Pseudomonas aeruginosa



ATM-AVI and CAZ-AVI exhibited potent activity against *P. aeruginosa* isolated from CF patients in the US and EU.



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Contact Information Helio S. Sader, MD, Ph.D.

JMI Laboratories 345 Beaver Kreek Centre, Suite A North Liberty, IA 52317 Phone: (319) 665-3370 Fax: (319) 665-3371 Email: helio-sader@jmilabs.com

- Pseudomonas aeruginosa is the most common cultured respiratory pathogen in individuals with cystic fibrosis (CF) and is associated with a more rapid decline in lung function.
- Aztreonam-avibactam (ATM-AVI) is under clinical development for the treatment of •^¦ã[`•Áã}~^&cã[}•Á&æ`•^åÁà^ÁÕ¦æ{Ë}^*æcãç^Áàæ&c^¦ãæÊÁã}&|`åã}*Á{^cæ||[Ë Ë|æ&cæ{æ•^Á (MBL) producers.
- Ø[`¦Á[c@^¦Á Ё|æ&cæ{æ•^Áã}@ãàãc[¦Á&[{àã}æcã[}•ÁÇÓŠÐÓŠQDÁ@æç^Áà^^}Á¦^&^}c|^Áæ]]¦[ç^åÁ by the US FDA: ceftazidime-avibactam (CAZ-AVI), ceftolozane-tazobactam (C-T), meropenem-vaborbactam (MEM-VAB), and imipenem-relebactam (IMI-REL).
- We evaluated the in vitroÁæ&cãçãc^Á [~Ác@^•^Á Í ÁÓŠÐÓŠQ•Áæ}åÁ& [{]ælæc [l•Áæ*æã } •cÁ P. aeruginosa causing CF pulmonary exacerbation.

Isolates were collected as part of SENTRY Antimicrobial Surveillance Program.

- Medical centers were asked to collect consecutive bacterial isolates from lower respiratory tract sites of CF patients in 2018–2021.
- Each participant center could contribute up to 40 *P. aeruginosa* isolates.
- Only isolates from invasive sampling, including transtracheal aspiration, bronchoalveolar lavage, protected brush samples, or qualified sputum samples, were accepted.
- The isolate collection included 383 P. aeruginosakie [|æc^ekçF0]æcia^}cDk-! [{ kHÍk { ^åi&ækek centers in the US (n=187) and 12 centers in Europe (EU; n=196; Figure 1).
- Isolates were categorized as multidrug-resistant (MDR) or extensively drug-resistant (XDR) according to criteria defined in 2012 by the joint European and US Centers for **Disease Control:**
- $T\ddot{O}\ddot{U}K\dot{A} [] \bullet \check{\bullet} \bullet A^{]} c\tilde{a}\dot{a} [\dot{A}c [\dot{A}F\dot{A}e * A] c\dot{A}\tilde{a}] \dot{A}^{-}H\dot{A}e] c\tilde{a} \{ \tilde{a} \& | [\dot{a}\tilde{a}e | \dot{A} \& | e \bullet A \bullet \dot{E}] c\tilde{a} = A \bullet \dot{E}]$ $\mathbf{\hat{Y}}\mathbf{\hat{U}}\mathbf{\hat{K}}\mathbf{\hat{A}}$
- Isolates were susceptibility tested by the CLSI broth microdilution method (M100; 2022).
- TQÔÁ!^• ~ [c•Á ^ !^Áã } c^!] !^c^åÁæ&& [!åã } * Ác [ÁÔŠÙQÁæ } åÐ [!ÁWÙÁØÖŒÁà !^æ \] [ã } c•Á 、@^ } Áæçæã|æà |^ÈÁ
- ŒÁ]¦[çã•ã[}æ|Áæ:c¦^[}æ{Ëæçãàæ&cæ{ÁÚSÐÚÖÁà¦^æ\][ã}cÁ[~ÁmÌÁ{*ЊÁ¸æ•Áæ]]|ã^åÁ~[¦Á comparison.
- MEM-VAB is not approved for *P. aeruginosa* treatment in the US; thus, MEM-VAB à¦^æ\][ã}c•Á]`à|ã•@^åÁ~[¦ÁÒ}c^¦[àæ&c^¦æ|^•ÁÇmIÐÌЬFĨÁ{ *ЊÁ~[¦ÁÙÐQÐÜDÁà^ÁÔŠÙQÁ ^!^Á applied for comparison.
- ATM-AVI (MIC I FOLLE ÊÁ I ÐNF Í Á { * ЊDÁã } @ãàãc^åÁ Ì HÈ I à Áæ } åÁ Ì Í ÈG à Á [~Áã• []æc^•Á~! [{ Ác@^ÁWÙÁæ } åÁ ÒWÁæcÁmÌÁ { *ЊÊÁ¦^•]^&cãç^|^ÁÇØã * `¦^ÁGDÈ
- CAZ-AVI (MIC í ∉ÐJ ∉ÊÁGÐÌÁ { *ЊLÁJÎÈHÃÐJÍÈIÃÁ•˘•&^]cãà|^ÁŽÙáÁã}ÁWÙÐÒWDÁ 、æ•Ác@^Á { [•cÁ æ&cãç^ÁÓŠÐÓŠQÁæ*^}cÊÁ~[||[^åÁà^ÁQ⊤QËÜÒŠÁÇJIÈÏÃÐJGÈÍÃÙÁã}ÁWÙÐÒWDÁæ}åÁÔËVÁ ÇÌJÈÌÃÐJFÈHÃÙÁã}ÁWÙÐÒWLÁØã*~¦^ÁGDÈÁ
- MEM-VAB (MIC_{1€ÐJ€}ÊÁ€ÈÍÐÌÁ { *ĐŠLÁ} [cÁæ]]¦[ç^åÁ~[¦ÁP. aeruginosa in the US) and MEM $(\mathsf{MIC}_{\mathsf{I}\in\mathsf{B},\mathsf{J}\in\mathsf{E}}) \in \hat{\mathsf{I}} = \hat$
- V[à!æ{^&ã}ÁÇVUÓDËÙÁ!æc^•Á, ^!^ÁÏHÈHÃÁæ}åÁÌÍÈÏÃÁã}ÁWÙÁæ}åÁÒWÊÁ!^•]^&cãç^|^ÁÇØã*`!^ÁGDÈÁ
- Œ{ [}*ÁVUÓ, } [}ËŲÁÇÞÙDÁã•[|æc^•ÊÁÌĮÈĨÃÁ,^¦^ÁÔŒZËŒXQ.ÙÁæ}åÁÏHÈFÃÁ,^¦^Áã}@ãàãc^åÁæcÁ ŒVŦËŒXQÁŦQÔÁ[~ÁmÌÁ { *ĐŠÁÇØã*`¦^ÁHDÈÁ
- ÔŒZËŒXQÁ¦^œã}^åÁ* [[åÁæ&cãçãc Âæ*æã } •cÁÔËV. ÞÙÁÇÎFÈFÃÙDÊÁQ TQËÜÒŠ. ÞÙÁÇÎGÈFÃÙDÊÁ]ã]^¦æ&ã||ã}Ёcæ:[àæ&cæ { ÁÇÚQŰËVŒZD.ÞÙÁÇÌÎÈÏÃÙDĚÁ { ^¦[]^}^ { ÁÇTÒTD.ÞÙÁÇÌÎÈĨÃÙDÊÁ æ}åÁ&ã]¦[~|[¢æ&ã}ÁÇÔQÚD.ÞÙÁÇJGÈFÃÙDÁã•[|æc^•ÁÇØã*`¦^ÁHDÈÁ
- ATM-AVI and TOB showed similar coverage against *P. aeruginosa*-resistant subsets (Figure 3).
- TÖÜÁæ}åÁÝÖÜÁ]@^}[c^]^•Á_^!^Á[à•^!ç^åÁæ{[}*ÁI€ÈFÃÐH€ÈFÃÁæ}åÆ}åÆ]ÈÍÃÐFÎÈÌÃÁ[~Á isolates from the US and EU, respectively (Figure 4).
- Œ { [} *ÁŦÖÜÁã•[|æc^•ÊÁÌÌÈFÃÁ、^¦^ÁÔŒZËŒXQ.ÙÊÁÎÍÈÏÃÁ、^¦^Áã}@ãàãc^åÁæcÁmÌÁ { *ĐŠÁ[~Á ŒVŦĔŒXQÊÁæ}åÁÍÏĖÍÃÁŢ^¦^ÁVŪÓËÙÁÇØã*˘¦^ÁHDÈÁ
- ŒV T ËŒXQÁæ}åÁVUÓÁ¦^cæã}^åÁæ&cãçãc^Áæ*æã}•cÁÍIÈIÃÁæ}åÁIJÈIÃÁ[~ÁÝÖÜÁã•[|æc^•ÊÁ, @^¦^æ•Á Ì GÈH Ã Á [~Ác@^•^Áã• [|æc^•Á ¸ ^¦^ÁÔŒZËŒXQ . ÙÁÇØã* ` ¦^ÁHDĚÁ