

Administration of Aztreonam-Avibactam

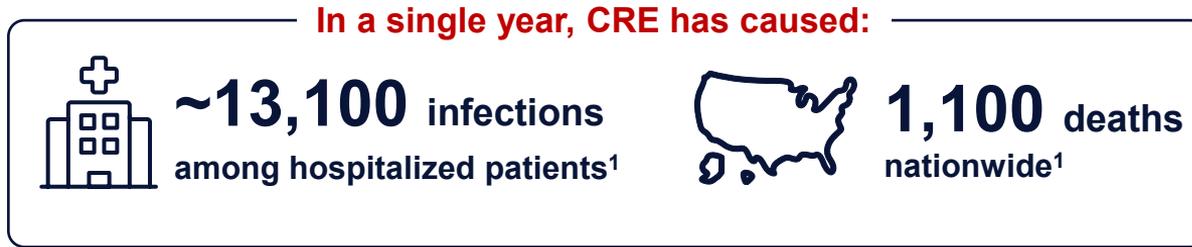
ICD-10 Coordination and Maintenance Committee Update
Spring 2025

abbvie

ATM-AVI is an investigational product and is not yet FDA approved. Prepared for ICD-10 Coordination & Maintenance Committee Update - Spring 2025

Antimicrobial resistance (AMR) is a major threat to human health

- CDC estimates that antibiotic resistant bacteria cause at least 2.8 million infections and 35,000 deaths a year in the US¹
- Carbapenem Resistant Enterobacterales (CRE) are characterized as an Urgent Threat:



2 TO 3X

Higher risk of mortality for patients with CRE vs those with carbapenem-susceptible Enterobacterales²

Despite continued stewardship, CRE is an ongoing threat with continuing prevalence and intensity

Product Overview

- Aztreonam-avibactam (ATM-AVI) is an investigational beta-lactam antibiotic/beta-lactamase inhibitor combination under development for the **treatment of complicated intrabdominal infections (cIAI)**, in combination with metronidazole, in patients with limited or no other treatment options.
- ATM-AVI has demonstrated in vitro activity against highly **antibiotic-resistant Gram-negative bacteria**, such as carbapenem resistant Enterobacterales (CRE), including those that produce metallo-beta-lactamases (MBLs), and *Stentrophomonas maltophilia*
- ATM-AVI is under consideration for fiscal year (FY) 2026 new technology add-on payment (NTAP)

ATM-AVI Product Components

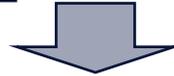
AZTREONAM (ATM)

- Monobactam beta-lactam antibiotic available since 1986
 - Binds to penicillin-binding proteins (PBPs), inhibiting peptidoglycan cell wall synthesis of Gram-negative bacteria, resulting in cell death
 - Not hydrolyzed by Class B MBLs, but susceptible to hydrolysis by Class A, C, and D serine beta-lactamases which are often co-expressed



AVIBACTAM (AVI)

- Beta-lactamase inhibitor that prevents the inactivation of ATM; available since 2015
 - Part of first β -lactamase inhibitor combination (AVYCAZ) effective against carbapenem resistant Enterobacterales (CRE)
 - Inhibits Class A, C, and some D serine beta-lactamases



ATM-AVI

Has in vitro activity against all 4 classes of beta-lactamases including Class B MBLs for which there are currently no effective inhibitors

ATM-AVI Recommended Dosage and Administration for cIAI¹

Recommended doses for adults with estimated CrCl >50 mL/min

Dose		Infusion Time	Dosing Interval
Loading	Maintenance	3 hours	Every 6 hours
ATM-AVI 2.67 g (aztreonam 2 grams and avibactam 0.67 grams)	ATM-AVI 2 g (aztreonam 1.5 grams and avibactam 0.5 grams)		

Dosage Forms and Strengths

ATM-AVI 2.0 g (aztreonam and avibactam) lyophilized powder for injection is supplied as a white to slightly yellow sterile powder for reconstitution in a single-dose, sterile, clear glass vial containing aztreonam 1.5 grams (equivalent to 1.5 grams of aztreonam) and avibactam 0.5 grams (equivalent to 0.542 grams of avibactam sodium).

Recommended doses for adults with estimated CrCl ≤50 mL/min

Estimated CrCl (mL/min)	Dose		Infusion Time	Dosing Interval
	Loading	Maintenance		
>30 to ≤50	ATM-AVI 2.67 g (aztreonam 2 grams and avibactam 0.67 grams)	ATM-AVI 1 g (aztreonam 0.75 grams and avibactam 0.25 grams)	3 hours	Every 6 hours
>15 to ≤30	ATM-AVI 1.8 g (aztreonam 1.35 grams and avibactam 0.45 grams)	ATM-AVI 0.9 g (aztreonam 0.675 grams and avibactam 0.225 grams)	3 hours	Every 8 hours
≤15 mL/min, including on hemodialysis	ATM-AVI 1.33 g (aztreonam 1 gram and avibactam 0.33 grams)	ATM-AVI 0.9 g (aztreonam 0.675 grams and avibactam 0.225 grams)	3 hours	Every 12 hours

Treatment of infections will be largely inpatient due to infusion time and frequency



Documentation of administration

- Intravenous infusion of aztreonam-avibactam is documented within medical records and would most commonly be found in the Medical Administration Record (MAR) and Electronic Health Record (EHR), progress reports and pharmacy records.
- Aztreonam-avibactam administration should be documented consistent with the documentation associated with other intravenous injections of antimicrobials

Two Phase 3 Studies for ATM-AVI



Summary of Proposed Indication: ATM-AVI, in combination with metronidazole, in adults with cIAI caused by susceptible Gram-negative microorganisms for which there are limited or no treatment options

Primary study (REVISIT study / C3601002)¹

A Phase 3 prospective, randomized, multicenter, open-label, central assessor-blinded, parallel group, comparative study

- 422 patients: 312 with cIAI or 110 with HABP/VABP
- Randomized 2:1 ATM-AVI ± MTZ versus meropenem ± colistin

Two Phase 3 studies

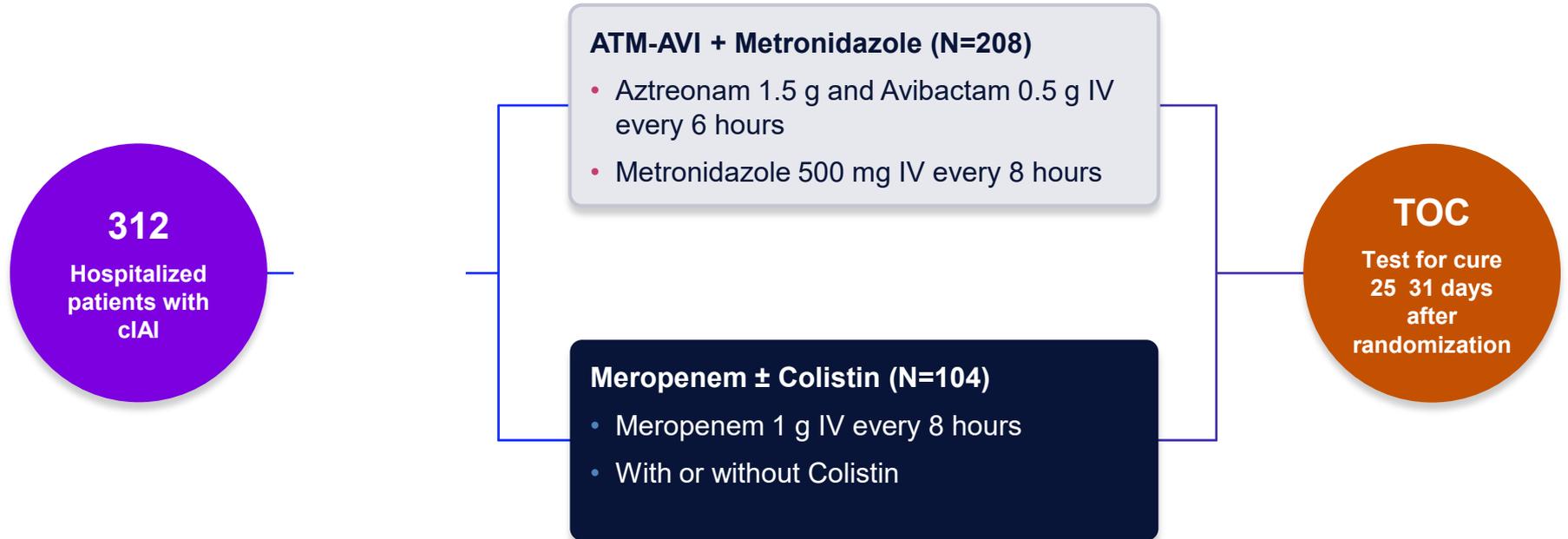
Resistant pathogen study (ASSEMBLE study / C3601009)²

A prospective, randomized, open-label, comparative study

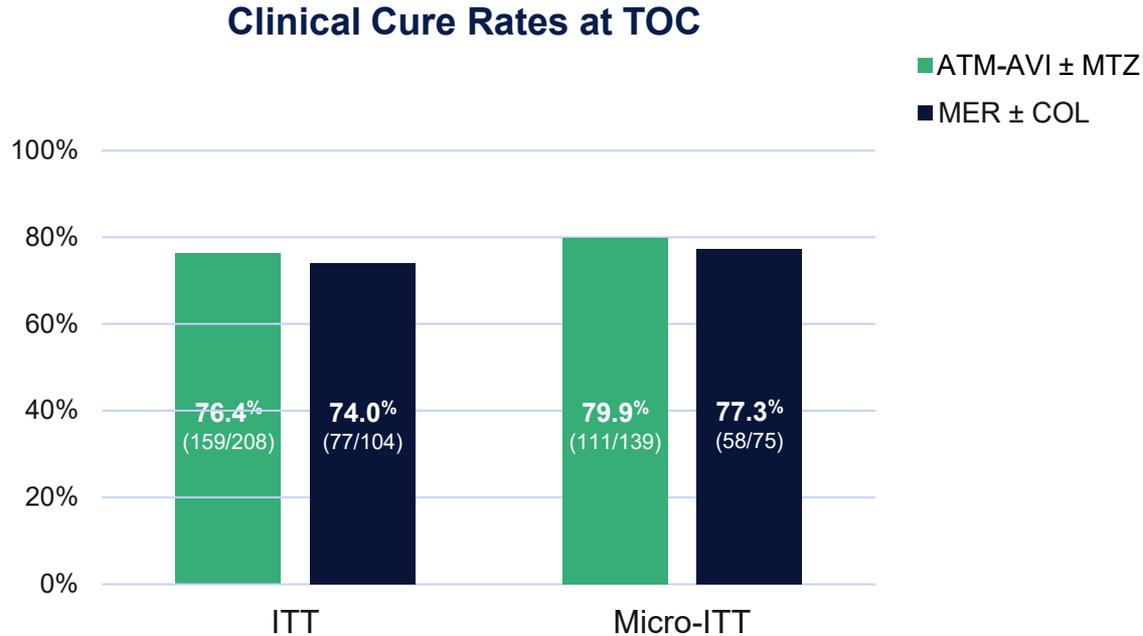
- 15 patients with cIAI, HABP/VABP, cUTI, and BSI with MBLs
- ATM-AVI ± MTZ versus BAT

REVISIT: Study Design

The REVISIT clinical trial was a phase 3 randomized, multinational, multicenter, open-label, central assessor-blinded trial.¹



REVISIT: Clinical Efficacy for Complicated Intra-abdominal Infections¹



The trial was not powered for a comparative inferential efficacy analysis.

ATM-AVI, aztreonam-avibactam; COL, colistin; ITT, intent-to-treat; MER, meropenem; micro-ITT, microbiological ITT; MTZ, metronidazole; TOC, test of cure.

1. Carmeli et al. Lancet Infect Dis. 2024 Oct 7:S1473-3099(24)00499-7

Safety Profile in Phase 2 and 3 Trials

- Most common Adverse Drug Reactions occurring in greater than 5% of patients included: anemia, diarrhea, ALT increased, and AST increased

Adverse Drug Reactions Occurring in 2% or More of ATM-AVI-treated Subjects in Phase 2 and 3 Trials

System Organ Class/Preferred Term	ATM AVI (N 305)	COMPARATOR (N 139)
Blood and lymphatic system disorders		
Anemia	6.9%	5.0%
Gastrointestinal disorders		
Diarrhea	6.2%	3.6%
Nausea	3.9%	2.2%
Vomiting	3.3%	1.4%
Abdominal pain	3.3%	4.3%
Investigations		
Alanine aminotransferase (ALT) increased	6.2%	5.0%
Aspartate aminotransferase (AST) increased	5.2%	3.6%
Vascular disorders		
Phlebitis	2.3%	0.0%
Skin and subcutaneous tissue disorders		
Rash	2.3%	0.0%
General disorders and administration site conditions		
Pyrexia	4.6%	5.0%
Participants with serious adverse events	20.7%	19.4%
Participants with fatal adverse events	7.2%	8.6%
Participants discontinued from the study due to adverse events	6.9%	9.4%
Participants discontinued study drug due to adverse event	4.3%	5.0%

ATM-AVI Clinical Efficacy and Safety Summary

Efficacy



- ATM-AVI MTZ was effective in treating patients with serious Gram-negative infections (cIAI)
- In vitro activity against beta-lactamase producing Enterobacterales, including those that produce Class B MBLs

Safety (Ph 2/3 Safety Population N=305)



- ATM-AVI was generally safe and well-tolerated
- The adverse drug reactions (ADRs) for ATM-AVI are consistent with those for aztreonam monotherapy