+	+	+	+
SHV	+	+	+	+	+	+
CTX-M	+	+	+	+	+	+
KPC	+	+	+	−	−	−
Class B						
MBL	−	−	−	−	−	−
Class C						
AmpC	+	+	+	−	±[a]	−
Class D						
OXA	±	−[b]	±	−	−	−
Reference	[5]	[5]	[5, 24]	[25, 26]	[27]	[27]

− no inhibitory activity, + inhibitory activity, *MBL* metallo-β-lactamase

[a]Enterobacteriaceae resist inhibition by sulbactam, although *Klebsiella* spp., *Salmonella* spp., and *Proteus* spp. normally do not harbor chromosomal bla_{AmpC} genes

[b]Limited data available

Zhanel et al. Drugs 2018

aztreonam

Table 2 Novel antimicrobial Ambler class activity

Drug	Ambler group A	Ambler group B	Ambler group C	Ambler group D	2019 CLSI Enterobacterales MIC breakpoint
			β-lactam/β-lactamase inhibitor		
Ceftazidime-avibactam	+	-	+	+ (OXA-48)	8/4
Meropenem-vaborbactam	+	-	+	-	4/8*
Imipenem-relebactam	+	-	+	-	1/4**
			Other novel antimicrobials		
Plazomicin	+	+	+	+	2**
Cefiderocol	+	+	+	+	2**
Fosfomycin	+	+	+	+	N/A

*Higher than meropenem breakpoint, avoid use in OXA endemic areas

**FDA minimum inhibitory concentration breakpoint

Modifiziert nach Lasko et al. Curr Infect Dis Rep 2020

Aztreonam/Avibactam (Emblaveo®)

1.5g Aztreonam und 0.5g Avibactam über 3h alle 6 h (Aufsättigung mit 2g AZT/0,67g Avi ?)

Indikation lt. Zulassung:

- Komplizierte intraabdominelle Infektionen (cIAI)
- Nosokomiale Pneumonien (HAP), einschließlich beatmungsassoziierter Pneumonien (VAP) Komplizierte Harnwegsinfektionen (cUTI), einschließlich Pyelonephritis
- Infektionen aufgrund aerober Gram-negativer Erreger bei erwachsenen Patienten mit begrenzten Behandlungsoptionen indiziert

Spektrum: Gramnegative Erreger (zusätzlich Erfassung der Ambler B Metallobetalaktamasen
nicht: Acinetobacter baumanii, keine GP, keine Anaerobier

Table 4
Antimicrobial susceptibility of carbapenem-resistant *Enterobacterales* stratified by region (2020–2022).

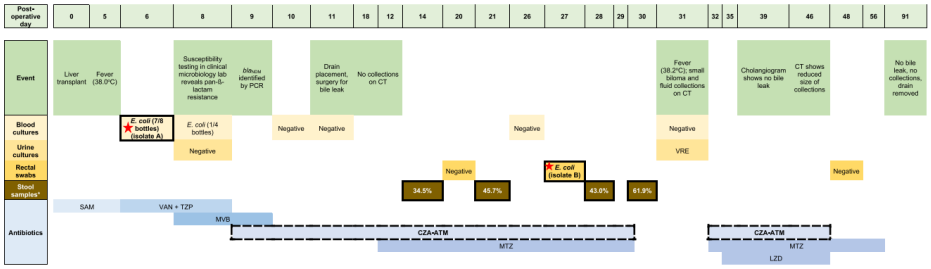
Antimicrobial agent	% Susceptible per CLSI or FDA criteria (no. of isolates)				
	W-EU (229)	E-EU (377)	APAC (148)	LATAM (262)	All (1016)
Aztreonam-avibactam	100.0[a]	99.5[a]	99.3[a]	99.6[a]	99.6[a]
Ceftazidime-avibactam	76.9	66.6	39.9	65.1	64.6
Meropenem-vaborbactam	72.5	46.7	37.8	70.6	57.4
Imipenem-relebactam	63.8[b]	43.5[b]	27.7[b]	62.7[b]	50.7[b]
Levofloxacin	12.7	5.3	11.5	14.5	10.3
Gentamicin	53.1	40.6	43.9	32.1	41.7
Amikacin	59.4	27.1	62.8	32.4	40.9
Tigecycline	94.8	93.4	95.3	92.7	93.8

[a] % inhibited at ≤8 mg/L.
[b] All *Enterobacterales* species were included in the analysis, but CLSI excludes *Morganella*, *Proteus*, and *Providencia* species.

Sader et al. Int J Antimicrob Agents 2024
Fachinformation Emblaveo

Emergence of high-level aztreonam–avibactam and cefiderocol resistance following treatment of an NDM-producing *Escherichia coli* bloodstream isolate exhibiting reduced susceptibility to both agents at baseline

Ghady Haidar[1,2], Ellen G. Kline[1], Georgios D. Kitsios[3,4], Xiaohong Wang[3,4], Eun Jeong Kwak[1], Anthony Newbrough[1], Kelly Friday[1], Kailey Hughes Kramer[1] and Ryan K. Shields[1,2,5]*



Resistenz-Selektion durch Ceftazidim /Avibactam gegenüber Reserve-AB bei reduzierter Empfindlichkeiten gegenüber AZT/Avi und Cefiderocol aufgrund einer Mutation im ftsI Gen (inkl. Auftreten neuer Mutationen)

Wichtig: Molekulare Resistenzanalyse bei MDR (Frühzeitig!!!)

Haidar et al. JAC Antimicrob Resist 2024

Cefiderocol-trojan horse (Fetcroia)

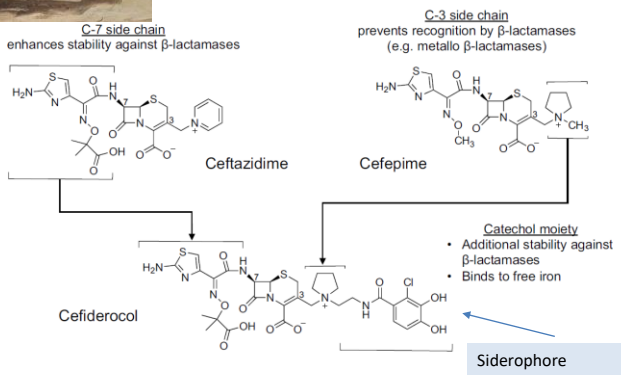


Fig. 2 Cefiderocol structure activity relationships

Zhanel et al. Drugs 2019

	Nosocomial pneumonia		Bloodstream infections or sepsis		Complicated urinary tract infections		Overall	
	Cefiderocol (n=45)	Best available therapy (n=22)	Cefiderocol (n=30)	Best available therapy (n=17)	Cefiderocol (n=26)	Best available therapy (n=10)	Cefiderocol (n=101)	Best available therapy (n=49)
Day 14	11 (24%; 12·9—39·5)						19 (19%; 11·7–27·8)	6 (12%; 4·6–24·8)
Day 28	14 (31%; 18·2–46·6)						25 (25%; 16·7–34·3)	9 (18%; 8·8–32·0)
End of study	19 (42%; 27·7–57·8)						34 (34%; 24·6–43·8)	9 (18%; 8·8–32·0)

Data are n (%; 95% CI) by clinical di… …mber of patients in the safety population who had the specified clinical diagn…

Table 5: All-cause mortality in t…

	Cefiderocol (n=101)	Best available therapy (n=49)
Acinetobacter spp*	21/42 (50%)	3/17 (18%)
Acinetobacter baumannii	19/39 (49%)	3/17 (18%)
Klebsiella pneumoniae	8/34 (24%)	4/16 (25%)
Without *Acinetobacter* spp	6/28 (21%)	4/15 (27%)
Pseudomonas aeruginosa	6/17 (35%)	2/12 (17%)

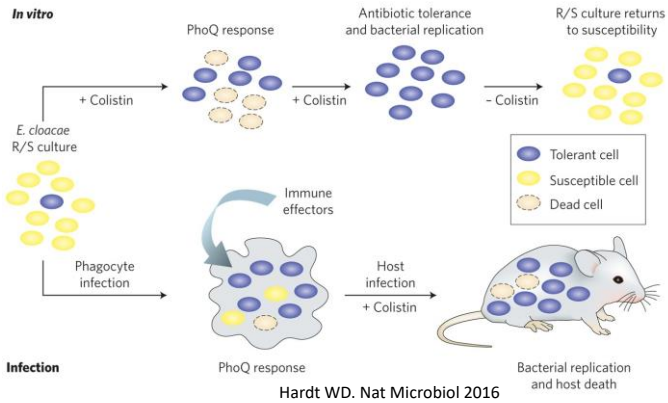
Interpretation Cefiderocol had similar clinical and microbiological efficacy to best available therapy in this heterogeneous patient population with infections caused by carbapenem-resistant Gram-negative bacteria. Numerically more deaths occurred in the cefiderocol group, primarily in the patient subset with *Acinetobacter* spp infections. Collectively, the findings from this study support cefiderocol as an option for the treatment of carbapenem-resistant infections in patients with limited treatment options.

Universitätsklinik für Innere Medizin II Innsbruck (Infektiologie, Immunologie, Tropenmedizin, Rheumatologie, Pneumologie)

Bassetti et al. Lancet ID 2021

MEDIZINISCHE UNIVERSITÄT INNSBRUCK

Heteroresistance– increase with exposure to antibiotic and reverses thereafter



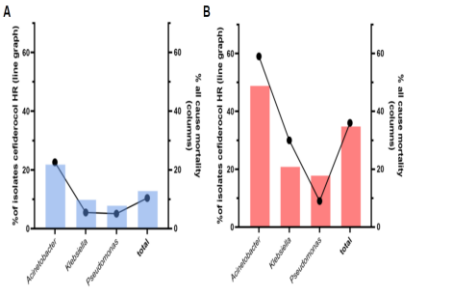
Hardt WD. Nat Microbiol 2016

Linked to observations in Acinetobacter infection upon treatment with Cefiderocol?– controversially discussed (Bassetti et al. Lancet Infect Dis 2001)

		Acinetobacter	*Klebsiella*	*Pseudomonas*	Total
Hetero-resistance GA, USA	Susceptible (S)[A]	11% [4/35]	0% [0/50]	5% [1/20]	5% [5/105]
	Cephalosporin-resistant[B]	44% [8/18]	12% [5/41]	5% [1/19]	18% [14/78]
	Carbapenem-resistant (CR)[2]	59% [64/108]	30% [27/89]	9% [6/69]	36% [97/266]
All-cause mortality	APEKS-NP[14,C]	22% [5/23]	10% [5/48]	8% [2/24]	13% [12/95]
	CREDIBLE-CR[15,C]	49% [19/39]	21% [6/28]	18% [2/11]	35% [27/78]

[A]These isolates are susceptible to meropenem, cefepime, ceftazidime, and ceftriaxone by clinical antimicrobial susceptibility testing.
[B]These isolates are carbapenem (meropenem) susceptible but resistant to at least one of the extended spectrum cephalosporins cefepime, ceftazidime, and ceftriaxone by clinical antimicrobial susceptibility testing.
[C]APEKS-NP involved only pneumonia patients while CREDIBLE-CR enrolled patients with pneumonia, bloodstream infections or urinary tract infections.

Table 1. The higher rate of all-cause mortality in the CREDIBLE-CR trial versus the APEKS-NP trial correlates with the increased frequency of cefiderocol heteroresistance among carbapenem-resistant relative to carbapenem-susceptible Gram-negative pathogens. Heteroresistance was determined by population

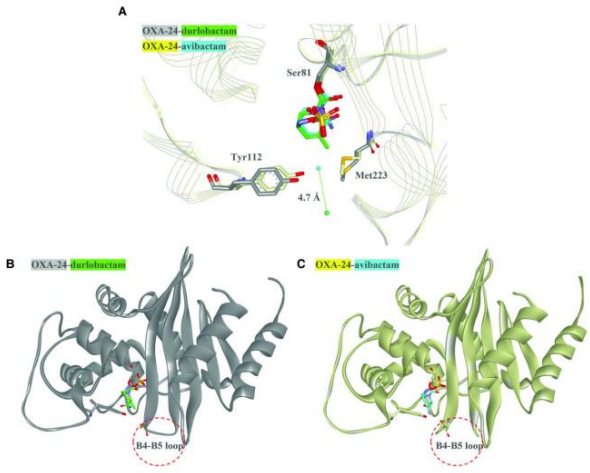


Supplemental Figure 2. Graphical representaion of the correlation between heteroresistance and all-cause mortality in the CREDIBLE-CR trial versus the APEKS-NP trial. The left axis and line graphs show the heteroresistance rates and the right axis and columns show the all-cause mortality rate for (A) carbapenem-susceptible isolates and the APEKS-NP trial and (B) carbapenem-resistant isolates and the CREDIBLE-CR trial.

Choby et al. Lancet Microbe 2021

DURLOBACTAM IS A DIAZABICYCLOOCTANE β-LACTAMASE INHIBITOR WITH BROAD-SPECTRUM INHIBITION OF SERINE β-LACTAMASES AND PBPs

Xacduro



Papp-Wallace et al CID 2023

Efficacy and safety of sulbactam–durlobactam versus colistin for the treatment of patients with serious infections caused by *Acinetobacter baumannii–calcoaceticus* complex: a multicentre, randomised, active-controlled, phase 3, non-inferiority clinical trial (ATTACK)

Keith S Kaye, Andrew F Shorr, Richard G Wunderink, Bin Du, Gabrielle E Poirier, Khurram Rana, Alita Miller, Drew Lewis, John O'Donnell, Lan Chen, Harald Reinhart, Subasree Srinivasan, Robin Isaacs, David Altarac

- Prospektive randomisierte Studie 2019-2021 bei Infektionen (VAP, Sepsis, cUTI) mit Carbapenem-resistentem A. baumannii
- Vergleich SD (1g/1g) alle 6h versus Colitistin jeweils plus Imipenem/Cil.
- Studie B: Salvage Therapie bei Colistin- Resistenz
- Outcome: 28 D Mortalität

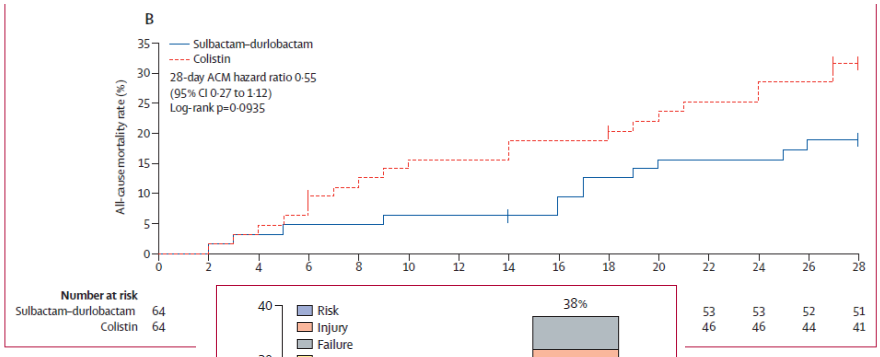


Figure 2: **All-cause mortality**

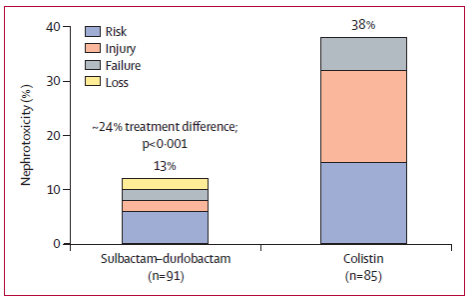


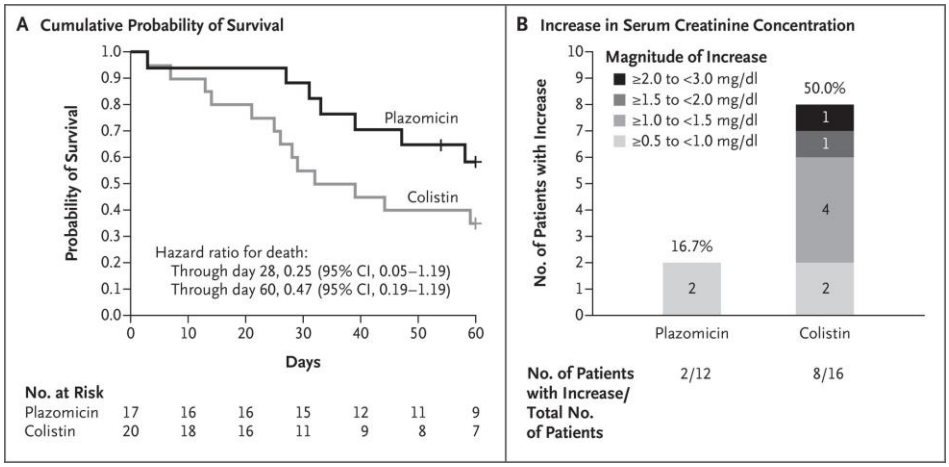
Figure 3: **Incidence of nephrotoxicity (at any visit after baseline), as measured by modified RIFLE criteria (part A, safety population)**

Universitätsklinik für Innere Medizin II Innsbruck (Infektiologie, Immunologie, Tropenmedizin, Rheumatologie, Pneumologie)

Kaye KS et al. Lancet ID 2024

Medizinische Universität Innsbruck

Plazomicin vs. Colistin in combination with Meropenem or Tigecyclin for CR- Enterobacteriaceae infection (BSI or VAP)



McKinell et al. NEJM 2019

Universitätsklinik für Innere Medizin II Innsbruck
(Infektiologie, Immunologie, Tropenmedizin, Rheumatologie, Pneumologie)

MEDIZINISCHE UNIVERSITÄT INNSBRUCK

Table 2. Characteristics of novel anti-Gram-negative antimicrobial agents in phase 3 clinical trials.

Drug	Drug Class	Bacterial Pectrum	Drug Stable to Beta-Lactamase Type					Potential Indications	Ongoing Trials (Phase 3)	Route//Dosage	Comment
			KPC	MBL	AmpC	OXA	ESBL				
Aztreonam/ avibactam	MB/BLI	GNB; less effective against MBL-producing *P. aeruginosa*	yes	yes	yes	yes	yes	cIAI, HAP, VAP, cUTI, BSI	NCT03580044	IV//500/167 mg loading dose, 1500/500 mg QDS	Combination that covers both serine and MBL carbapenemases
Cefepime/ enmetazobactam	BL/BLI	GNB, GPB; ineffective against *A. baumannii*, CRE, and MRSA	no	no	yes/no	no	yes	cUTI, HAP, VAP	NCT03687255	IV//2 g/500 mg TDS	Excellent class A, anti-ESBL activity; Potential carbapenem-sparing drug; Penetrates ELF easily
Cefepime/ zidebactam	BL/BLI	GPB (no MRSA); GNB (not *A. baumannii*)	yes	yes	yes	yes	yes	cUTI	NCT04979806	IV//2 g/1 g TDS	Phase 3 study recruiting patients
Cefepime/ taniborbactam	BL/BLI	GPB (not MRSA), GNB, (not *A. baumannii*)	yes	yes	yes	yes	yes	cUTI	NCT03840148	IV//2 g/0.5 g TDS	Preliminary results from phase 3 cUTI study: comparable efficacy to MER
Sulbactam/ durlobactam	BL/BLI	GNB, particularly *Acinetobacter* spp.; active against *Burkholderia cepacia*; not *P. aeruginosa*	yes	no	yes	yes	yes	*Acinetobacter* infections	NCT03894046	1 g/1 g QDS	Phase 3, pneumonia and BSI study. Better clinical cure and less nephrotoxicity than colistin (preliminary results)
Sulopenem	CP	GPB (not MRSA); GNB (not *P.aeruginosa*, *Stenotrophomonas maltophilia*, *B. cepacia*)	no	no	yes	no	yes	cUTI, uUTI, cIAI	NCT03357614, NCT03358576	Oral//sulopenem etzadroxil 500 mg/probenecid 500 mg BD; IV//1000 mg OD	Phase 3 trial of uncomplicated UTI, recruiting patients
Tebipenem	CP	GPB (not MRSA); GNB (not *P.aeruginosa*, *A. baumannii*)	no	no	yes	no	yes	cUTI	NCT03788967	Oral//600 mg TDS	Excellent anti-ESBL activity
Benapenem	CP	Like other CPs	no	no	yes	no	yes	cUTI	NCT04505683	IV//1000 mg OD	Excellent anti-ESBL activity

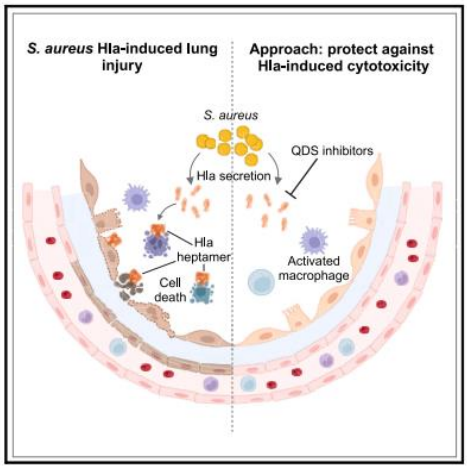
Abbreviations: AmpC—chromosomally encoded beta-lactamase; BD—twice daily; BL—beta-lactam; BLI—beta-lactamase inhibitor; BSI—bloodstream infection; CP—carbapenem; CR—Carbapenem resistant; CRE—Carbapenem-resistant Enterobacteriaceae; cIAI—complicated intraabdominal infections; cUTI—complicated urinary tract infections; ELF—epithelial lining fluid; ESBL—Extended Spectrum Beta-Lactamase; GNB—Gram-positive bacteria; GPB—Gram-positive bacteria; HAP—hospital acquired pneumonia; KPC—*Klebsiella pneumoniae* carbapenemase; MB—monobactam; MER—meropenem; MBL—metallo-β-lactamases; MDR—Multidrug-resistant; OD—once daily; OXA—oxacillinase; QDS—four times daily; TDS—thrice daily; VAP—ventilator associated pneumonia.

Karvouniaris et al. Antibiotics 2023

Universitätsklinik für Innere Medizin II Innsbruck
(Infektiologie, Immunologie, Tropenmedizin, Rheumatologie, Pneumologie)

MEDIZINISCHE UNIVERSITÄT INNSBRUCK

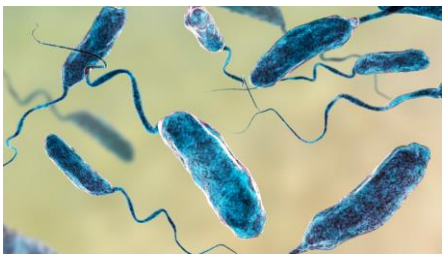
Highly potent quinoxalinediones inhibit α-hemolysin and ameliorate *Staphylococcus aureus* lung infections



- A cellular screen identified QDS, small molecule inhibitors of *S. aureus* α-hemolysin
- QDS revert the hallmarks of α-hemolysin pathogenicity
- QDS prevent the formation of functional pores by interacting with α-hemolysin
- The QDS analog H052 is active *in vivo* when given prophylactically or therapeutically

Shekhar et al. Cell Host&Microbe 2025

Assoziation von Pathogenen im Wasser und höheren Temperaturen



V. parahaemolyticus and *V. vulnificus*	Shellfish	Increased levels at higher temperatures	A	DePaola et al., 1990; Lhafi & Kühne, 2007; Parveen et al., 2008
Campylobacter, Salmonella	Surface waters	Varying associations with temperature	B	Haley et al., 2009; Martinez-Urtaza, 2008; Simental & Vereen Jr et al., 2013; Vereen et al., 2007
Vibrio spp.	Coastal waters	Increased levels at higher temperatures	A	Johnson et al., 2012; Louis et al., 2003; Vezzulli, 2012

*Refer to Box 1 for a description of the levels used to rate the strength of the scientific evidence

Hellberg et al. Crit Rev Microbiol 2015

Wien Klin Wochenschr. 2016; 128: 141–145.
Published online 2016 Jan 29. doi: 10.1007/s00508-015-0944-y
PMCID: PMC4771811
PMID: 26825075

Necrotizing fasciitis due to *Vibrio cholerae* non-O1/non-O139 after exposure to Austrian bathing sites

Sonja Hirk, MD, Steliana Huhulescu, MD, Franz Allerberger, MD, MPH,✉ Sarah Lepuschitz, BSc, Sonja Rehak, Sandra Weil, Elisabeth Gschwandtner, MD, Michael Hermann, MD, Stephanie Neuhold, MD, Alexander Zoufaly, MD, and Alexander Indra, MD

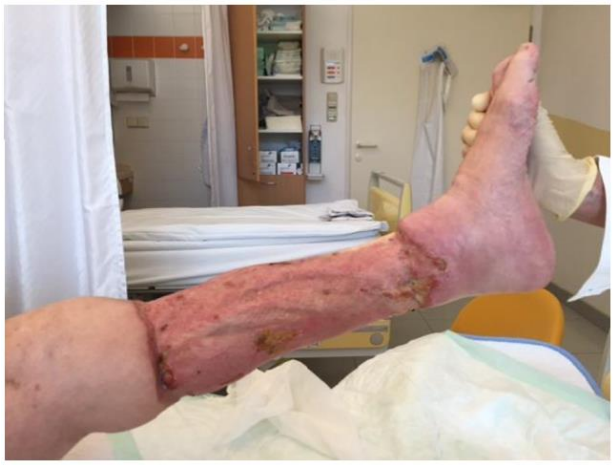


Table 1

Table 2

Summarized data of EU bathing waters harboring *Vibrio cholerae* non-O1/non-O139 in Austria, August 2015

Body of water	Bathing site	Province	*V. cholerae* non-O1/non-O139 in MPN/100 ml	Water temperature in °C	pH
Lake Neusiedl	Weiden	Burgenland	> 11,000	24.9	8.8
	Neusiedl		360	24.6	8.7
	Breitenbrunn		4,600	24.4	8.8
	Rust		4,600	25.5	8.6
	Podersdorf		11,000	23.8	8.9
	Illmitz		> 11,000	24.9	8.9
	Mörbisch		11,000	25.4	8.8
Lake Andau	Lake Andau	Burgenland	930	25.5	8.4
Lake Apetlon	Lake Apetlon	Burgenland	2,400	25.0	8.6
Zicksee	St. Andrä	Burgenland	2,100	21.3	8.9
Ausee	Blindenmarkt	Lower Austria	150	23.1	8.4
Lake Hohenau	Lake Hohenau	Lower Austria	1,500	24.2	9.0
Lake Seeschlacht	Langenzersdorf	Lower Austria	> 11,000	24.6	8.4

Hirk et al. Wi Kli Wo 2016

Mycoplasma pneumoniae infection in adult inpatients during the 2023–24 outbreak in France (MYCADO): a national, retrospective, observational study

Ariane Gavaud, Matthieu Holub, Antoine Asquier-Khati, Karine Faure, Sophie Leautez-Nainville, Gwenael Le Moal, François Goehringer, David Luque Paz, Bérangère Arnould, Victor Gerber, Guillaume Martin-Blondel, Charles Declerck, Sandrine Gazaignes, Sophie Blanchi, Paul Loubet, Natacha Mroz[illegible], Florence Tubac

	Total (n=1309)	Severity of infection	
		Severe outcome (n=424)	No severe outcome (n=885)
Age, years	43 (31-63)	46 (32-65)	42 (31-61)
Sex			
Male	718 (54·9%)	254 (59·9%)	464 (52·4%)
Female	591 (45·1%)	170 (40·1%)	421 (47·6%)
Respiratory diseases			
COPD or emphysema	90 (6·9%)	39 (9·2%)	51 (5·8%)
Asthma	141 (10·8%)	49 (11·6%)	92 (10·4%)
Chronic interstitial pneumonia	12 (0·9%)	4 (0·9%)	8 (0·9%)
Any kind of chronic respiratory failure*	288 (22·0%)	113 (26·7%)	175 (19·8%)
Symptoms before and at hospital admission			
Fever	1023 (78·2%)	322 (75·9%)	701 (79·2%)
Fatigue	550 (42·0%)	173 (40·8%)	377 (42·6%)
Headache	211 (16·1%)	48 (11·3%)	163 (18·4%)
Confusion or altered level of consciousness	52 (4·0%)	26 (6·1%)	26 (2·9%)
Cough	1098 (83·9%)	336 (79·3%)	762 (86·1%)
Dyspnoea	948 (72·4%)	356 (84·0%)	592 (66·9%)
Expectorations	473 (36·1%)	156 (36·8%)	317 (35·8%)
Rhinitis, pharyngitis, tonsillitis, or otitis	202 (15·4%)	53 (12·5%)	149 (16·8%)
Diarrhoea	138 (10·5%)	50 (11·8%)	88 (9·9%)

Gavoud et al. Lancet ID 2025

	Total (n=1309)	Severity of infection

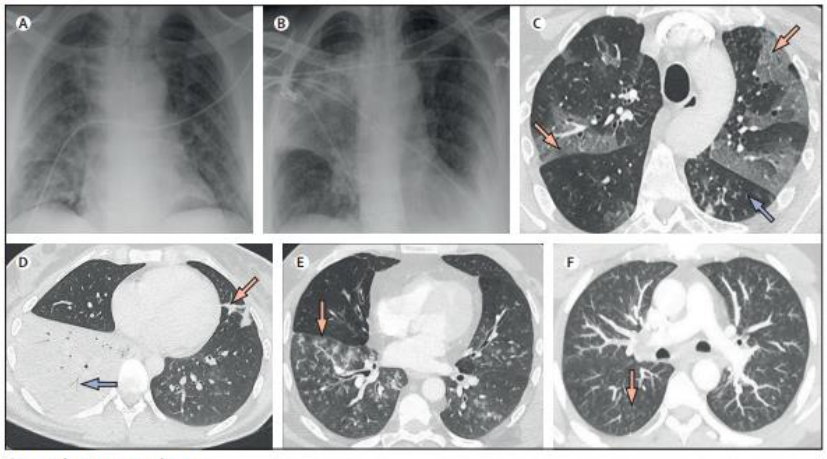
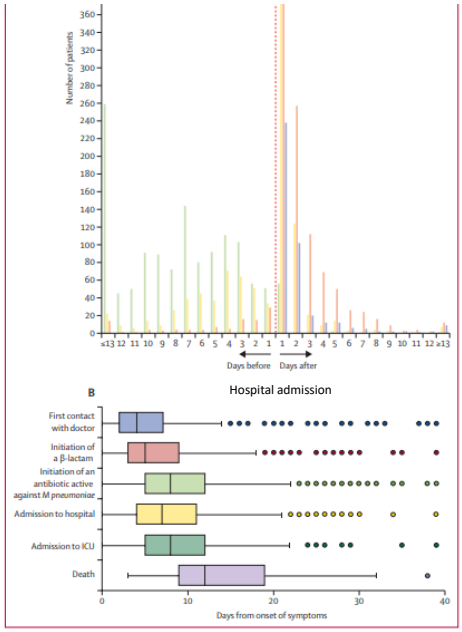


Figure 3: Pulmonary x-rays and CT scans

Universitätsklinik für Innere Medizin II Innsbruck
(Infektiologie, Immunologie, Tropenmedizin, Rheumatologie, Pneumologie)

Gavoud et al. Lancet ID 2025

MEDIZINISCHE UNIVERSITÄT INNSBRUCK



31,7% ICU admission

2.1% lethalithy

Universitätsklinik
für Innere Medizin II Innsbruck
(Infektiologie, Immunologie, Tropenmedizin, Rheumatologie, Pneumologie)

Gavoud et al. Lancet ID 2025

MEDIZINISCHE UNIVERSITÄT INNSBRUCK

Circulation of avian *Chlamydia abortus* in the Netherlands and community-acquired pneumonia: an outbreak investigation and retrospective cohort study

Sert Doornenbal, Miriam Maas, Pieter Jacobs, Ingrid Keur, Frederika Dijkstra, Daphne Reukers, rgen Mager, Joan Totté, Saara Vainio, Maarten Bongaerts, Edou Heddema

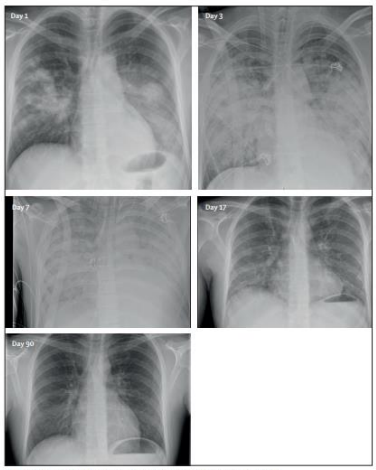


Figure 2: X-rays showing the disease course of avian *Chlamydia abortus* in patient 1
The initial x-ray (day 1) showed bilateral infiltrates, which progressed (day 3) and resulted in acute respiratory distress syndrome (day 7). Radiographic abnormalities improved on treatment with doxycycline and dexamethasone (day 17) and eventually the opacities were resorbed (day 90).

Findings An avian *C abortus* strain caused a cluster of respiratory illness in four family members. Three patients were hospitalised with community-acquired pneumonia, one of whom was admitted to the intensive care unit. The faeces of wild birds were considered a probable source for the index infection. For two family members, human-to-human transmission was a plausible route. Ten historical cases could be identified with avian *C abortus* with the same *ompA* genotype. All patients had been admitted to hospital, at least five developed pneumonia, and one died.

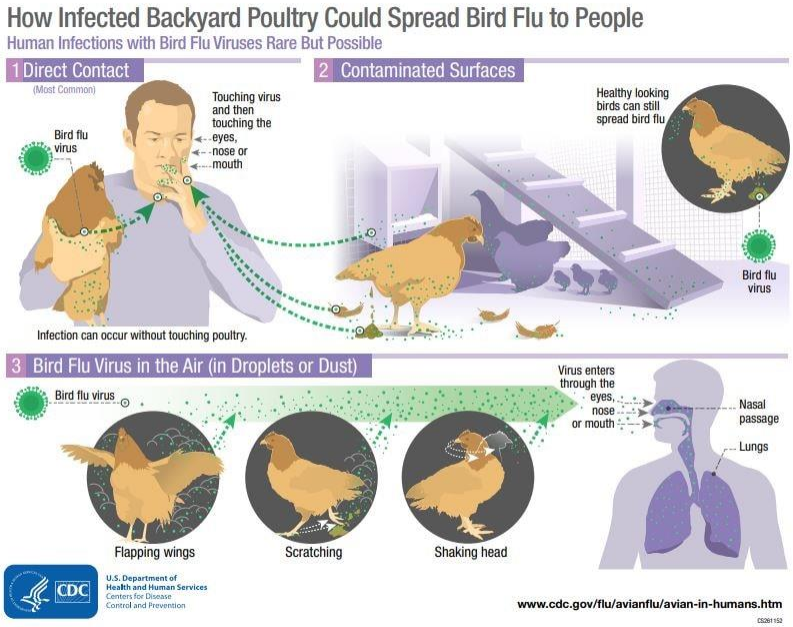
Interpretation This cluster supports that avian *C abortus* strains can cause human infections and underlines that human-to-human transmission should be considered when tracing the source of such infections.

Implications of all the available evidence
Our findings underscore the zoonotic potential of avian *C abortus* to cause community-acquired pneumonia in humans. Human-to-human transmission should be considered when investigating potential sources of this particular avian *C abortus* strain. We show the need for a multidisciplinary approach, which was indispensable in the detection of avian *C abortus* as a causative agent of human pneumonia and the subsequent source investigation reported here. Future studies will need a

Universitätsklinik
für Innere Medizin II Innsbruck
(Infektiologie, Immunologie, Tropenmedizin, Rheumatologie, Pneumologie)

Raven et al. Lancet ID 2025

MEDIZINISCHE UNIVERSITÄT INNSBRUCK



Case Fatality Proportion According to Clade or Subclade and Median Time from Onset of Illness to Hospitalization or Death in Patients with Confirmed Influenza A (H5N1) Illness

Table 1. Case Fatality Proportion According to Clade or Subclade and Median Time from Onset of Illness to Hospitalization or Death in Patients with Confirmed Influenza A (H5N1) Illness.

Country	Predominant Clade or Subclade*	Case Fatality Proportion	Onset of Illness to Hospitalization		Onset of Illness to Death	
		no. of patients/ total no. (%)	*days*	*no. of patients*	*days*	*no. of patients*
Cambodia, Thailand, Vietnam†	1	66/123 (54)	4	109	9	65
Indonesia	2.1	76/96 (79)	5	64	9	72
Azerbaijan, Djibouti, Egypt, Iraq, Nigeria, Turkey	2.2	26/59 (44)	3	36	9	24
China, Laos	2.3	17/26 (65)	5	16	10	17

* The presumed clade or subclade assignment is based on the known geographic distribution of the viruses and is not verified by individual patient data. Few sequences are available for human isolates in the public database for some countries. Multiple clades and subclades have circulated in China in poultry. The numbers of patients for whom data were available are listed. The analysis was provided by Dr. Christoph Steffen and Dr. Julia Fitzner, WHO, Geneva.

† Among 61 patients with documented clade 1 infection, the case fatality proportion was 75%; the median time from the onset of illness to hospitalization was 5 days in 48 patients, and the median time from the onset of illness to death was 9 days in 46 patients.

. N Engl J Med 2008;358:261-273

New outbreaks of H5N1

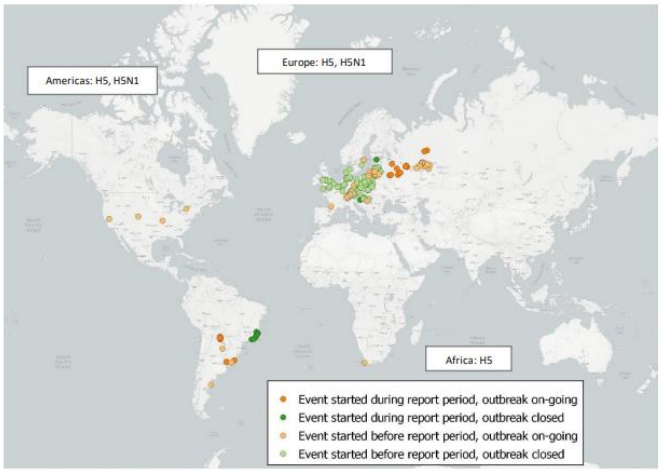
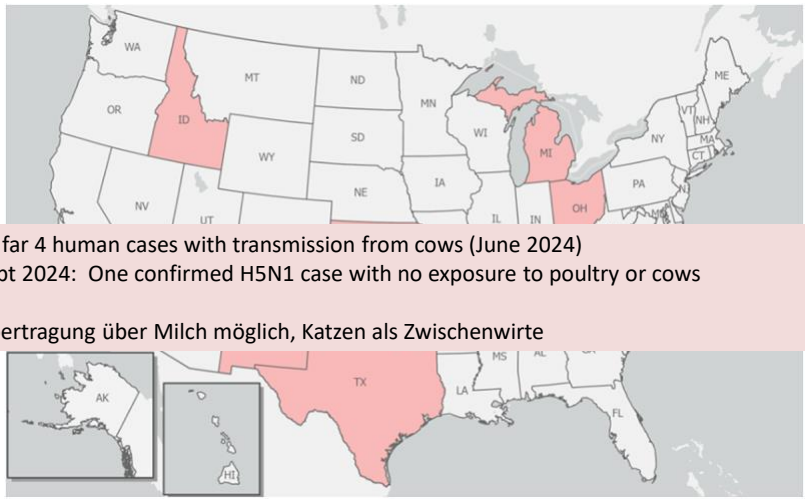


Figure 4. Distribution of HPAI new outbreaks in non-poultry animals, and corresponding subtypes.

WHO Avian influenza report, 10.6.2023

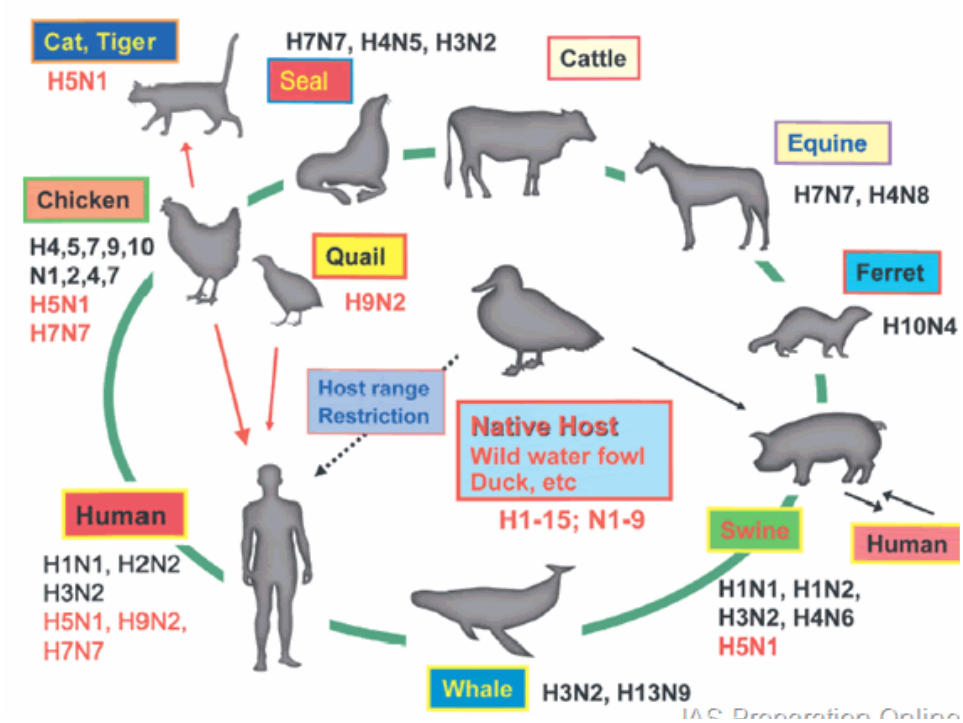
Confirmed cases of H5N1 in Diary herds in US (May 2024)



So far 4 human cases with transmission from cows (June 2024)
Sept 2024: One confirmed H5N1 case with no exposure to poultry or cows

Übertragung über Milch möglich, Katzen als Zwischenwirte

Ly H et al. Virulence 2024

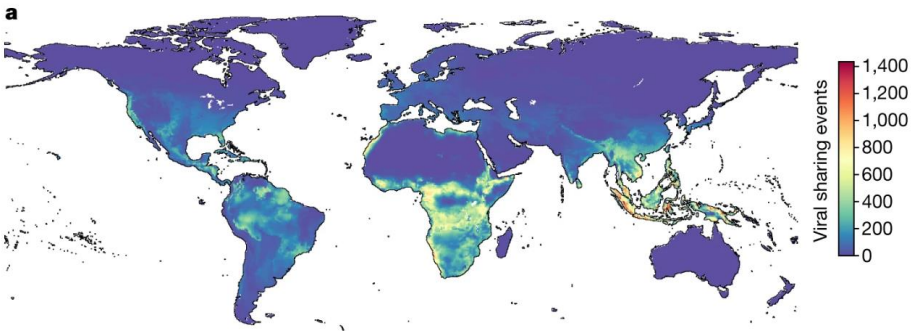


Human case of H5N1 transmitted from cattle

Stamm—hohe Ähnlichkeit mit H5N1 Impfstamm

Uyeki et al. NEJM 2024

Circa 10.000 Viren sind potentiell humanpathogen, der Großteil zirkuliert in wilden Tieren– durch Klimaänderungen und Bevölkerungsausbreitung kommt es zu vermehrten Übertragung solchen Viren auf den Menschen (spillover)

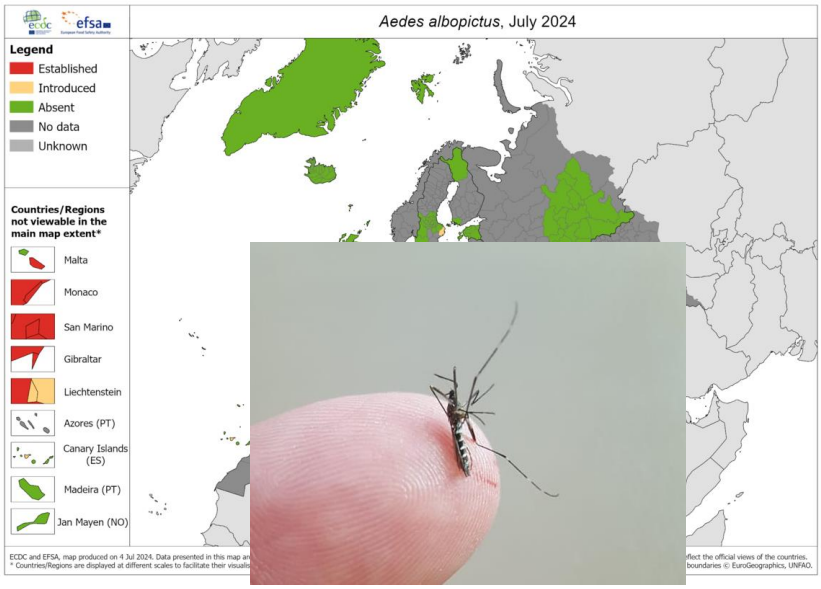


The projected number of novel viral sharing events among mammal species in 2070 based on geographical range shifts of the 3139 host species from changes in climate and land use

Carlson CC et al. Nature 2022

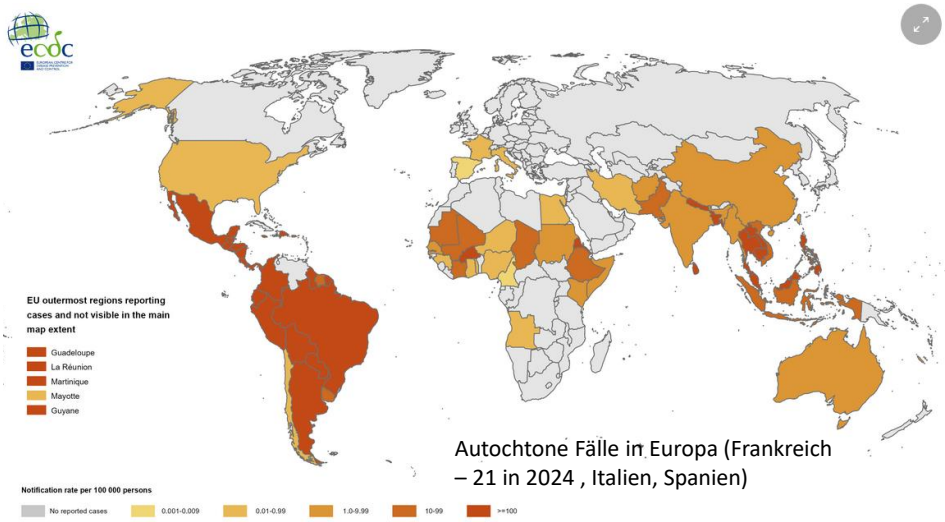
Universitätsklinik
für Innere Medizin II Innsbruck
(Infektiologie, Immunologie, Tropenmedizin, Rheumatologie, Pneumologie)

MEDIZINISCHE UNIVERSITÄT INNSBRUCK



Innsbruck Juli 2020

Dengue August 2023- Juli 2024



Autochtone Fälle in Europa (Frankreich – 21 in 2024 , Italien, Spanien)

Autochtone Fälle in der EU

Year	Country	Department or regions affected	Number of autochthonous cases	Probable period of virus circulation
2010	Croatia	Korčula Island and the Pelješac peninsula	10	August–October
2010	France	Alpes-Maritimes department	2	August–September
2013	France	Bouches-du-Rhône department	1	September-October
2014	France	Var and Bouches-du-Rhône departments	4	July-September
2015	France	Gard department	8	July–September
2018	France	Alpes Maritimes, Hérault, and Gard departments	8	September–October
2018	Spain	Catalonia region, Murcia region or province of Cádiz	6	August-October
2019	Spain	Catalonia region	1	September
2019	France	Alpes-Maritimes and Rhône departments	9	July-September
2020	France	Hérault, Var, Alpes-Maritime, and Gard departments	13	July-October
2020	Italy	Veneto region	10	August
2021	France	Var and Hérault departments	2	July and September
2022	France	Pyrénées-Orientales, Hautes-Pyrénées, Haute-Garonne, Tarn et Garonne, Var, Alpes-Maritime, and Corsica departments	65	June-September
2022	Spain	Ibiza	6	August-October
2023	France	Île-de-France (3 cases), Bouches-du-Rhône (14 cases in 2 clusters), Pyrénées-Orientales (11 cases), Hérault (2 cases), Gard (9 cases), Alpes-Maritimes (2 cases) and Auvergne Rhône-Alpes (2 cases) departments.	43	July-October
2023	Italy	Lodi (41 cases), Rome (38 cases in the Rome metropolitan city and 1 case in Anzio) and Latina (2 cases) provinces.	82	End of July-November
2023	Spain	Catalonia (3 cases)	3	August-October

https://www.ecdc.europa.eu/en/all-topics-z/dengue/surveillance-and-disease-data/autochthonous-transmission-dengue-virus-euea, last accessed 22.01.2024

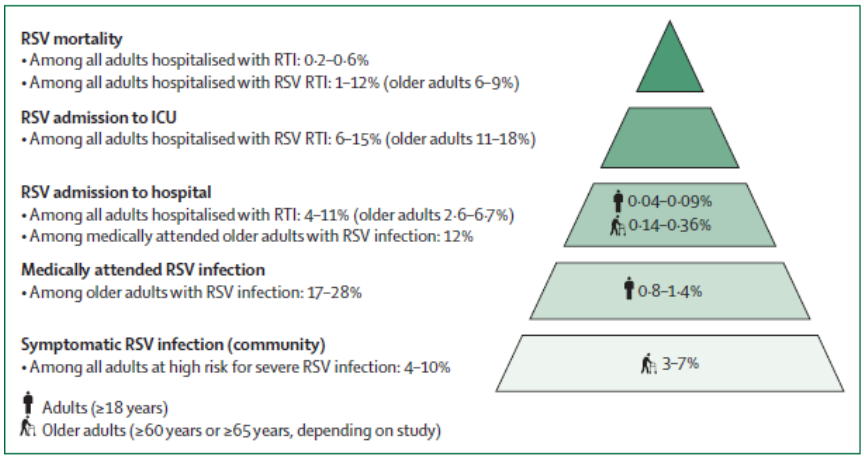
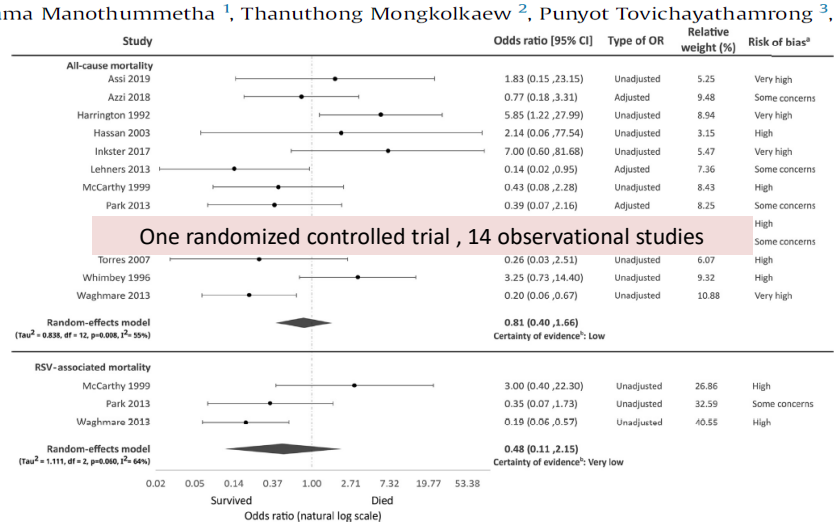


Figure 1: **RSV incidence in adults**

Wildenbeest et al. Lancet 2024

Ribavirin treatment for respiratory syncytial virus infection in patients with haematologic malignancy and haematopoietic stem cell transplant recipients: a systematic review and meta-analysis

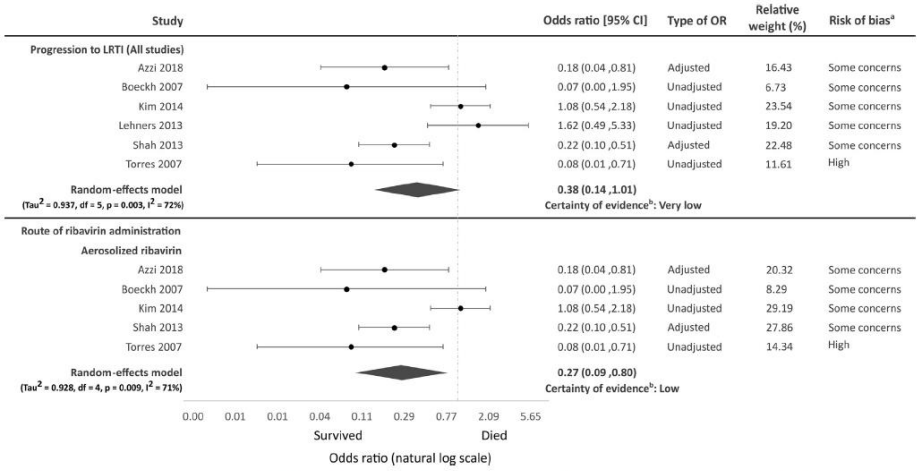
Kasama Manothummetha [1], Thanuthong Mongkolkaew [2], Punyot Tovichayathamrong [3],



One randomized controlled trial , 14 observational studies

Fig. 1. Pooled ORs of ribavirin use and mortality. [a]The risk of bias in non-randomized studies of exposure was used for assessing the risk of bias. [b]Grading of recommendation

Manothummetha et al. CMI 2023



ig. 3. Pooled ORs of ribavirin and progression to LRTI from RSV. [a]The risk of bias in non-randomized studies of exposure was used for assessing the risk of bias. [b]Grading o

No signifcant reduction of mortality; trends towards reduction in patients with LRTI

Manothummetha et al. CMI 2023

Humanes Metapneumovirus

- Pneumoviridae, which comprises large enveloped negative-sense RNA viruses
  - Orthopneumovirus (including RSV)
  - Metapneumovirus (including hMPV)
- Two subgroups of hMPV, subgroups A and B, and two clades within each of these subgroups (designated A1, A2, B1, and B2)
- Geringe genetische Diversität

Crowe et al. UptoDate2024

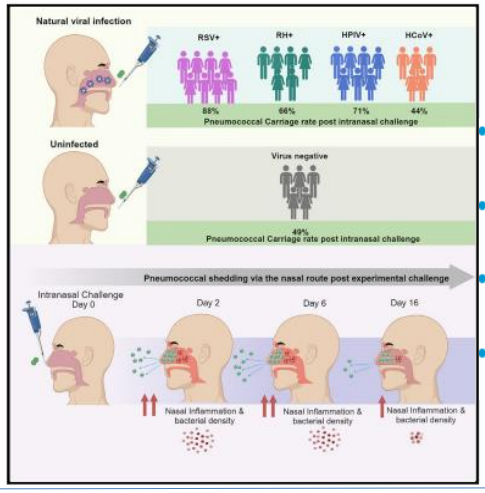
Epidemiologie

- Inkubationszeit: 5-9 d
- Indexpatienten v.a. Kinder
  - Ca. 15 Mio Infektionen /Jahr bei Kindern unter 5 a
- Saisonale Variation- EU&USA—Spätwinter/Frühling
- Infektion v.a. bei Kindern, bei Erwachsene als LTRI selten
- Symptome va. Husten (100%), Schnupfen (85%), Fieber selten
- Dg: RT-PCR bei klin. Verdacht
- Bis zu 4% der hospitalisierten CAP (Jain S et al. NEJM 2015)
- Evt. prolongierte Symptomatik v.a. bei Immunocompr. Patienten
  - 428 allogene HCT Patienten– bis zu 10% positiv; häufig als Co-Infektionen (mit Pseudomonas/Pilze –cave multiplex PCR); bei UTRI 2%, bei LTRI 21% Mortalität (Pinana et al. JID 2024)

Crowe et al. UptoDate2024

Cell Host & Microbe

RSV and rhinovirus increase pneumococcal carriage acquisition and density, whereas nasal inflammation is associated with bacterial shedding



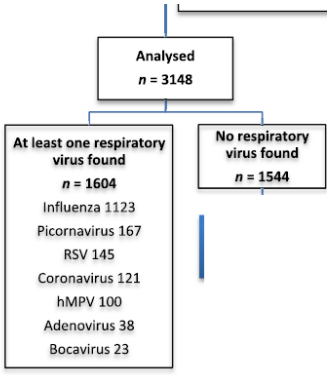
- Primary RSV or rhinovirus infection predisposed to pneumococcal carriage
- Asymptomatic RSV infection increased bacterial colonizing density by 2-log
- Nasal inflammation associated with pneumococcal shedding via the nose
- Adults may also act as a reservoir of pneumococcal transmission

Mitsi et al. CHM 2024

Characteristics of human metapneumovirus infection in adults hospitalized for community-acquired influenza-like illness in France, 2012–2018: a retrospective observational study

P. Loubet [1,2,*,‡], P. Mathieu [3,‡], N. Lenzi [2], F. Galtier [2,4], F. Lainé [2,5], Z. Lesieur [2],

- Beobachtungsstudie- retrospektive von Pat. mit ILI



Universitätsklinik für Innere Medizin II Innsbruck (Infektiologie, Immunologie, Tropenmedizin, Rheumatologie, Pneumologie)

Loubet et al. CMI 2021

MEDIZINISCHE UNIVERSITÄT INNSBRUCK

Table 1
Clinical characteristics and outcomes of hospitalized patients infected with human Metapneumovirus compared with p

	hMPV-($n = 3048$)	hMPV+ ($n = 90$)	Univariate analysis
Baseline characteristics			
Gender			
Women, *n* (%)	1390/3048 (46%)	50/90 (56%)	0.06
Men, *n* (%)	1658/3048 (54%)	40/90 (44%)	
Median age, years (IQR)	71 (56–82)	78 (70–86)	<0.001
Age >65 years, *n* (%)	1904/3048 (62%)	76/90 (84%)	<0.001
Median BMI, kg/m^2 (IQR)	24.8 (21.5–28.5)	25.4 (21.1–29.3)	
Symptoms			
Fever or feverishness, *n* (%)	2562/3045 (84%)	79/90 (88%)	0.40
Cough, *n* (%)	2360/3045 (78%)	75/90 (83%)	0.18
Dyspnea, *n* (%)	1739/2199 (79%)	76/90 (84%)	0.54
Weakness/malaise, *n* (%)	821/3041 (27%)	13/90 (14%)	0.007
Headache, *n* (%)	755/3032 (25%)	16/90 (18%)	0.08
Myalgia, *n* (%)	734/3029 (24%)	19/90 (21%)	0.45
At least one complication during the hospital stay, *n* (%)	1648/3148 (52%)	56/90 (62%)	0.13
Pneumonia*, *n* (%)	918/3124 (29%)	32/89 (36%)	0.27
Respiratory failure, *n* (%)	873/3124 (28%)	32/89 (36%)	0.17
Acute heart failure, *n* (%)	420/3122 (13%)	22/89 (25%)	0.004
Acute respiratory distress syndrome, *n* (%)	257/3123 (8%)	8/89 (9%)	0.85
Median length of stay, days (IQR)	5 (3–9)	7 (4–13)	0.50
ICU admission after hospitalization in acute care, *n* (%)	543/2283 (24%)	15/90 (17%)	0.60
Death, *n* (%)	137/3131 (4%)	4/90 (4%)	1

THERAPIE: symptomatisch, Ribavirin in vitro wirksam (wie bei RSV)

Universitätsklinik für Innere Medizin II Innsbruck (Infektiologie, Immunologie, Tropenmedizin, Rheumatologie, Pneumologie)

Loubet et al. CMI 2021

MEDIZINISCHE UNIVERSITÄT INNSBRUCK

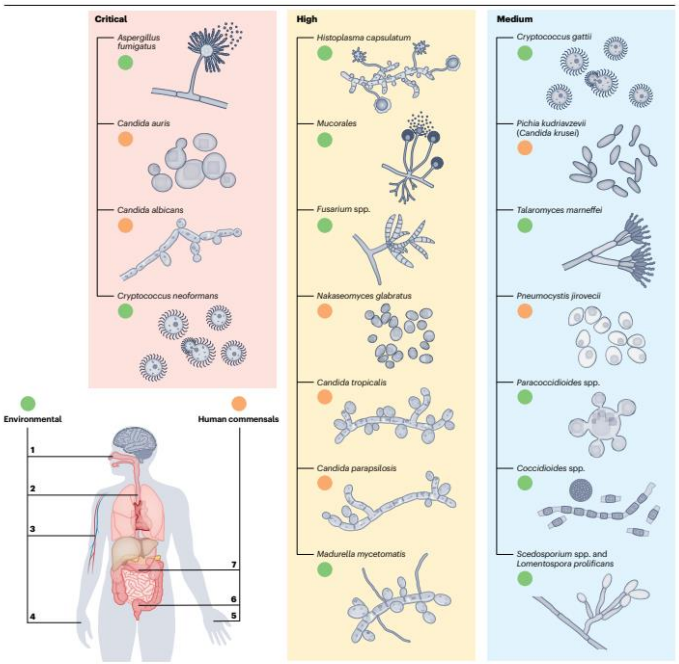


Fig. 1 | **Human pathogenic fungi designated as critical, high and medium risk by the WHO.** Shown are 18 fungal pathogens that have been categorized as critical, high or medium risk to human health by the WHO during compilation for pathogens of environmental origin (for example, soil or airborne fungi) or orange circles for pathogens derived from human commensal mycobiota. Fungal pathogens acquired from environmental sources may generally human

Brown et al. Nat Rev Microbiol 2024

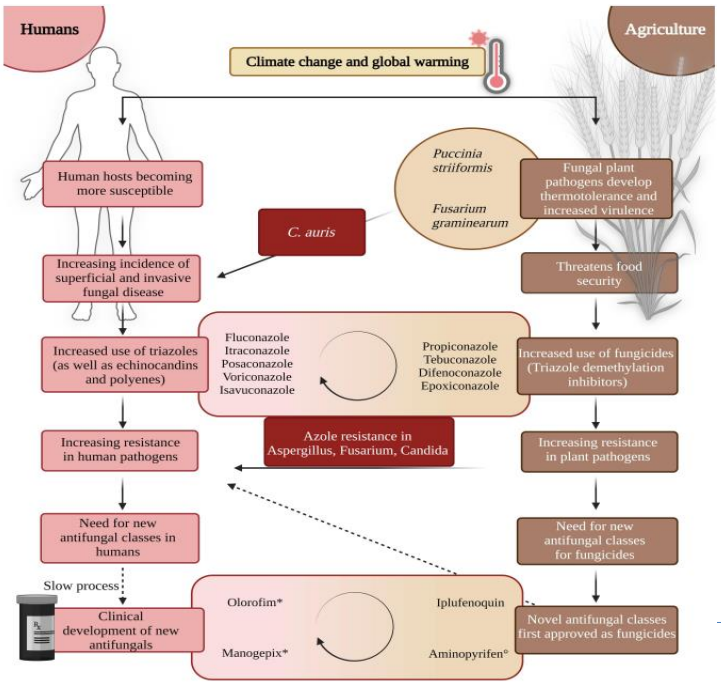
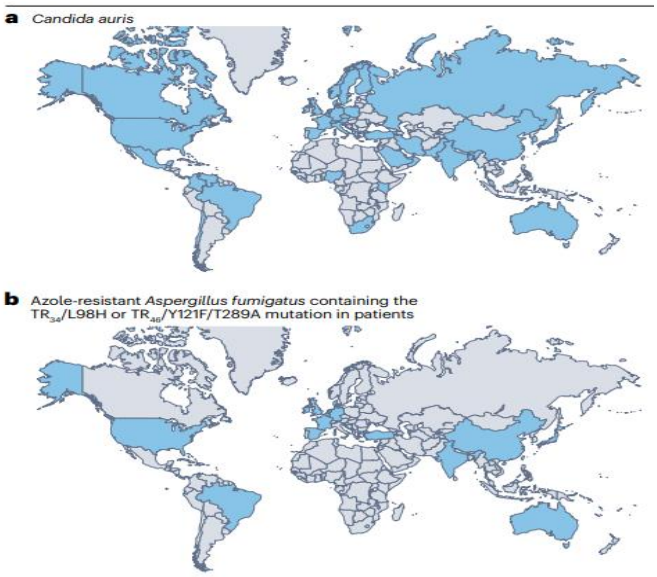


FIG 1 Climate change and antifungal use and resistance in agriculture and humans.

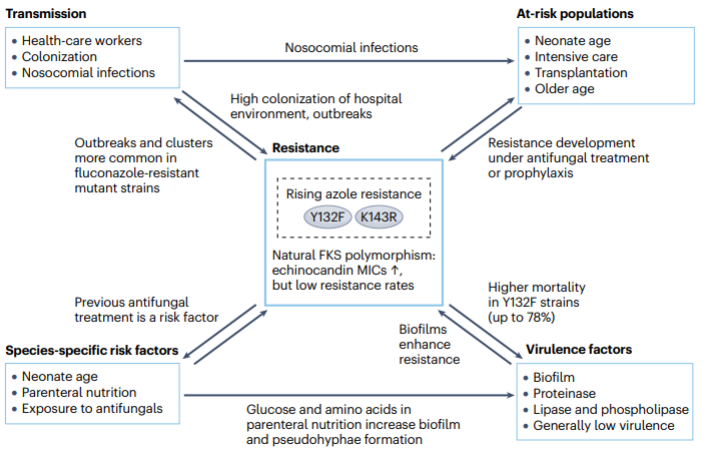
Hoenigl M et al. Crit Rev Microbiol 2024



Lockhart et al. Nat Rev Microbiol 2023

Candida parapsilosis complex in the clinical setting

Miriam Govrins & Cornelia Lass-Flörl



Nat Rev Microbiol 2023

Table 1 | Features of *Candida auris*, azole-resistant *Aspergillus fumigatus* and *Trichophyton indotineae*

Feature	*C. auris*	Azole-resistant *A. fumigatus*	*T. indotineae*
Antifungal resistance	Nearly all isolates are fluconazole resistant; amphotericin B, echinocandin and flucytosine resistance have been recorded	TR_{34} and TR_{46} mutants are resistant to itraconazole and voriconazole, respectively; through additional mechanisms, some isolates may become pan-azole resistant	Frequently resistant to terbinafine, sometimes resistant to azole antifungals (for example, itraconazole)
Country or region where first cases have been identified	East Asia, Indian subcontinent, South Africa and Venezuela	The Netherlands and elsewhere in Europe	Southern and Southeast Asia
Current treatment options	For azole-resistant and amphotericin B-resistant isolates, the treatment of choice is an echinocandin; for pan-resistant isolates, there are ongoing clinical trials for the new antifungals ibrexafungerp and fosmanogepix	Amphotericin B; there are ongoing clinical trials for the new antifungals ibrexafungerp and olorofim	Terbinafine remains a treatment option, but for resistant isolates, itraconazole or other triazoles are an option
Current distribution	Worldwide distribution, predominantly from the clades that originate from the Indian subcontinent, South Africa and Venezuela	Predominant in Europe but has been identified in Africa, North America, South America, Asia and Australia	Predominantly in India; cases have been reported throughout Asia, Europe, Africa and North America; cases in Europe have generally been associated with travel or migration
Clinical presentation	Can be present as a commensal microorganism both on the skin and in the urinary tract with no symptoms or as a pathogen in the bloodstream with typical symptoms of candidaemia	Typical presentation for aspergillosis but may be refractory to initial therapy	Inflammatory dermatophyte infection, most commonly affecting the face and body, occasionally affecting nails

Lockhart et al. Nat Rev Microbiol 2023

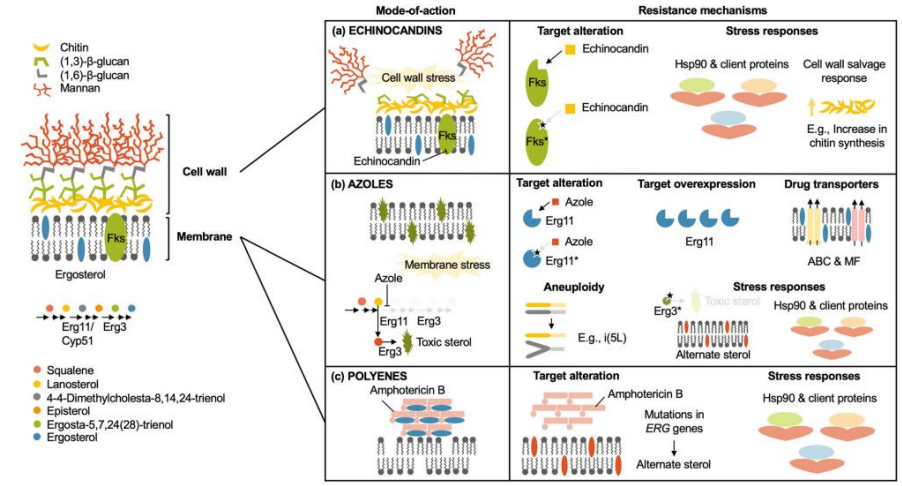


Fig. 1 Antifungal mode-of-action and mechanisms of resistance. a The echinocandins function by inhibiting (1,3)-β-D-glucan synthase, disrupting cell wall integrity and causing severe cell wall stress. Echinocandin resistance is primarily mediated by mutations in the drug target

Lee Y et al. Antimicrob Resistance 2023

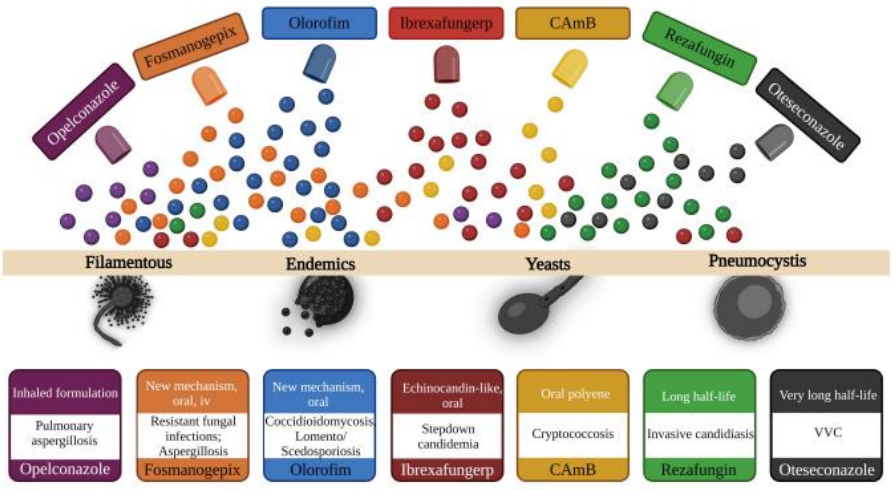
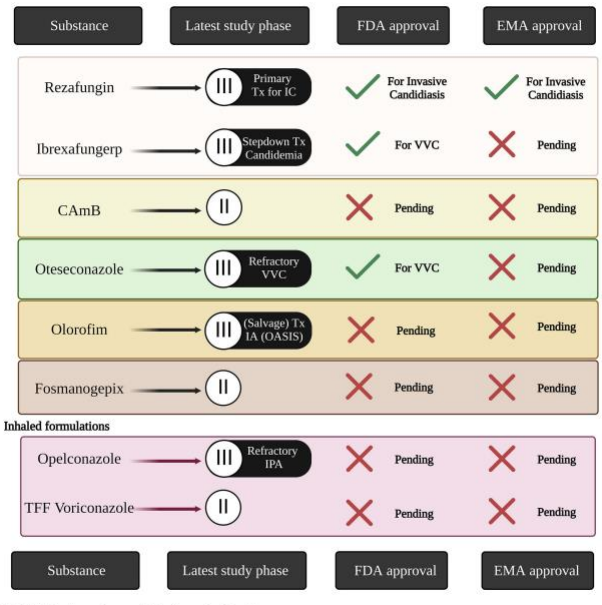


FIG 5 Indications for novel antifungal drug classes and situations where they might be used off-label.

Hoenigl M et al. Crit Rev Microbiol 2024



4 Clinical trials timeline and approval status for novel antifungals.

Hoenigl M et al. Crit Rev Microbiol 2024


DANKE

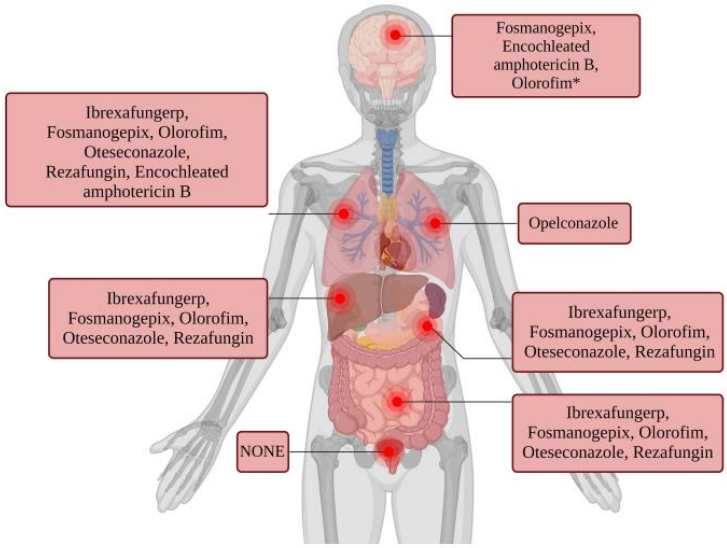


FIG 7 Tissue penetration of new antifungals. CAmB is not displayed: while tissue presentation is thought to mirror that of other AmB formulations, there are no animal data or human data supporting this assumption in the public domain.

Universitätsklinik für Innere Medizin II Innsbruck (Infektiologie, Immunologie, Tropenmedizin, Rheumatologie, Pneumologie)

Hoenigl M et al. Crit Rev Microbiol 2024

MEDIZINISCHE UNIVERSITÄT INNSBRUCK

TABLE 2 Drug-drug interactions of novel antifungals

	Substrate	Inhibitor	Inducer	Transporter	
Ibrexafungerp	Substrate 3A4	Strong inhibition of CYP2C8 and moderate inhibition of CYP3A4		P-gp, BCRP, BSEP, MRP2, and OATP1B3 inhibitor.	(462)
Fosmanogepix		Weak inhibitor of CYP2C9 and CYP2D6	Weak inducer of CYP2B6; a moderate inducer of CYP1A2, CYP2C19, and CYP3A4	Ibrexafungerp may be an inhibitor of MDR1, OATP1B3, and weakly BSEP	(463, 464)
Olorofim	Substrate 3A4	Weak inhibitor of 3A4 and 2D6	Weak inducer 1A2 and 2B6		
Rezafungin	Not a substrate, inducer, or inhibitor				(465)
Oteseconazole		Inhibitor of CYP3A4/5	Inducer of CYP3A4/5	Inhibitor of BCRP	(466)
Opelconazole	Substrate for CYP3A4 and CYP2C9[a]	No inhibition expected at clinical steady-state concentrations	No induction expected at clinical steady-state concentrations	As the expected clinical steady-state systemic C_{max} for opelconazole is ≤0.01 µM (≤6830 pg/mL), it is considered improbable that inhibitory interactions with the substrates of uptake and efflux transporters will occur	Source: data on file, provided by Sponsor
Encochleated amphotericin B					

[a]Expected to be of little clinical relevance in patients with pulmonary aspergillosis, given the delivery of the drug directly to the respiratory system via inhalation and the low systemic concentration of opelconazole.

Universitätsklinik für Innere Medizin II Innsbruck (Infektiologie, Immunologie, Tropenmedizin, Rheumatologie, Pneumologie)

Hoenigl M et al. Crit Rev Microbiol 2024

MEDIZINISCHE UNIVERSITÄT INNSBRUCK