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Monoclonal Antibody-Based Immunotherapy as an Adjunct to Antibiotics in Pseudomonas Aeruginosa Infections: A Clinical Perspective

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Abstract. Multidrug-resistant Pseudomonas aeruginosa has heightened global public health challenges. New treatment methods must be investigated to assist antibiotics and inhibit the evolution of antibiotic resistance in pathogens. Monoclonal antibody (mAb)-based immunotherapy shows great promise, as it utilises our own immune defence to fight infections, with fewer side effects and less selective pressure. This literature review focuses on monoclonal antibody-based immunotherapy as a potential adjunct or alternative to antibiotics. The review examines the published studies that target key bacterial components such as PcrV, PsI and lipopolysaccharide in MDR-P. aeruginosa using specific mAbs, evaluating target identification and underlying mechanisms. The study aims to identify whether monoclonal antibodies can enhance antibiotic therapy or serve as standalone treatments by analysing the experimental results and trial outcomes. Preclinical studies have reported multiple cases in which anti-checkpoint mAbs successfully suppressed P. aeruginosa infection in animal models. However, the clinical evidence suggests that mAb therapy may not be sufficient on its own due to the complex clinical conditions in ICU patients, but could serve as a valuable adjunct to antibiotic treatment. Monoclonal Antibody-Based Immunotherapy is a promising approach for treating MDR-P. aeruginosa as an adjunct to antibiotics, but its potential for use alone requires further study.

Keywords: Pseudomonas aeruginosa, Monoclonal antibody-based immunotherapy, antibiotics, combination, antibiotics-resistance

1. Introduction

Pseudomonas aeruginosa is a Gram-negative opportunistic pathogen which accounts for 7.1 to 7.3% of all healthcare-associated infections and is the most common etiological agent of nosocomial pneumonia [1]. Antibiotics are considered the best course of action; however, this theory is undermined by the rise of antimicrobial resistance (AMR) in pathogens. Multidrug-resistant (MDR) Pseudomonas aeruginosa accounted for 32,600 infections and 2,700 deaths in the United States in 2017, with an estimated healthcare burden exceeding $767 million [1]. In broader terms, AMR represents a major global public health challenge, contributing to higher rates of morbidity,

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mortality, and therapeutic failure in infectious diseases, while also imposing substantial economic burdens on individuals and healthcare systems [2]. The management of the infections caused by P. aeruginosa is challenging due to the rise of antibiotic resistance and multidrug-resistant strains [3]. Deploying antibiotics such as Carbapenems against them only creates selective pressure, which contributes to the evolution of antibiotic-resistant strains [3]. Although other drug classes are typically reserved for treating multidrug-resistant bacterial infections, they still prove effective; however, this trend is not promising. If this trend continues, more antibiotics will become ineffective against pathogens over the next 10–20 years. This leads to increased restrictions on using antibiotics to treat MDR-P. aeruginosa; Immunotherapy serves as a potential treatment approach, as it only weakens the pathogen or exposes it to the immune system, thereby creating less selective pressure. Alternative treatments must be investigated as adjuncts or replacements to antibiotics. There is a novel treatment method that utilises our own immune system rather than chemicals, known as immunotherapy. Administering antibodies as therapeutics, which is referred to as passive immunisation, could serve as a secondary approach to these superbugs. This literature will discuss the potential of monoclonal antibody-based immunotherapy as an adjunct to the traditional antibiotic treatment by comparing the literature and analysing its findings. This literature offers new clinical insights for developing future strategies against superbugs such as MDR-P. aeruginosa, including whether combination therapy can enhance treatment efficacy and whether monoclonal antibody-based immunotherapy could help limit the spread of antibiotic resistance across strains.

2. Antibody targets and mechanisms

Antibody therapy exploits the innate functions of antibodies, which are typically generated in response to infection or immunisation. Antibodies perform multiple roles, such as attaching to bacterial cells or neutralising toxins, facilitating phagocyte-mediated clearance through opsonophagocytosis, and activating complement pathways, and thereby enabling pathogen elimination [1]. One example is bezlotoxumab (Clostridium difficile treatment), which is one of the few mAb drugs approved by the FDA that inhibits these properties to fight bacterial and viral pathogens [4].

2.1. Target identification

The type III secretion system (T3SS) is a specialised protein translocation pathway employed by various pathogenic bacteria to manipulate host cellular processes, enabling immune evasion and enhancing dissemination in the host [5]. P. aeruginosa also has this structure, which releases proteinaceous toxins known as effectors to target cells, inhibiting cellular biochemical and enzymatic reactions necessary for the body's immune defenses against bacterial infection [5]. Although the mechanism behind the T3SS activation is still shrouded, the evidence proves that a needle-tip protein located at the top of the P. aeruginosa T3SS structure (needle-like structure) known as PcrV, is essential to the activation and regulated delivery of those effectors [5]. It has been identified as an important therapeutic target because it plays a central role in T3SS regulation and is abundant in patients' blood [5].

Another potential target would be Psl, which is an abundantly expressed exopolysaccharide composed of mannose, rhamnose, and glucose. It is important for P. aeruginosa's antibiotic-resistant biofilm formation and maintenance [6]. Moreover, Psl facilitates bacterial adherence to epithelial cells while blocking complement deposition, thereby allowing P. aeruginosa to escape detection and clearance by the host immune system. These characteristics make them a key therapeutic target [6].

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The evidence supports this claim, suggesting that targeting PsI (and PcrV) with an antibody can inhibit acute lung injury and bacterial numbers in tissue in an impactful way (reducing the body-to-weight ratio by about half compared to control) [7]. In addition, other targets have been identified as well, such as lipopolysaccharide (LPS), an essential virulence factor which promotes evasion of host defences and establishment of infection in the pathogenesis of P. aeruginosa infections [8]. LPS is a potent stimulator of the innate immune system, which can trigger a robust immune response by activating toll-like receptor 4 [8]. However, when unregulated, it causes intense inflammation due to the excessive release of pro-inflammatory cytokines [8]. By targeting LPS as a therapeutic target, the evidence shows that the bacterial burden was reduced and the survival rate of the experimental animals increased (bacterial burden had a 4.68 log reduction in the lung) [8].

2.2. Mechanism of action

Monoclonal antibody-based immunotherapy works under different mechanisms in different bacterial pathogens. In the case of P. aeruginosa, the different targets have varied mechanisms. In the case of P. aeruginosa, antibodies against PcrV block the type III secretion system, preventing toxin injection into host cells and neutralising this key virulence mechanism [5]. Antibodies targeting surface components such as Psl or LPS enhance bacterial recognition by the immune system, promoting opsonophagocytosis and complement-mediated killing [8,9]. Unlike antibiotics, which directly kill bacteria and exert strong selective pressure for resistance, antivirulence antibodies may reduce the likelihood of resistance development while still enabling pathogen clearance.

3. Preclinical & translational evidence

Numerous studies over the decades have explored monoclonal antibody-based immunotherapy in preclinical models, with many yielding promising results. The first example is mAb166 which was investigated in 2003, which markedly reduced alveolar epithelial damage and lung edema within 4 hours of bacterial instillation, whereas the group that received phosphate-buffered saline exhibited significant increases in lung epithelial injury and oedema [10]. Another example is the anti-PcrV antibody, COT-143, which is a novel humanised anti-PcrV monoclonal antibody desired by Shionogi & Co., Ltd. Numata et al., 2024 found that COT-143 inhibited T3SS-mediated effects of P. aeruginosa lung infection. The bacterial cells have been significantly decreased in a dose-dependent manner. In addition, COT-143 enhanced bacterial phagocytosis by neutrophils, with concurrent decreases in neutrophil apoptosis and viable bacterial counts [5].

Many studies also investigated the antibody against another therapeutic target, such as DiGiandomenico et al., 2012, where a mAb called Cam-003 provided promising protection to mice infected with strain PAO1 and improved the survival rate of mice infected with strain 6294 in a concentration-dependent manner [11]. Another example involves Psl: Ray et al. conducted an experiment to determine whether anti-Psl recognises Psl within P. aeruginosa biofilms and whether its inhibition of bacterial growth occurs independently or in conjunction with innate immune effector cells [9]. The result confirms that Psl is a highly abundant target and accessible to mAb. Furthermore, Anti-Psl monoclonal antibodies interfered with early biofilm formation by blocking bacterial surface attachment and intercellular aggregation, with effects determined by epitope specificity. Similar outcomes were observed for LPS as well. One study investigated the therapeutic efficiency of using two anti-LPS mAbs, WVDC-0357 and WVDC-0496, against P. aeruginosa PAO1 [8]. The results indicate that two mAbs have induced bacterial aggregation and mediate direct antibacterial activity against P. aeruginosa.

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The multiple-targeting mAb has also been tested and is currently undergoing a preclinical study. One example is gremubamab, a Bispecific Monoclonal Antibody that targets both PcrV and PsI to enhance Neutrophil-Mediated Killing of P. aeruginosa in patients with bronchiectasis [12]. The results indicated that both mAbs induced bacterial aggregation and exerted direct antibacterial activity against P. aeruginosa. Although the anti-PcrV played a major role in patients' serum, the anti-PsI has limited activity. In conclusion, these results prove that Monoclonal Antibody-Based Immunotherapy has excellent potential in treating P. aeruginosa; thus, it needs to be further evaluated in clinical trials.

4. Clinical trials / human studies

Several monoclonal antibody-based immunotherapies for P. aeruginosa have entered clinical trials; however, results were not always encouraging. The first example is gremubamab (MEDI3902), which entered phase 2 of clinical trials in 2015 [13]. The original result from phase 1 shows good patient tolerability and dose-dependent increases in serum anticytotoxic and opsonophagocytic killing activities. However, in Phase 2, gremubamab failed to achieve a 50% reduction in the incidence of P. aeruginosa pneumonia. The heterogeneity of P. aeruginosa pneumonia in critically ill patients may limit the therapeutic benefit of Gremubamab. The result indicates that the baseline inflammation state significantly influenced the pharmacokinetic profile of Gremubamab; patients with a low inflammation state respond better to the therapy. High baseline inflammatory states or cachexia-associated changes in protein metabolism and pharmacokinetics may reduce antibody availability and efficacy [13]. Although it has an acceptable safety profile, its therapeutic efficacy remains a critical problem. There are several reasons that may lead to this. The first is the study's limitation, as described by the researchers: these limitations include a slow rate of subject enrollment, some errors in randomisation, and the possibility of misdiagnosis, which may underpower the analysis. The second is the therapeutic efficiency of the antibody. Monoclonal antibodies enhance bacterial clearance by neutralising virulence factors and promoting immune-mediated killing. If the immune system is already compromised by factors such as severe inflammation, the therapy may be less effective.

However, not all clinical trials failed. Another phase 2a clinical trial focused on panobacumab, a fully human anti-LPS mAb [14]. They examined its impact on Nosocomial P. aeruginosa pneumonia, and the results are promising. They found that panobacumab has a good safety profile, was well tolerated and showed no signs of immunogenicity; it was also detected in respiratory samples. It has a pharmacokinetic profile like that in healthy volunteers, and all 13 volunteers who received three doses survived. It shows high clinical cure and survival rates in patients with nosocomial P. aeruginosa O11 pneumonia, which suggests that further trials are needed [14].

In general, the clinical evidence regarding the efficacy and safety of monoclonal antibody-based immunotherapies for P. aeruginosa is minimal, with only one case showing a positive outcome. The FDA currently approves no monoclonal antibody for use against P. aeruginosa. However, the concept of using monoclonal antibodies as immunotherapy to fight bacterial pathogens is valid. The success of bezlotoxumab against C. difficile demonstrates the clinical feasibility of antibody-based antibacterial therapy [15]. However, its administration strategies must be further investigated to ensure sufficient therapy exposure in the patient under clinical conditions.

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5. Adjunct strategies / combinations

5.1. Antibiotics

Although multiple studies report that the use of monoclonal antibody-based immunotherapies alone may not achieve therapeutic efficacy, much research does justify their potential role as adjunct therapy. Le et al. 2019 elevate the therapeutic efficiency of MEDI3902 (a bispecific mAb) as an adjunct with meropenem [16]. The findings indicate that combining meropenem with MEDI3902 significantly prolonged survival time, even at relatively low doses, compared to when either treatment was administered alone. The evidence was provided by the same literature we discussed above, which examined the effect of panobacumab on critical patients with nosocomial P. aeruginosa O11 pneumonia [14]. The results indicated that it could serve as a good adjunct therapy to antimicrobial therapy. The patients have been pre-treated with antimicrobial therapy for >1 day. Additionally, the recurrence rate of P. aeruginosa infection ranges from 25% to 40% after the first infection, indicating panobacumab may inhibit this recurrence rate due to the prolonged biological effects of the antibody in patients' tissues. From a molecular mechanism perspective, MEDI3902 targets PcrV and Psl: one is essential for regulating toxin production, and the other is critical for biofilm formation. Theoretically, by blocking these factors (especially for Psl), the penetration of antibiotics could be increased because bacteria have weaker biofilm [16]. And for panobacumab, although the molecular mechanisms have not been provided in evidence, in theory, it could indirectly support the antibiotics by immune effector enhancement [14]. In general, monoclonal antibodies do not directly support antibiotic activity, as they act through distinct mechanisms, neutralising bacterial virulence factors and promoting immune-mediated clearance rather than directly killing the bacteria. Their role is to weaken the pathogen and enhance immune recognition, while antibiotics target essential bacterial processes and kill them.

5.2. New combination strategies

Apart from antibiotics, other combination strategies are also being explored; one is with bacteriophages. Bacteriophages (phages) are viruses that use bacteria as hosts. They represent a targeted approach effective against MDR bacteria. Junya et al., 2024 explored this possibility by combining an anti-PcrV mAb with Pseudomonas virus ΦR18 against P. aeruginosa PA103 [17]. The results suggested that the combination therapy was more effective, as shown by the significant differences in survival rates between the saline-treated control group and the combination therapy group, along with marked reductions in bacterial load, MPO activity, and intrapulmonary IL-6 levels compared to the other treatment groups. The combination therapy helped reduce lung edema and bacterial proliferation, protecting the mice from developing fatal septic shock [17]. This observation provides new insights for researchers: bacteriophages are natural predators of bacteria, and bacteria do not develop resistance to phages in the same way they do to antibiotics.

6. Challenges and future directions

The current state of mAb immunotherapy remains immature. Several challenges must be addressed before the mAbs can be used in clinical practice. The main problem is heterogeneity; the mAb may struggle in the critical patient with a complex condition, such as a high inflammatory state. Studies have shown that the efficacy of mAbs can be influenced by host-pathogen interactions, including factors such as immune response modulation and tissue penetration [18]. Additionally, there is

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evidence that mAb therapy is more effective in the early stages of the disease. However, the clinical trial, like Chastre et al. 2022 included critically ill patients, which could hinder the real efficiency of mAb [13]. Antibody therapy may need to be given early to reach its maximum effects, which is problematic because many patients discovered their disease way past the early stage. Moreover, the manufacturing costs of bispecific antibodies may prove challenging due to their complex structure. The next focus should be to identify the potential benefits of mAb immunotherapy for the patient group with P. aeruginosa. The therapy could still be valuable even if it is only effective in the early disease stage. In addition, mAb therapy shows strong promise when used as an adjunct to antibiotics, but future studies should also explore its role as an independent strategy, particularly considering the rise of antibiotic resistance. A new treatment route is still needed, and mAb immunotherapy is one of them.

7. Conclusion

In conclusion, mAbs hold great promise for treating MDR-P. aeruginosa as an adjunct to antibiotics. By targeting specific proteins in P. aeruginosa, mAbs disrupt its virulence and expose it to the host immune system. By doing that, they weaken the pathogen rather than kill it, which avoids natural selection and slows the spread of antibiotic-resistant strains. Although pre-clinical studies show promising results, there is currently no mAb therapy that has passed clinical trials. Both clinical and pre-clinical observations indicated it could serve as a good adjunct to antibiotics. However, future studies and trials should focus on identifying patient subgroups that benefit from mAbs and developing targeted therapeutic strategies for these groups.

References

[1] A. M. Horspool et al., 2023. “Development of an anti-Pseudomonas aeruginosa therapeutic monoclonal antibody WVDC-5244, ” Front. Cell. Infect. Microbiol., vol. 13, no. April, pp. 1–12.
[2] C. for D. C. and Prevention, 2019. “Antibiotic resistance threats in the United States, ” Cdc, p. 148.
[3] Ramatla, T., et al., 2025. Global prevalence and antibiotic resistance profiles of carbapenem-resistant Pseudomonas aeruginosa reported from 2014 to 2024: a systematic review and meta-analysis. Frontiers in Microbiology, 16, 1599070.
[4] S. Johnson and D. N. Gerding, 2019. “Bezlotoxumab, ” Clin. Infect. Dis., vol. 68, no. 4, pp. 699–704.
[5] S. Numata et al., 2024. “Novel humanized anti-PcrV monoclonal antibody COT-143 protects mice from lethal Pseudomonas aeruginosa infection via inhibition of toxin translocation by the type III secretion system, ” Antimicrob. Agents Chemother., vol. 68, no. 10, doi: 10.1128/aac.00694-24.
[6] D. E. Tabor et al., 2018. “Pseudomonas aeruginosa PcrV and Psl, the Molecular Targets of Bispecific Antibody MEDI3902, Are Conserved Among Diverse Global Clinical Isolates, ” J. Infect. Dis., vol. 218, no. 12, pp. 1983–1994, doi: 10.1093/infdis/jiy438.
[7] H. N. Le et al., 2018. “MEDI3902 correlates of protection against severe pseudomonas aeruginosa pneumonia in a rabbit acute pneumonia model, ” Antimicrob. Agents Chemother., vol. 62, no. 5, pp. 1–11.
[8] J. Kang et al., 2023. “Monoclonal antibodies against lipopolysaccharide protect against Pseudomonas aeruginosa challenge in mice, ” Front. Cell. Infect. Microbiol., vol. 13, no. June, pp. 1–18.
[9] V. A. Ray et al., 2017. “Anti-Psl Targeting of Pseudomonas aeruginosa Biofilms for Neutrophil-Mediated Disruption, ” Sci. Rep., vol. 7, no. 1, pp. 1–12, doi: 10.1038/s41598-017-16215-6.
[10] K. Faure et al., 2003. “Effects of monoclonal anti-PcrV antibody on Pseudomonas aeruginosa-induced acute lung injury in a rat model, ” J. Immune Based Ther. Vaccines, vol. 1, doi: 10.1186/1476-8518-1-2.
[11] A. DiGiandomenico et al., 2012. “Identification of broadly protective human antibodies to Pseudomonas aeruginosa exopolysaccharide Psl by phenotypic screening, ” J. Exp. Med., vol. 209, no. 7, pp. 1273–1287.
[12] M. B. Long et al., 2024. “A Bispecific Monoclonal Antibody Targeting Psl and PcrV Enhances Neutrophil-Mediated Killing of Pseudomonas aeruginosa in Patients with Bronchiectasis, ” Am. J. Respir. Crit. Care Med., vol. 210, no. 1, pp. 35–46, doi: 10.1164/rccm.202308-1403OC.

DOI: 10.54254/2753-8818/2026.AU29755

[13] J. Chastre et al., 2022. “Safety, efficacy, and pharmacokinetics of gremubamab (MEDI3902), an anti-Pseudomonas aeruginosa bispecific human monoclonal antibody, in P. aeruginosa-colonised, mechanically ventilated intensive care unit patients: a randomised controlled trial, ” Crit. Care, vol. 26, no. 1, pp. 1–14.
[14] Q. Lu et al., 2011. “Pharmacokinetics and safety of panobacumab: Specific adjunctive immunotherapy in critical patients with nosocomial Pseudomonas aeruginosa O11 pneumonia, ” J. Antimicrob. Chemother., vol. 66, no. 5, pp. 1110–1116, doi: 10.1093/jac/dkr046.
[15] A. M. Skinner et al., 2023. “Efficacy of bezlotoxumab to prevent recurrent Clostridioides difficile infection (CDI) in patients with multiple prior recurrent CDI, ” Anaerobe, vol. 84, no. June, p. 102788.
[16] Le, Hoan N., et al., 2019. "Treatment efficacy of MEDI3902 in Pseudomonas aeruginosa bloodstream infection and acute pneumonia rabbit models." Antimicrobial agents and chemotherapy 63.8: 10-1128.
[17] Junya, O. et al., 2024. Effects of the combination of anti-PcrV antibody and bacteriophage therapy in a mouse model of Pseudomonas aeruginosa pneumonia. Microbiology Spectrum, 12(12), e01781-24.
[18] M. Piscaglia et al., 2025. “Exploring Human Use of Monoclonal Antibodies Against Critical Bacteria: A Scoping Review of Clinical Trials, ” Infect. Dis. Ther., vol. 14, no. 8, pp. 1619–1647.