

Erika Matuschek¹, Laura Koeth², Andreas Petersen³, Gregory Stone⁴, Jenny Åhman¹ and Gunnar Kahlmeter¹

¹EUCAST Development Laboratory, Växjö, Sweden; ²Laboratory Specialists, Inc., Westlake, OH, USA; ³Statens Serum Institut, Copenhagen, Denmark; ⁴AstraZeneca Pharmaceuticals, Waltham, MA, USA

Introduction

The antimicrobial agent ceftazidime-avibactam (CAZ-AVI) is a combination of ceftazidime and a novel non-β-lactam β-lactamase inhibitor, avibactam. For disk diffusion antimicrobial susceptibility testing, the EUCAST disk mass for CAZ-AVI is set to 10-4 µg (presented at ECCMID 2014, poster 221), but clinical breakpoints and disk quality control (QC) criteria are yet to be determined.

Objective

The objective of this study was to establish EUCAST zone diameter ranges and targets for relevant QC strains.

Methods

QC ranges for ceftazidime-avibactam were established according to EUCAST SOP 9.0 (www.eucast.org/documents/sops/) using EUCAST disk diffusion methodology for *Escherichia coli* ATCC 25922 (EC), *Pseudomonas aeruginosa* ATCC 27853 (PA) and *Klebsiella pneumoniae* ATCC 700603 (KP). All testing was performed with the same lots of CAZ-AVI disks from two manufacturers (BD and Oxoid/Thermo Fisher Scientific). In the initial two-site study, performed at EUCAST Development Laboratory and Statens Serum Institut, tentative QC ranges were established using Mueller-Hinton agar from four manufacturers (BBL/BD, bioMérieux, Bio-Rad and Oxoid). Data from five additional European laboratories (see acknowledgements) were used to validate the tentative ranges using site specific Mueller-Hinton agar (10 repetitions per disk and site). For PA, additional validation was performed at Clinical Microbiology in Växjö, Sweden (n=20). Ceftazidime 10 µg and piperacillin-tazobactam 30-6 µg (Oxoid) were used as comparative disks in all studies.

For more information, please contact:
erika.matuschek@escmid.org

Table 1. Results from EUCAST QC study for ceftazidime-avibactam 10-4 µg.

Results /QC strain	<i>E. coli</i> ATCC 25922	<i>P. aeruginosa</i> ATCC 27853	<i>K. pneumoniae</i> ATCC 700603
Mean (mm) Initial two-site study*	27.1	24.6	21.4
Mean (mm) Validation study**	26.9	24.4	21.3
Median (mm) Initial two-site study*	27	25	21
Median (mm) Validation study**	27	24	21

* 240 observations (239 for *E. coli*), ** 100 observations (5 sites x 2 disks x 10 repetitions)

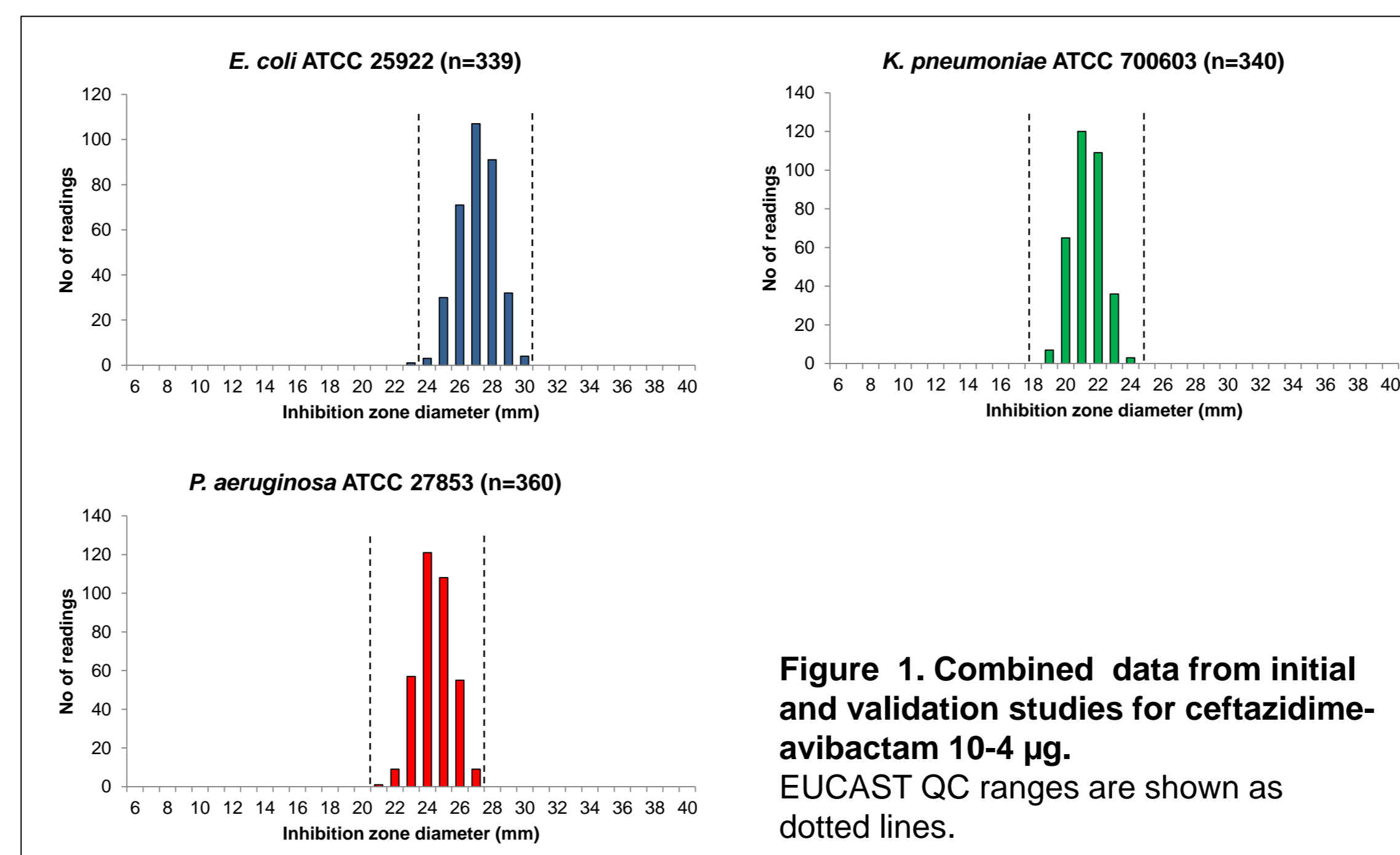


Table 2. EUCAST QC targets and ranges for ceftazidime-avibactam 10-4 µg.

Final targets and ranges /QC strain	<i>E. coli</i> ATCC 25922	<i>P. aeruginosa</i> ATCC 27853	<i>K. pneumoniae</i> ATCC 700603
EUCAST target (mm)	27	24	21
EUCAST range (mm)	24-30	21-27	18-24
Readings within range (%)*	99.7	100	100

* 240 observations (initial and validation studies)

Results

Mean and median values for CAZ-AVI zones from both studies are shown in Table 1. The final EUCAST targets and ranges are shown in Table 2.

The initial two-site study resulted in 240 readings per QC strain. Tentative ranges were based on median values ± 3 mm, which included all but one reading for EC and all readings for PA and KP. All readings for the comparative agents were within QC ranges, with median values on target ± 1 mm.

Median values from the validation study were identical to those of the two-site study for EC and KP, but for PA, the median values differed 1 mm. Further testing for PA in Växjö (n=20) resulted in zone diameters in the lower part of the tentative range. Based on all results for PA (n=360), we decided on a range of 24 ± 3 mm. This range included all readings from the initial and validation studies. Combined inhibition zone distributions are shown in Figure 1.

Conclusions

This EUCAST QC study following the EUCAST SOP 9.0 resulted in zone diameter targets and ranges for ceftazidime-avibactam 10-4 µg for *E. coli* ATCC 25922, *P. aeruginosa* ATCC 27853 and *K. pneumoniae* ATCC 700603 (Table 2). These ranges will be published in EUCAST QC tables when clinical breakpoints have been established.

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