Analysis of the clinical antibacterial and antituberculosis pipeline

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Table 1: Antibiotics and combinations containing a new chemical entity that are being developed against priority pathogens, approved by FDA 2017/2018

Name (trade name)	Approved by (date)	Antibiotic class	Route of administration (market authorization holder)	Expected activity against priority pathogens				Innovation			
				CRAB	CRPA	CRE	OPP	NCR	CC	T	MoA
Delafloxacin (Baxdela)	FDA (6/2017)	Fluoroquinolone	iv & oral (Melinta)	○	○	○	●	—	—	—	—
Vaborbactam + meropenem (Vabomere)	FDA (8/2017)	Boronate BLI + carbapenem	iv (Melinta)	○	○	●[1]	/	?	✓	—	—
Plazomicin (Zemdri)	FDA (6/2018)	Aminoglycoside	iv (Achaogen)	○	○	●	/	—	—	—	—

Table 2: Antibiotics and combinations containing a new chemical entity that are being developed against priority pathogens

Name (synonym)	Phase	Antibiotic class	Route of administration (developer)	Expected activity against priority pathogens				Innovation			
				CRAB	CRPA	CRE	OPP	NCR	CC	T	MoA
Eravacycline	NDA[1] MAA[1]	Tetracycline	iv (Tetraphase)	?	○	●	/	—	—	—	—
Omadacycline (Nuzyra)	NDA[2]	Tetracycline	iv & oral (Paratek)	○	○	○	●	—	—	—	—
Iclaprim	NDA[3]	DHFR inhibitor	iv (Motif Bio)	/	/	/	●	—	—	—	—
Lascufloxacin	NDA[4]	Fluoroquinolone	iv & oral (Kyorin)	○	○	○	?	—	—	—	—
Relebactam + imipenem/cilastatin	3	DBO-BLI + carbapenem/ degradation inhibitor	iv (MSD)	○	?	●[5]	/	—	—	—	—
Cefiderocol	3	Siderophore cephalosporin	iv (Shionogi)	●	●	●	/	?	—	—	—
Lefamulin	3	Pleuromutilin[6]	iv & oral (Nabriva)	/	/	/	●	?	✓[6]	—	✓
Sulopenem, sulopenem etzadroxil/ probenecid	3	Penem	iv (Iterum) oral (Iterum)	○	○	○[7]	/	—	—	—	—
Murepavadin (POL 7080)	3	Novel membrane targeting antibiotic	iv & inhaled (Polyphor)	/	●	/	/	✓	✓	✓	✓
Solithromycin	3[8]	Macrolide	iv & oral (Cempra/Melinta)	/	/	/	●	—	—	—	—
Levonadifloxacin Alalevonadifloxacin	3[9]	Fluoroquinolone	iv (Wockhardt) oral (Wockhardt)	○	○	○	?	—	—	—	—
Cefilavancin (TD-1792)	3[10]	Glycopeptide cephalosporine conjugate	iv (Thervance/ R-Pharm)	/	/	/	●	—	—	—	—
AAI101 + Cefepime	3	β-lactam BLI + cephalosporin	iv (Allecra)	○	○	○[11]	/	—	—	—	—
Contezolid Contezolid acefosamil	2/3[12]	Oxazolidinone	oral (MicuRx) iv (MicuRx)	/	/	/	●	—	—	—	—

Pathogen activity: ● active; ? possibly active; ○ not or insufficiently active; / activity not assessed.
Innovation assessment: ✓ criterion fulfilled; ? inconclusive data or no agreement among the advisory group; — criterion not fulfilled.

OPP (Other Priority Pathogens) include usually Gram-positive cocci, in the case of gepotidacin, zoliflodacin, solithromycin and delafloxacin, also *Neisseria gonorrhoeae*

NCR, no cross-resistance to other antibiotic classes; CC, new chemical class; T, new target; MoA, new mode of action;

Table 2: cont.

Name (synonym)	Phase	Antibiotic class	Route of administration (developer)	Expected activity against priority pathogens				Innovation			
				CRAB	CRPA	CRE	OPP	NCR	CC	T	MoA
Gepotidacin	2	NBTI (Triazaacenaphthylene)	iv & oral (GSK)	/	/	/	●	✓	✓	–	✓
Zoliflodacin	2	NBTI (Spiropyrimidenetrione)	oral (Entasis/GARDP)	/	/	/	●	✓	✓	–	✓
ETX2514 + sulbactam	2	DBO-BLI /PBP2 binder + β-lactam-BLI/PBP1,3 binder	iv (Entasis)	●	○	○	/	–	–	–	–
Nafithromycin (WCK 4873)	2	Macrolide	oral (Wockhardt)	/	/	/	●	–	–	–	–
Afabicin(Debio-1450)	2	FabI inhibitor	iv & oral (Debiopharm)	/	/	/	●	✓	✓	✓	✓
BOS-228 (LYS-228)	2	Monobactam	iv (Boston Pharmaceuticals)	○	○	●	/	–	–	–	–
Zidebactam + cefepime	1	DBO-BLI/ PBP2 binder + cephalosporin	iv (Wockhardt)	○	?	●	/	–	–	–	–
Nacubactam + meropenem	1	DBO-BLI/ PBP2 binder + meropenem	iv (Roche)	○	?	●[5]	/	–	–	–	–
VNRX-5133 + cefepime	1	Boronate-BLI + cephalosporin	iv (VenatoRX)	?	?	●	/	?	–	–	?
ETX0282 + cefpodoxime	1	DBO-BLI + cephalosporin	oral (Entasis)	○	○	●[5]	/	–	–	–	–
SPR 741 + β-lactam	1	Polymyxin + β-lactam	iv (Spero)	?	?	?	/	–	–	–	–
KBP-7072	1	Tetracycline	oral (KBP BioSciences)	○	○	○	●	–	–	–	–
TP-271	1	Tetracycline	iv & oral (Tetraphase)	?	○	○	●	–	–	–	–
TP-6076	1	Tetracycline	iv (Tetraphase)	●	○	?	/	–	–	–	–
TNP-2092	1	Rifamycin-quinolizinone hybrid	iv & oral (TenNor)	/	/	/	?	–	–	–	–
AIC 499 + unknown BLI	1	β-lactam + BLI	iv (AiCuris)	?	?	?	/	–	–	–	–

Pathogen activity: ● active; ? possibly active; ○ not or insufficiently active; / activity not assessed.
Innovation assessment: ✓ criterion fulfilled; ? inconclusive data or no agreement among the advisory group; – criterion not fulfilled.

[1] MAA submitted on 17 August 2017, CHMP has adopted positive opinion for approval.; NDA submitted on 2 January 2018 for the iv form only for cIAI, PDUFA date August 28, 2018

[2] NDA submitted on 5 February 2018, PDUFA date October 2018

[3] Completed NDA submission 14 June 2018

[4] NDA in Japan only

[5] Active against *K. pneumoniae* carbapenemase (KPC) but not metallo-β-lactamase-producing Enterobacteriaceae

[6] First systemic formulation of this class, which has been used topically and in animals previously

[7] Active against extended-spectrum β-lactamase-producing cephalosporin-resistant but not carbapenem-resistant Enterobacteriaceae

[8] withdrawn MAA, FDA complete response letter, currently no development activities outside of Japan

[9] Phase-3 trial ongoing only in India, phase-1 oral studies in the USA in 2014 (alalevonadifloxacin)

[10] Developed only for Russia

[11] Active against extended-spectrum β-lactamase-producing cephalosporin-resistant and some KPC producing carbapenem-resistant Enterobacteriaceae

[12] Contezolid acefosamil: Phase 2 in USA not yet recruiting. Contezolid: NDA in China expected end of 2018

Table 3: Biological antibacterial agents in clinical development

Name (synonym)	Phase	Antibiotic class	Route of administration (developer)	Expected activity against priority pathogens		
				PA	SA	CD
SAL-200	2	Phage endolysin	iv (Intron)	/	●	/
CF-301	2	Phage endolysin	iv (Contrafect)	/	●	/
Suvratoxumab[1]	2	Anti-*S. aureus* IgG monoclonal antibody	iv (MedImmune)	/	●	/
MEDI-3902[1]	2	Anti-*P. aeruginosa* IgG monoclonal antibody	iv (MedImmune)	●	/	/
AR-105 (Aerucin)	2	Anti-*P. aeruginosa* IgG monoclonal antibody	iv (Aridis)	●	/	/
IMM-529	1/2	Anti-*C. difficile* polyclonal antibody	oral (Immuron)	/	/	●
AR-301 (tosatoxumab)	1/2	Anti-*S. aureus* IgM monoclonal antibody	iv (Aridis)	/	●	/
514G3	1/2	Anti-*S. aureus* IgG monoclonal antibody	iv (XBiotech)	/	●	/
DSTA 4637S	1	Anti-*S. aureus* IgG monoclonal antibody/rifamycin	iv (Genentech/Roche)	/	●	/
PolyCab	1	Anti-*C. difficile* polyclonal antibody	iv (MicroPharm)	/	/	●

Pathogen activity: ● *active;* / *not applicable.*

PA: *Pseudomonas aeruginosa*
SA: *Staphylococcus aureus*
CD: *Clostridium difficile*
[1] These products are in trials for pre-emptive indications only.

Table 4: Antibiotics for the treatment of tuberculosis in clinical development

Name (synonym)	Phase	Antibiotic class	Route of administration (developer)	Innovation			
				NCR	CC	T	MoA
Pretomanid (PA 824)	3	Nitroimidazole	oral (TB Alliance)	?	—	—	?
SQ-109[1]	2/3	Diamine	oral (Sequella/Infectex)	?	—	✓	✓
Delpazolid (LCB01-0371)[2]	2	Oxazolidinone	oral (LegoChem)	—	—	—	—
Sutezolid[3]	2	Oxazolidinone	oral (TB Alliance/Sequella)	—	—	—	—
Telacebec (Q 203)	2	Imidazopyridine amide	oral (Qurient/Infectex)	✓	✓	✓	✓
Macozinone (PBTZ 169)	1 (2)	DprE1 inhibitor (benzothiazinone)	oral (Innovative Medicines for Tuberculosis Foundation/ Nearmedic Plus[4])	✓	✓	✓	✓
GSK-070 (GSK-3036656)	1	Leu RS inhibitor (oxaborole)	oral (GlaxoSmithKline)	✓	✓	✓	✓
OPC-167832	1	DprE1 inhibitor	oral (Otsuka)	?	✓	✓	✓
TBA-7371	1	DprE1 inhibitor	oral (TB Alliance)	✓	✓	✓	✓
TB-166[5]	1	Riminophenazine (clofazimine-analogue)	oral (Institute of Materia Medica, Chinese Academy of Medical Sciences & Peking Union Medical College)	—	—	—	—

Innovation assessment: ✓ *criterion fulfilled;* ? *inconclusive data;* — *criterion not fulfilled.*

[1] Chemically close to ethambutol
[2] Delpazolid also completed a phase-1 trial as injectable for MRSA and vancomycin-resistant *Enterococcus* spp. infections
[3] Developed by Sequella and independently by the Global Alliance for TB Drug Development, non-exclusive patent held by Sequella and by The Medicines Patent Pool
[4] In Russia developed by Nearmedic Plus
[5] Clofazimine is approved for leprosy and used for TB