02091

Characterization of co-infecting gram-negative pathogens isolated in addition to *Acinetobacter baumannii-calcoaceticus* complex (ABC) at baseline from patients enrolled in ATTACK

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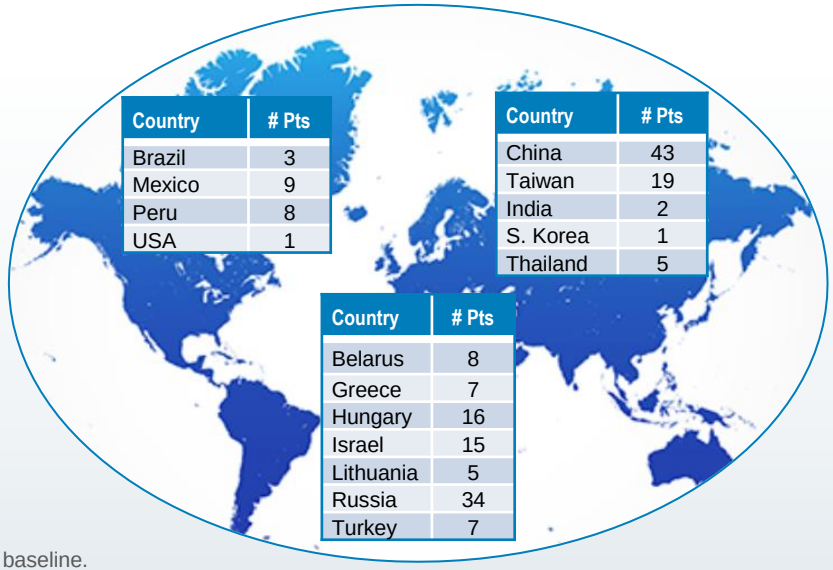
Background

- ATTACK was a global, Phase 3 trial conducted to evaluate the efficacy and safety of sulbactam-durlobactam (SUL-DUR) versus colistin (COL) for patients with ABC infections, including multidrug-resistant (MDR) strains
- Imipenem/cilastatin was added as background therapy to both arms to treat any non-ABC, co-infecting gram-negative pathogens (since SUL-DUR is ABC pathogen-focused and some serious infections can be polymicrobial)
- In the ATTACK trial, 36% of m-MITT patients had polymicrobial ABC infections at baseline
- Because DUR is a potent inhibitor of serine carbapenemases, the activity of imipenem might be restored against carbapenem-resistant co-infecting gram-negative organisms when combined therapeutically with SUL-DUR
- Here, we summarize the species identification and in vitro susceptibility of co-infecting gram-negative pathogens isolated at baseline from patients in the m-MITT population in ATTACK

183 patients from 16 countries enrolled in m-MITT population



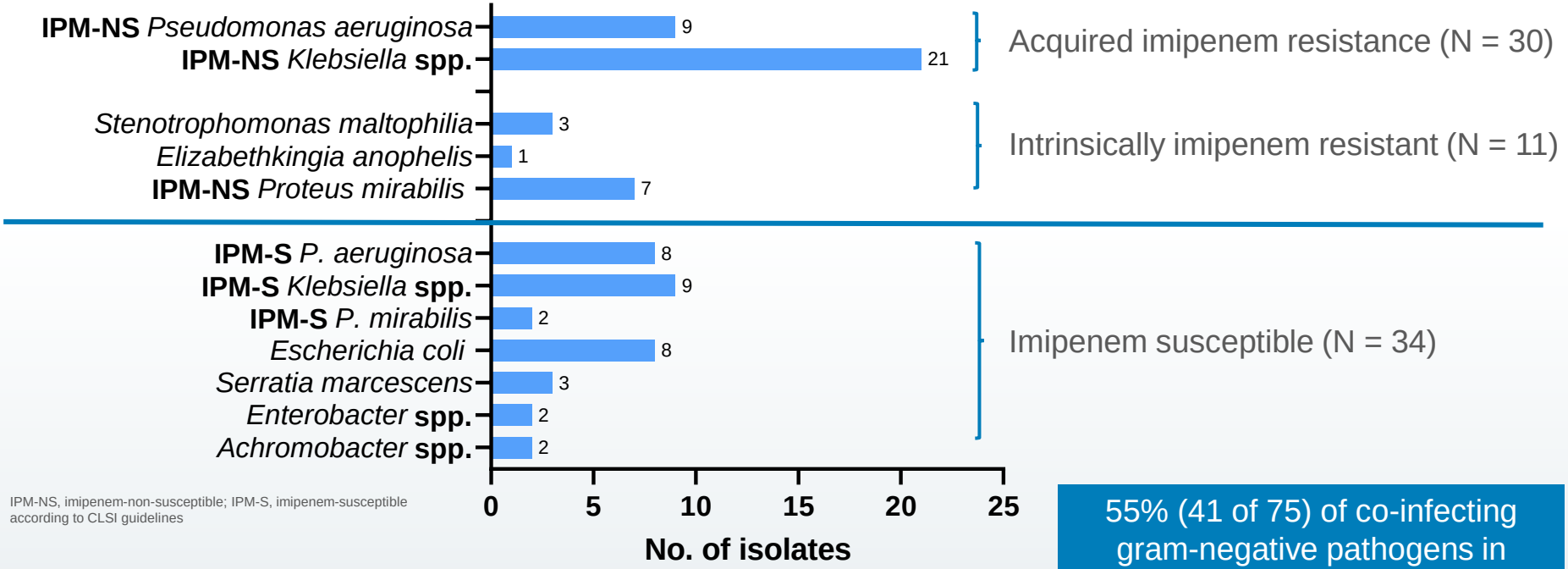
Country	# Pts
Brazil	3
Mexico	9
Peru	8
USA	1

Country	# Pts
China	43
Taiwan	19
India	2
S. Korea	1
Thailand	5

Country	# Pts
Belarus	8
Greece	7
Hungary	16
Israel	15
Lithuania	5
Russia	34
Turkey	7

m-MITT, patients in the ITT population who received any study drug and had an ABC organism isolated at baseline.

Results: Species identification and imipenem susceptibility of 75 co-infecting gram-negative pathogens isolated from 60 m-MITT patients with baseline polymicrobial infections



IPM-NS, imipenem-non-susceptible; IPM-S, imipenem-susceptible according to CLSI guidelines

Methods: Baseline gram-negative isolates were speciated by MALDI-TOF and antibiotic susceptibility was determined by broth microdilution using CLSI methodology and interpretive criteria at IHMA, Inc, Schaumburg, IL, USA, and IHMA-China, Shanghai

55% (41 of 75) of co-infecting gram-negative pathogens in ATTACK were non-susceptible to imipenem

Results: Durlobactam restored imipenem susceptibility to imipenem-nonsusceptible gram-negative co-infecting pathogens

Bacterial Species	% of Total (N)	% IPM-S[a]	% IPM-S (N) with SUL-DUR Added	% IPM-S (N) with DUR Added
Acquired imipenem resistance; N = 30				
Klebsiella spp.	28% (21)	0% (0)	23% (17)	23% (17)
P. aeruginosa	12% (9)	0% (0)	5.3% (4)	5.3% (4)
Intrinsically imipenem resistant; N = 11				
E. anopheles	1.3% (1)	0% (0)	0% (0)	0% (0)
P. mirabilis	9.3% (7)	0% (0)	0% (0)	0% (0)
S. maltophilia	4% (3)	0% (0)	0% (0)	0% (0)
Imipenem susceptible; N = 34				
Achromobacter spp.	2.7% (2)	2.7% (2)	2.7% (2)	2.7% (2)
Enterobacter spp.	2.7% (2)	2.7% (2)	2.7% (2)	2.7% (2)
Escherichia coli	10.7% (8)	10.7% (8)	10.7% (8)	10.7% (8)
Klebsiella spp.	12% (9)	12% (9)	12% (9)	12% (9)
P. aeruginosa	10.7% (8)	10.7% (8)	10.7% (8)	10.7% (8)
P. mirabilis	2.7% (2)	2.7% (2)	2.7% (2)	2.7% (2)
S. marcescens	4% (3)	4% (3)	4% (3)	4% (3)
Total percent (N)	**100% (75)**	**45% (34)**	**73% (55)**	**73% (55)**

[a]IPM-S = imipenem-susceptible according to CLSI guidelines. IPM, imipenem; SUL, sulbactam; DUR, durlobactam

SUL-DUR or DUR alone restored imipenem susceptibility to 70% of isolates (21 of 30) with acquired imipenem resistance

SUL-DUR or DUR alone had no effect on intrinsically imipenem-resistant species

No antagonism was observed between imipenem and SUL-DUR or DUR alone

Of the 75 baseline co-infecting gram-negative pathogens
- 34 (45%) were susceptible to imipenem alone
- 55 (73%) were susceptible to imipenem-SUL-DUR or imipenem-DUR

Conclusions

- Results presented in the current study suggest that for patients with polymicrobial ABC infections,
  SUL-DUR may restore imipenem susceptibility to imipenem-resistant co-infecting pathogens
- The primary efficacy and safety results from the ATTACK trial (02060, 02093 and 02145) suggest that, if approved, SUL-DUR could be an important option for the treatment of ABC infections, including carbapenem-resistant and MDR strains

Other sulbactam-durlobactam presentations at ECCMID 2022:

- **02060:** Primary outcomes for efficacy and safety of SUL-DUR vs. colistin in ATTACK
- **02093:** Efficacy and safety of SUL-DUR in the open label Part B of ATTACK
- **02145:** Safety profile of SUL-DUR vs. colistin in patients enrolled in ATTACK
- **02051:** Characterization of baseline ABC from patients in ATTACK
- **02037:** SUL-DUR in vitro dose response studies -/+ carbapenems vs. *A. baumannii* in the hollow-fiber infection model
- **01106:** In vitro activity of SUL-DUR against ABC isolates from a five-year surveillance program (2016-2020)