



(REVIEW ARTICLE)



## CD23-TARGETED IMMUNOTHERAPY FOR GIANT CELL MYOCARDITIS

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### ABSTRACT

Giant cell myocarditis (GCM) is a rare, rapidly progressive cardiac disorder characterized by giant, multinucleated cells that contribute to severe myocardial damage. Existing combination immunosuppressive therapies, although directed at immune-mediated injury, lack precision and are associated with considerable adverse effects. A CD23-targeted intervention holds promise as a more selective, safer adjunctive treatment. This review evaluates a strategy centered on the low-affinity IgE receptor (CD23/FcεRII), predominantly expressed on alternatively activated (M2a) macrophages and B cells. The proposed method uses engineered anti-IgE-IgE complexes to engage CD23, inhibiting macrophage fusion—a defining feature of GCM—and fostering a more anti-inflammatory immune milieu. This therapy also aims to protect myocardial tissue by suppressing pathogenic T-cell responses and slowing disease progression. The review details the scientific basis for this approach, outlines laboratory testing protocols, suggests optimal delivery systems, and considers translational hurdles to clinical implementation.

**Keywords:** Giant Cell Myocarditis, CD23, M2a Macrophages, Anti-IgE:IgE Complexes, Immunomodulation, Macrophage Fusion

### 1 INTRODUCTION

Giant cell myocarditis (GCM) is a rapidly progressive and lethal form of myocardial inflammation clinically distinguished by its aggressive presentation, including refractory ventricular arrhythmias, high-degree heart block, and cardiogenic shock. The disease course is notably fulminant, frequently culminating in death or the necessity for mechanical circulatory support and orthotopic heart transplantation within days to weeks of symptom onset. Histologically, GCM is characterized by widespread cardiomyocyte necrosis, intensive polymorphic inflammatory cell infiltration, and the pathognomonic presence of multinucleated giant cells [1].

The current gold standard of care relies heavily on combinations of high-dose corticosteroids, cyclosporine, azathioprine, or anti-thymocyte globulin. While these regimens have extended median transplant-free survival from less than three months to about one year, they carry serious clinical caveats. Broad-spectrum immunosuppression causes significant systemic toxicity, increases the risk of opportunistic infections, and does not selectively halt the cellular cascades driving ongoing autoimmune destruction of cardiac parenchyma [2].

Does inhibiting fusion reduce myocardial injury and improve meaningful cardiac outcomes, or does it mainly alter histological appearance? Recent advances in cellular immunology show that GCM is driven by coordinated, maladaptive

crosstalk between antigen-presenting cell (APC) subsets and autoreactive T lymphocytes. Standard immunosuppressive therapies temper general lymphocyte proliferation but do not alter the distinct phenotypic switches or physical cell fusion events that sustain localized myocardial destruction [3]. Consequently, clinicians urgently need targeted, disease-modifying therapies that interrupt these specific immunopathogenic axes without causing systemic immune collapse. Clinicians urgently need disease-modifying therapies that target the underlying immune mechanisms and interrupt these immunopathogenic axes without causing systemic immune collapse.

## 2 DISCUSSION

### 2.1 Treating Giant Cell Myocarditis: Targeting the Immune System for Heart Protection

Giant cell myocarditis (GCM) begins and worsens when certain immune cells, called monocytes and macrophages, become chronically activated and change their shape and behavior in the heart. In the highly inflamed environment of GCM, resident and newly arrived macrophages each take on distinct roles. Some, known as M1 macrophages, trigger fast and intense inflammation. Others, called M2a macrophages, play a larger role in long-term tissue remodeling and the body's response to what it perceives as foreign material [3].

A defining surface marker of this pathogenic M2a phenotype is CD23, the low-affinity IgE receptor (FcεRII). Under sustained pro-inflammatory stimulation and exposure to local interleukins, these CD23-expressing M2a macrophages undergo extensive cell-to-cell membrane fusion, forming multinucleated giant cells. This fusion event is a highly coordinated biophysical process. It relies on sequential surface receptor-ligand interactions, cytoskeletal reorganization, and specific membrane-docking proteins, including CD44 and the macrophage fusion receptor (MFR) [4]. Studies of MFR and CD44 establish that macrophage fusion can be altered through specific surface interactions [5]. It's hypothesized that sufficiently multivalent CD23-engaging complexes could also influence fusion, although this effect has not been demonstrated.

Once formed, these multinucleated giant cells act as localized physical and chemical disruptors within the myocardium. They release high concentrations of matrix metalloproteinases (MMPs), oxidative radicals, and pro-inflammatory cytokines that degrade the extracellular matrix and compromise mechanical cardiac structural integrity. Concurrently, these cells, along with neighboring dendritic cells, serve as highly efficient APCs. They process and present cardiac self-antigens (such as cardiac  $\alpha$ -myosin heavy chain) to naive T lymphocytes, driving their differentiation into destructive, tissue-specific cytotoxic effectors. Intercepting the CD23 axis on these cells therefore offers a unique dual opportunity: halting the physical manifestation of giant cell formation while disrupting downstream autoimmune signaling.

Most importantly, GCM involves T-cell-mediated inflammation, macrophage recruitment, multinucleated giant-cell formation, and myocardial injury. Whether a CD23-expressing macrophage subset contributes to fusion or sustains disease is an unresolved question central to this hypothesis.

### 2.2 How Special Antibody Complexes Could Calm the Immune System in Giant Cell Myocarditis

Do disease-relevant GCM macrophages express sufficient CD23? Can complex engagement also alter their fusion or inflammatory activity? Related hypothesis-generating reviews have proposed CD23-engaging anti-IgE:IgE complexes for cystic fibrosis and as adjuncts to CAR T-cell therapy in autoimmune disease. These proposals provide conceptual background for the present GCM hypothesis but do not directly establish inhibition of macrophage fusion, induction of cardiac antigen-specific tolerance, or efficacy in myocarditis [6,7].

Preformed anti-IgE:IgE complexes are a theoretical construct in GCM because these specially designed molecules can strongly bind to CD23 receptors on different immune cells. Rather than simply blocking the receptor like a typical antibody, these complexes bridge immune cells together and calm the overactive immune response in the heart.

When preformed anti-IgE:IgE complexes are introduced, they may act as high-affinity, multivalent structures that can simultaneously bind CD23 receptors on different immune cells, including M2a macrophages and B cells.

This CD23 cross-linking triggers two main effects. In M2a macrophages, CD23 engagement leads to a shift toward a more tolerogenic, less inflammatory phenotype. This limits their ability to promote multinucleated giant cell formation, which is associated with chronic inflammation.

This attenuates B cell activation and reduces stimulation of cytotoxic T cells. A related review has proposed inhaled CD23-engaging anti-IgE:IgE complexes for immune modulation in cystic fibrosis. The present hypothesis extends this platform to GCM, where effects on macrophage fusion and cardiac immune injury remain untested [6].

Overall, the dual action—modifying both macrophage phenotype and B cell activation—may help create a more regulated and less inflammatory immune environment in and around the heart.

### 2.3 How Antibody Complexes Prevent Harmful Immune-Cell Fusion in Giant Cell Myocarditis

The preformed anti-IgE:IgE complex works like a protective shield. When given as a treatment, it quickly attaches to CD23 receptors on M2a macrophage surfaces. This binding covers parts of the cell, making it harder for immune cells to interact in harmful ways.

By creating a dense steric barrier, the large protein complexes impede the close cellular apposition necessary for membrane-to-membrane docking. They could interfere with receptor-ligand interactions essential for fusion, such as those between MFR and its ligands. Without direct plasma membrane contact, independent macrophages cannot fuse, which would inhibit the formation of new pathognomonic multinucleated giant cells; this requires experimental confirmation. CD23-engaging anti-IgE:IgE complexes have also been proposed as adjuncts to CAR T-cell therapy for autoimmune disease. Their ability to influence macrophage fusion remains unestablished. [7].

### 2.4 How Blocking CD23 Reprograms Immune Cells to Protect the Heart

Blocking CD23 on immune cells does more than just prevent them from fusing. When these antibody complexes bind to CD23, they send powerful signals inside the cell. This changes how monocytes, macrophages, and dendritic cells behave at the genetic level, turning off the usual aggressive inflammatory response and pushing them toward a calmer, more protective state.

This reprogramming may create a temporary "tolerogenic window" by altering the secretome and surface topography of the APCs:

- Down-regulation of Co-stimulation: Engaged APCs down-regulate critical co-stimulatory molecules, specifically CD80 and CD86, which are mandatory for delivering "Signal 2" during T-cell activation.
- Altered Cytokine Kinetics: APCs' secretory profile shifts definitively. Production of classic Th1-priming cytokines—such as Tumor Necrosis Factor-alpha (TNF- $\alpha$ ) and Interleukin-2 (IL-2)—is sharply suppressed. Conversely, homeostatic, tissue-protective factors like Interleukin-10 (IL-10) and Transforming Growth Factor-beta (TGF- $\beta$ ) are upregulated [8].

### 2.5 Stopping T Cells from Attacking the Heart in Giant Cell Myocarditis

In giant cell myocarditis, certain aggressive T cells (CD4+ Th1 and CD8+ cytotoxic T cells) mistakenly attack and destroy heart muscle cells. These specially designed antibody complexes help by altering how other immune cells (APCs) present signals to these T cells, stopping the attack before it causes serious damage.

When autoreactive T cells encounter cardiac autoantigens on CD23-modulated APCs, the lack of CD80/CD86 co-stimulation may deliver an anergic signal rather than an activating one. Deprived of essential survival and proliferative stimuli, the T cells are functionally starved.

Furthermore, localized IL-10 elevation may directly dampen T-cell receptor (TCR) signal transduction, suppressing transcription and release of cytotoxic effector molecules, including perforin, granzyme B, and Interferon-gamma (IFN- $\gamma$ ). This multi-pronged dampening of T-cell activation directly preserves viable myocardium [9].

### 2.6 How Antibody Complexes Help B Cells Calm the Immune System

B-cells naturally express high basal levels of CD23, an endogenous regulatory checkpoint for humoral immunity. Cross-linking CD23 on the B cell with a preformed complex may engage a definitive negative feedback loop [10].

This engagement may temper B-cell receptor (BCR) activation and minimize potentially pathogenic antibody production. Because B cells serve as critical co-stimulatory and cytokine-producing partners for T cells within tertiary lymphoid structures, modulating B-cell reactivity may indirectly break the chronic cellular crosstalk required to sustain long-term cardiac autoimmunity [11,12].

### 2.7 Making Sure the Therapy Reaches and Stays in the Heart

To turn this idea into a real treatment, scientists need to carefully make these antibody complexes in the right amounts and find ways to deliver the complexes so they stay in the heart without spreading too much through the rest of the body [13].

## 2.8 How to Safely Make and Mix Antibody Complexes for Heart Therapy

The proposed strategy requires an anti-IgE antibody whose binding epitope preserves IgE-mediated engagement of CD23. UB-221/8D6 provides proof of principle for this molecular property, whereas omalizumab is unsuitable as the default CD23-engaging construct because it inhibits the IgE–CD23 interaction. How well this therapy works and how safe it is depends largely on achieving the right balance when mixing the antibodies. To make these special complexes, two carefully purified human components are needed, and they're made to reduce the risk of allergic reactions.

- **Anti-IgE Monoclonal Antibody:** This is a lab-made antibody adjusted to work in people and designed to bind very strongly to its target. Certain types, like 8D6 and CUE-221, can be used as long as they stay flexible enough to bind properly to the CD23 receptor.
- **Passive IgE Antigen:** This is a pure form of human IgE that has been processed so it won't cause allergic reactions and doesn't stick to heart proteins. Its only job here is to help form the antibody complex structure.

Mix these two ingredients in a special solution that keeps them stable and prevents clumping. Keep the amounts balanced, using either equal parts or twice as much IgE, so the complexes stay the right size and don't cause problems in the blood vessels.

The mixture is then gently warmed for about an hour, which helps the antibodies and IgE molecules lock together into stable complexes. After that, tests confirm everything has combined correctly and that the complexes are the right size to be safe and effective [14].

## 2.9 New Ways to Deliver Heart Treatments Precisely Where They're Needed

Because giant cell myocarditis comes on suddenly and can get worse very quickly, simply giving the treatment through a regular IV may not be enough—and can even cause unwanted side effects in other parts of the immune system. That's why researchers are developing new delivery methods to ensure the therapy goes straight to where it's needed most: the heart.

- **Enzyme-Responsive Nanocarriers:** When the heart is inflamed, certain enzymes called MMPs become much more active in the affected area. Scientists can put the antibody complexes inside tiny, safe particles or gels that break open and release the treatment only when they encounter these enzymes in the inflamed heart. This keeps the medicine safe and unused in the bloodstream and may release it only where it's needed [15,16].
- **Ultrasound-Targeted Microbubble Destruction (UTMD):** In this approach, the antibody complexes are attached to tiny bubbles that are injected into the bloodstream. When these bubbles reach the heart, doctors use focused ultrasound waves to pop them. This may temporarily open small spaces in the heart's blood vessels, allowing the treatment to reach heart tissue more effectively [17].
- **Multi-Specific Nanobody Conjugates:** Here, the antibody complexes are connected to special delivery systems that can find and attach to the exact immune cells involved in the disease. By designing these carriers to target markers on specific T cells or monocytes, the treatment may reach the heart where inflammation is most active [18].
- **Co-delivery with Tolerogenic Peptides:** Another idea is to combine the antibody complexes with small protein pieces from the heart itself and deliver them together in tiny particles. This helps teach the immune system not to attack the heart, encouraging a more peaceful response and the development of protective immune cells [19].

## 2.10 Overcoming Hurdles: Making Advanced Heart Therapies Safe, Effective, and Ready for Patients

As a biological therapeutic, translating preformed anti-IgE:IgE complexes from concept to clinical trials requires careful mitigation of distinct pharmacokinetic, immunological, and stability challenges.

## 2.11 How the Therapy Moves Through and Leaves the Body

When these special antibody complexes are given by IV, they behave differently in the body than regular antibody treatments. Their unique structure makes them too large for the kidneys to filter out quickly, so they stay in the bloodstream longer—usually about one to two weeks.

The body mainly removes these complexes slowly through the liver and spleen. To help the treatment last longer during a heart crisis, scientists can make small changes to the antibody's structure. For example, adjusting the antibody so it binds less readily in the liver lets it stay active in the bloodstream longer, giving the heart more time to benefit from the therapy [20].

## 2.12 Keeping Antibody Therapies Safe and Effective During Storage

These antibody complexes are delicate and can fall apart or clump if stored improperly. In liquid form, they stay stable in the fridge for just a few weeks. To keep them viable for several months, they must be frozen quickly and stored at -80°C in special freezers that don't thaw automatically.

To protect the complexes from damage during freezing, researchers add extra sugars like trehalose or sucrose to the solution. Because they can't use dangerous preservatives, researchers must keep everything sterile through careful handling and filtration. The best way to store these treatments long-term is freeze-drying, which keeps them safe for years, but they must be rehydrated very carefully before they can be given to patients [21,22].

## 2.13 Balancing Safety: Preventing Side Effects and Unwanted Immune Reactions

The biggest safety concern is ensuring the antibodies are mixed in the right amounts during production. If the balance is off, the immune system could overreact, causing side effects such as widespread inflammation or serum sickness. Because people with giant cell myocarditis have very different immune profiles than lab animals, it's also difficult to predict the right dose for each patient.

Treatment could also weaken the body's defenses against infections, either in the heart or throughout the body. That's why early clinical trials must carefully monitor unwanted immune reactions and ensure the treatment doesn't impair the patient's ability to fight off germs [23,24].

## 2.14 Proving the Therapy Works and Is Safe—First Steps Before Human Trials

Before scientists can test this CD23-targeted therapy in people, they must carefully test it in animal models that closely mimic how giant cell myocarditis works in humans. This helps ensure the treatment is safe and improves the disease.

## 2.15 How Scientists Test Therapy in Animal Models Before Moving to Human Trials

To study this therapy before trying it in people, scientists use a well-established animal model called Experimental Autoimmune Myocarditis (EAM). This model uses rats or specially bred mice modified to resemble the human immune system. Researchers use these animals because, under the microscope, the disease looks very similar to giant cell myocarditis in humans, with the same harmful cells and rapid progression. To start the disease, researchers give the animals a mix of heart muscle proteins and special immune-boosting substances on Day 0 and Day 7 [25].

Animals are randomized into three distinct experimental cohorts:

- Cohort A (Negative Control): Sham-immunized with PBS/CFA to establish baseline parameters.
- Cohort B (Positive Control / Vehicle): Myosin-immunized, receiving only empty vehicle buffer treatments.
- Cohort C (Experimental Treatment): Myosin-immunized, receiving active treatment with the preformed anti-IgE:IgE complexes.

## 2.16 How and When the Therapy Is Given in Animal Studies

In one group of animals, treatment starts on Day 10 after the disease is triggered—when harmful T cells begin invading the heart but before the heart tissue is badly damaged. The therapy is given through a simple injection into the tail vein, at carefully chosen doses (for example, 5–20 mg per kilogram of body weight). Animals receive these injections every three days until the study ends on Day 21.

## 2.17 How Scientists Measure Success in Animal Studies—and What They Hope to See

On Day 21, all cohorts undergo final functional assessments followed by humane sacrifice for comprehensive tissue and cellular analysis:

- Tissue Analysis: After the study, the hearts are removed and examined under a microscope using special stains to look for signs of damage. If the therapy works, scientists expect to see fewer giant cells in the heart muscle, healthier heart tissue, less scarring, and lower inflammation in treated animals than in the untreated group.
- Immune Cell Analysis: Scientists also break down the heart and nearby lymph nodes into single cells to figure out exactly what types of immune cells are present and how active they are. They look for evidence that the therapy is attaching to the right cells and calming down the most aggressive immune responses, with fewer "attack signals" showing up in the treated animals.
- Blood and Tissue Signals: The research team measures certain chemical signals in the blood and heart tissue. A successful therapy should lower the "bad" inflammatory signals and increase the "peaceful" signals that show the immune system is calming down and protecting the heart instead of attacking it.

- Heart Function Tests: Throughout the study, ultrasound scans check how well the heart pumps. In animals that don't receive therapy, heart function usually worsens significantly. In those that receive the therapy, researchers hope their hearts keep pumping strongly, suggesting the treatment protects heart function [26].

### 3 CONCLUSION

CD23-engaging anti-IgE:IgE complexes represent a candidate strategy for investigating macrophage fusion and immune regulation in GCM. Their value depends on demonstrating disease-relevant CD23 expression, beneficial receptor-dependent effects, and improved myocardial outcomes without unacceptable immune activation.

### STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

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Michael John Dochniak used the program "Grammarly" for grammar, spelling, and punctuation throughout the preparation of the review article. Mr. Dochniak used Grammarly, version 14.1271.0 (Grammarly Inc., San Francisco, CA). Dochniak used Grammarly to review and edit the entire article for grammatical accuracy, clarity, and readability. Grammarly's AI-powered writing assistant suggested improvements to sentence structure, word choice, and tone consistency, which the author reviewed and selectively incorporated. The author did not use it to generate original scientific content or research conclusions. The author takes full responsibility for the integrity of all content generated and presented in this review article.

#### *Disclosure of conflict of interest*

The author claims no conflict of interest.

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Michael John Dochniak is an independent medical researcher who has authored several books on Alzheimer's disease, Artificial Intelligence, Autism Spectrum Disorders, and Climate Change through Cambridge Scholars Publishing and Nova Science Publishers. Mr. Dochniak has also written extensively with GSC Online Press and appreciates its dedicated service.

### REFERENCES

- [1] Cooper LT Jr, Berry GJ, Shabetai R; Multicenter Giant Cell Myocarditis Study Group Investigators. Idiopathic giant-cell myocarditis—natural history and treatment. *N Engl J Med*. 1997;336(26):1860–1866. doi:10.1056/NEJM199706263362603.
- [2] Bang V, Ganatra S, Shah SP, et al. Management of patients with giant cell myocarditis: JACC review topic of the week. *J Am Coll Cardiol*. 2021;77(8):1122–1134.
- [3] Velders I, Westphal M, et al. Giant cell myocarditis: from immune pathogenesis to contemporary clinical management. *Clin Res Cardiol*. 2026;115(8):1241–1255.
- [4] Rószter T. Understanding the Mysterious M2 Macrophage through Activation Markers and Effector Mechanisms. *Mediators Inflamm*. 2015;2015:816460. doi:10.1155/2015/816460.
- [5] Sterling H, Saginario C, Vignery A. CD44 Occupancy Prevents Macrophage Multinucleation. *J Cell Biol*. 1998;143(3):837–847.
- [6] Dochniak MJ. Inhaled anti-IgE: IgE complexes as a mutation-agnostic biologic therapy for cystic fibrosis with rare mutations. *GSC Advanced Research and Reviews*. 2026;29(1):49–56. doi:10.30574/gscarr.2026.29.1.0262.
- [7] Dochniak MJ. Harnessing anti-IgE: IgE complexes to enhance CAR T-cell therapy for autoimmune diseases. *GSC Advanced Research and Reviews*. 2026;28(3):177–181. doi:10.30574/gscarr.2026.28.3.0237.
- [8] Bettini M, Bettini ML. Function, Failure, and the Future Potential of Tregs in Type 1 Diabetes. *Diabetes*. 2021 Jun 1;70(6):1211–1219. doi: 10.2337/dbi18-0058.

- [9] Zhuang Q, Cai H, Cao Q, Li Z, Liu S, Ming Y. Tolerogenic Dendritic Cells: The Pearl of Immunotherapy in Organ Transplantation. *Front Immunol.* 2020; 11:552988. doi: 10.3389/fimmu.2020.552988.
- [10] Veneri D, Ortolani R, Franchini M, Tridente G, Pizzolo G, Vella A. Expression of CD27 and CD23 on peripheral blood B lymphocytes in humans of different ages. *Blood Transfus.* 2009 Jan;7(1):29-34. doi: 10.2450/2008.0007-08.
- [11] Chen W, Zhang L, Gao M, Zhang N, Wang R, Liu Y, Niu Y, Jia L. Role of tertiary lymphoid structures and B cells in clinical immunotherapy of gastric cancer. *Front Immunol.* 2025 Jan 7; 15:1519034. doi: 10.3389/fimmu.2024.1519034.
- [12] Mallat Z, Binder CJ. The why and how of adaptive immune responses in ischemic cardiovascular disease. *Nat Cardiovasc Res.* 2022 May; 1:431-444. doi: 10.1038/s44161-022-00049-1.
- [13] Sahoo S, Kariya T, Ishikawa K. Targeted delivery of therapeutic agents to the heart. *Nat Rev Cardiol.* 2021 Jun;18(6):389-399. doi: 10.1038/s41569-020-00499-9.
- [14] Kuo BS, Li CH, Chen JB, Shiung YY, Chu CY, Lee CH, et al. IgE-neutralizing UB-221 mAb, distinct from omalizumab and ligelizumab, exhibits CD23-mediated IgE downregulation and relieves urticaria symptoms. *J Clin Invest.* 2022 Aug 1;132(15):e157765. doi: 10.1172/JCI157765. PMID: 35912861; PMCID: PMC9337824.
- [15] Nguyen MM, Carlini AS, Chien MP, Sonnenberg S, Luo C, Braden RL, Osborn KG, Li Y, Gianneschi NC, Christman KL. Enzyme-responsive nanoparticles for targeted accumulation and prolonged retention in heart tissue after myocardial infarction. *Adv Mater.* 2015;27(37):5547–5552. doi:10.1002/adma.201502003.
- [16] George TA, Hsu CC, Meeson A, Lundy DJ. Nanocarrier-based targeted therapies for myocardial infarction. *Pharmaceutics.* 2022;14(5):930. doi:10.3390/pharmaceutics14050930.
- [17] Yang S, Zhang R, Zhang H, Lu Y. Ultrasound-targeted microbubble destruction: a prospective strategy for treating cardiovascular disease. *Front Cardiovasc Med.* 2025; 12:1634059. doi: 10.3389/fcvm.2025.1634059.
- [18] Li H, Zhou Q, Cao N, Hu C, Wang J, He Y, Jiang S, Li Q, Chen M, Gong L, Luo M, Deng X, Luo Z. Nanobodies and their derivatives: pioneering the future of cancer immunotherapy. *Cell Commun Signal.* 2025 Jun 5;23(1):271. doi: 10.1186/s12964-025-02270-4.
- [19] Scotland BL, Shaw JR, Dharmaraj S, Caprio N, Cottingham AL, Martín Lasola JJ, Sung JJ, Pearson RM. Cell and biomaterial delivery strategies to induce immune tolerance. *Adv Drug Deliv Rev.* 2023; 203:115141. doi: 10.1016/j.addr.2023.115141.
- [20] Liu L. Pharmacokinetics of monoclonal antibodies and Fc-fusion proteins. *Protein Cell.* 2018 Jan;9(1):15-32. doi: 10.1007/s13238-017-0408-4.
- [21] Wang W. Lyophilization and development of solid protein pharmaceuticals. *Int J Pharm.* 2000;203(1-2):1-60.
- [22] Wang W, Singh S, Zeng DL, King K, Nema S. Antibody structure, instability, and formulation. *J Pharm Sci.* 2007;96(1):1–26. doi:10.1002/jps.20727.
- [23] Chung L, Berry GJ, Chakravarty EF. Giant cell myocarditis: a rare cardiovascular manifestation in a patient with systemic lupus erythematosus. *Lupus.* 2005;14(2):166-169. doi: 10.1191/0961203305lu2040cr.
- [24] Vosko I, Wallner M. Giant cell myocarditis: from immune pathogenesis to contemporary management. *Heart Fail Rev.* 2026 Aug 21;31(1):95. doi: 10.1007/s10741-026-10668-6.
- [25] Błyszczuk P. Myocarditis in Humans and in Experimental Animal Models. *Front Cardiovasc Med.* 2019 May 16; 6:64. doi: 10.3389/fcvm.2019.00064.
- [26] Liu H, Li W, Gu W, Kong Y, Yang N, Chen L. Immunoregulatory effects of carvedilol on rat experimental autoimmune myocarditis. *Scand J Immunol.* 2010 Jan;71(1):38-44. doi: 10.1111/j.1365-3083.2009.02347.x.