Annals of Gastroenterology (2026) **39,** 1-4

Granulocyte and monocyte adsorptive apheresis for ulcerative colitis: mechanisms, clinical evidence, and future perspectives

Tomotaka Tanaka, Yoshikazu Yoshifuku, Hajime Teshima, Hirona Konishi, Kazuyoshi Nakata, Kosei Kitamura, Nodoka Otabe, Takeshi Mori, Songde Cho, Michihiro Nonaka, Yoshifumi Fujimoto

JA Hiroshima General Hospital, Japan

Abstract

Ulcerative colitis (UC) is a chronic, idiopathic inflammatory bowel disease characterized by continuous mucosal erosions and ulcers in the colon. In recent years, biologics and small-molecule agents have revolutionized UC management; however, these therapies may be limited by risks such as infections, secondary loss of response, or intolerance. Granulocyte and monocyte adsorptive apheresis (GMA), developed in Japan, offers a non-pharmacologic and selective immunomodulatory approach by removing activated myeloid cells and modulating the inflammatory milieu. In this review, we summarize the mechanisms of action of GMA, including its effects on proinflammatory cytokines and regulatory T-cell responses. We also examine the clinical evidence, from randomized controlled trials and observational studies, that supports its efficacy, particularly in steroid-dependent and elderly patients. While mucosal healing rates with GMA may be lower than those achieved with biologics, its favorable safety profile may support its use as an adjunctive or bridging strategy in selected patients. However, evidence supporting these roles remains limited and is derived mainly from observational studies. Future directions include integration with personalized medicine, biomarker development and global expansion. GMA remains a viable option in the therapeutic landscape of UC.

Keywords Ulcerative colitis, granulocyte monocyte adsorptive apheresis, Adacolumn

Ann Gastroenterol 2026; 39 (XX): 1-4

Introduction

Ulcerative colitis (UC) is a chronic, idiopathic inflammatory bowel disease characterized by continuous erosions and ulcers in the colonic mucosa. The number of patients with UC continues to increase worldwide, including in developed countries such as Japan [1,2], significantly affecting both patients' quality of life (QOL) and healthcare resources. The mainstay of treatment includes 5-aminosalicylic acid (5-ASA) preparations, corticosteroids, immunomodulators, and more recently, molecular-targeted therapies such as biologic agents and small molecules. These therapies include anti-tumor necrosis factor [TNF]-α antibodies (infliximab, adalimumab, golimumab), the anti-interleukin [IL]-12/23p40 antibody (ustekinumab) [3], the anti-α4β7 integrin antibody (vedolizumab) [4], and Janus kinase (JAK) inhibitors (tofacitinib, upadacitinib, filgotinib) [5].

However, these agents are associated with several limitations, including increased infection risk due to immunosuppression, secondary loss of response, serious adverse events, and drug intolerance. Nevertheless, despite decades of clinical use in Japan, GMA has not been widely adopted globally. Potential reasons include limited availability outside Japan, the predominance of small single-country studies, lack of large multinational randomized controlled trials, procedural burden, and the increasing availability of highly effective biologic therapies. Therefore, non-pharmacological approaches are being reconsidered, especially in populations such as the elderly, pregnant women, or patients for whom immunosuppression is contraindicated. One such therapy is granulocyte and monocyte adsorptive apheresis (GMA), a unique treatment modality developed in Japan. This article comprehensively reviews the mechanism of action, clinical evidence,

Department of Gastroenterology, JA Hiroshima General Hospital, Japan (Tomotaka Tanaka, Yoshikazu Yoshifuku, Hajime Teshima, Hirona Konishi, Kazuyoshi Nakata, Kosei Kitamura, Nodoka Otabe, Takeshi Mori, Songde Cho, Michihiro Nonaka, Yoshifumi Fujimoto)

Conflict of Interest: None.

Correspondence to: Tomotaka Tanaka, MD, PhD, Department of Gastroenterology, JA Hiroshima General Hospital, Japan, e-mail: tomotaka@c.do-up.com

Received 24 December 2025; accepted 19 March 2026; published online 11 June 2026

DOI: https://doi.org/10.20524/aog.2026.1076

comparison with other therapies, and future perspectives of GMA based on the latest findings.

In addition, particular emphasis is placed on detailed mechanistic pathways, the study design characteristics of key clinical trials, safety considerations—including repeated treatment cycles and combination use with biologics—and the practical positioning of GMA within the modern therapeutic algorithm of UC. To improve clarity and reader accessibility, schematic figures and summary tables of major clinical studies are also provided.

Mechanism of action of GMA

GMA is an extracorporeal apheresis therapy performed using the Adacolumn®, developed by JIMRO Co., Ltd. The column is filled with cellulose acetate beads, which selectively adsorb neutrophils and monocytes through affinity for Fcγ receptors and complement receptors on leukocytes [6]. Importantly, adsorption is biased toward activated myeloid lineage cells, which express higher levels of Fcγ and complement receptors, whereas most lymphocytes and hematopoietic stem cells are largely spared. This cellular selectivity explains why GMA does not induce broad systemic immunosuppression and preserves adaptive immune function. As these cells secrete proinflammatory cytokines, such as IL-1β, IL-6 and TNF-α, GMA allows the physical removal of key mediators of inflammation [6]. In addition to direct cell removal, contact between leukocytes and the adsorption carrier can trigger functional changes, including reduced activation status and altered cytokine release profiles in circulating cells. These effects may contribute to downstream anti-inflammatory signaling beyond the absolute number of cells removed.

Apart from simple leukocyte removal, GMA also contributes to immune modulation. In fact, post-treatment increases in regulatory T cells (Tregs) and the anti-inflammatory cytokine IL-10 have been observed, suggesting not only local inflammation suppression but also restoration of systemic immune homeostasis. These characteristics establish GMA as a unique, non-pharmacological, selective immunomodulatory therapy.

A schematic overview of the cellular adsorption process and downstream immunological effects is shown in Fig. 1. In addition to leukocyte removal, GMA has been reported to modulate cytokine profiles and immune responses [6].

- Peripheral blood inflammation → Extracorporeal circulation → Adacolumn adsorption column
- Selective removal:
- - Activated granulocytes
- - Activated monocytes
- Downstream effects:
- ↑ TNF-α, IL-1β, IL-6
- ↓ IL-10, Treg activity
- Reduced mucosal inflammation

Figure 1 Mechanism of granulocyte and monocyte adsorptive apheresis (GMA). During extracorporeal circulation, activated granulocytes and monocytes are selectively adsorbed onto cellulose acetate beads in the Adacolumn® through Fcγ and complement receptor–mediated interactions. This results in reduction of circulating proinflammatory myeloid cells and downstream cytokines, along with secondary immunomodulatory effects including increased regulatory T-cell activity and anti-inflammatory cytokine production
GMA, granulocyte and monocyte adsorptive apheresis; TNF, tumor necrosis factor; IL, interleukin; Treg, regulatory T cell

Clinical evidence

Clinical studies, including a systematic review, have suggested that granulocyte and monocyte adsorptive apheresis can induce clinical remission in patients with UC, particularly in selected populations such as those with steroid dependence or intolerance to conventional therapies [2]. Importantly, not all studies have demonstrated consistent efficacy of GMA, particularly regarding mucosal healing and long-term remission maintenance [7]. Differences in study design, patient selection, treatment intensity, and outcome definitions complicate interpretation of the available evidence. Furthermore, many studies have been observational or conducted in limited geographic regions, and high-quality multinational randomized controlled trials remain scarce.

However, the majority of available evidence is derived from single-country studies, and large-scale international randomized controlled trials remain limited. In addition, while GMA may improve clinical symptoms, its efficacy in achieving mucosal healing appears to be lower compared with biologic therapies [3-5].

This geographic concentration of evidence represents an important limitation when extrapolating results to broader patient populations. Intensive GMA (i.e., twice-weekly sessions) has also been investigated. However, the mucosal healing rate with GMA is reportedly lower than that achieved with biologic agents. Some patients exhibit discordance between symptomatic and endoscopic improvement. Therefore, GMA is often positioned as a treatment aimed at "symptom relief" or a "drug-sparing/bridging" strategy, rather than full mucosal healing. Direct head-to-head comparative trials between GMA and biologic or small-molecule therapies are currently scarce [7], and most available data derive from indirect comparisons across separate studies. This should be considered when positioning GMA relative to advanced pharmacologic therapies. Moreover, the overall evidence base remains limited. Current evidence mainly supports the use of GMA for induction therapy in active UC, whereas evidence supporting maintenance therapy remains limited. A summary of representative clinical studies of GMA in UC is provided in Table 1.

Comparison with other therapies

Biologic and molecular-targeted therapies have significantly revolutionized UC management. Anti-TNF-α

antibodies have demonstrated significant improvements in remission and mucosal healing rates in trials such as ACT-1/ACT-2 (infliximab) and ULTRA-1/ULTRA-2 (adalimumab). Similarly, the efficacy of ustekinumab and vedolizumab has been well established [3-5]. A comparative summary of GMA and advanced pharmacologic therapies is shown in Table 2.

However, direct head-to-head comparative trials between GMA and these advanced pharmacologic therapies are limited, and most comparisons rely on indirect cross-study interpretation rather than randomized parallel comparisons. In comparison, GMA is generally associated with a lower risk of systemic immunosuppression-related complications compared with biologic or small-molecule therapies.

This makes it particularly suitable for elderly patients, pregnant women, or those intolerant to immunosuppressive agents. GMA may also be considered in selected patients with loss of response or intolerance to biologic agents, particularly when further immunosuppressive escalation is undesirable or contraindicated. Although GMA is generally well tolerated, procedure-related adverse events have been reported, including transient headache, nausea, hypotension, vascular access complications, and anticoagulation-related events. Most adverse events are mild and self-limited, and discontinuation rates are generally low.

Additionally, GMA is feasible in outpatient settings, making it a practical option for patients who cannot be hospitalized or who have difficulty with oral medications. From a practical standpoint, GMA requires specialized equipment and repeated treatment sessions, and cost-effectiveness may vary depending on healthcare system structure and reimbursement policies. These logistical factors should be considered when selecting candidates for therapy. The cost-effectiveness of GMA remains uncertain because repeated extracorporeal treatment sessions require specialized equipment, trained personnel, and repeated hospital visits. Economic impact may vary depending on healthcare reimbursement systems and local infrastructure. As a combination therapy, GMA may serve as a bridging treatment to control early inflammation in conjunction with agents like ustekinumab, mirikizumab, or vedolizumab, which have a delayed onset of action. A schematic overview of the clinical positioning of GMA within the current UC therapeutic algorithm, including its role as monotherapy and adjunct or bridging therapy, is shown in Fig. 2. Adsorptive apheresis has also been proposed as a drug-sparing therapeutic strategy in inflammatory bowel disease [6].

Future perspectives

Future developments in GMA are expected to focus on the following areas:

Establishment as a combination therapy

Recent studies suggest that combining GMA with biologics may yield synergistic effects, particularly during the induction phase with agents that have a slow onset of action. This strategy is biologically plausible, because GMA can rapidly reduce

Table 1 Major clinical studies of granulocyte and monocyte adsorptive apheresis in ulcerative colitis

Study [ref.]	Design	Population	Main findings	Major limitations
Sands *et al* [7]	Sham-controlled trial	Moderate-to-severe UC	No significant superiority over sham in primary endpoint	High placebo response
Thanaraj *et al* [2]	Systematic review	UC patients treated with GMA	Suggested clinical benefit in selected populations	Heterogeneity among included studies
Saniabadi *et al* [6]	Review article	IBD patients	Discussed drug-sparing and safety advantages	Mostly observational evidence

UC, ulcerative colitis; IBD, inflammatory bowel disease; GMA, granulocyte and monocyte adsorptive apheresis

Table 2 Comparison of GMA with advanced pharmacologic therapies in ulcerative colitis

Feature	GMA	Biologics	JAK inhibitors/S1P modulators	Clinical implication
Mechanism	Cell adsorption	Targeted immune blockade	Intracellular signaling/ trafficking	Different levels of immune modulation
Systemic immunosuppression	No	Yes	Yes	GMA safer in high-risk patients
Infection risk	Low	Moderate	Moderate–high	Important for elderly/pregnancy
Onset of action	Often rapid	Variable	Often rapid	GMA useful as bridge
Mucosal healing	Moderate	High	High	Biologics superior for deep remission
Use in intolerance	Suitable	Limited	Limited	GMA option when drugs not tolerated

GMA, granulocyte and monocyte adsorptive apheresis; JAK, Janus kinase; S1P, sphingosine-1-phosphate

- Active UC → Assess immunosuppression suitability
- If suitable → Biologic/JAK/S1P therapy
- Delayed onset → Add GMA bridge
- If high risk/intolerant → Consider GMA
- - Monotherapy (mild–moderate)
- - Adjunct therapy
- Best candidates:
- Elderly, infection risk, pregnancy,
- steroid-dependent, biologic LOR

Figure 2 Clinical positioning of granulocyte and monocyte adsorptive apheresis (GMA) within the therapeutic algorithm of ulcerative colitis. GMA may be used as monotherapy in selected mild-to-moderate cases, and as adjunctive or bridging therapy in patients receiving biologic or small-molecule agents, particularly when immunosuppression is undesirable or when rapid inflammatory load reduction is needed
UC, ulcerative colitis; GMA, granulocyte and monocyte adsorptive apheresis; JAK, Janus kinase; S1P, sphingosine-1-phosphate; LOR, loss of response

circulating activated myeloid cells and inflammatory cytokine load, potentially stabilizing disease activity while slower-acting biologic agents reach therapeutic effect.

Integration with personalized medicine

The development of predictive biomarkers, such as peripheral neutrophil ratios, serum IL-6, and CRP, may help identify responders and facilitate the incorporation of GMA into personalized treatment plans. Prospective validation studies are needed to confirm the predictive performance of these biomarkers and to define clinically useful cutoff values before routine implementation in treatment algorithms.

Global expansion

Given its safety profile, expansion of GMA use to other countries, including those in Europe and emerging markets, is anticipated. International collaborative studies are expected to support this expansion. Standardization of treatment protocols, outcome definitions and study endpoints across regions will be essential to enable meaningful international comparison and guideline-level recommendations. Taken together, future research should aim not only to expand the evidence base, but also to clarify the optimal clinical niche of GMA within increasingly complex, multi-option UC treatment strategies.

Concluding remarks

GMA offers a relatively safe therapeutic option for UC by physically removing inflammatory leukocytes without pharmacologic immunosuppression. It holds particular value in cases of steroid dependence, intolerance to immunosuppressive agents, and in vulnerable populations such as the elderly or pregnant women. At the same time, the current evidence base is characterized by a predominance of single-country studies and a limited number of large, fully blinded randomized trials.

While the advent of molecular-targeted therapies has somewhat limited the role of GMA, it is increasingly being reevaluated as an adjunctive or bridging therapy. Direct comparative studies against biologic and small-molecule therapies remain limited, and future head-to-head trials will be important to more precisely define its relative efficacy. Moving forward, the identification of suitable candidates via biomarkers and optimization of combination strategies will be crucial. In this context, GMA should be viewed as a complementary modality within the modern step-up and treat-to-target therapeutic algorithms, rather than a replacement for advanced pharmacologic therapies. GMA is expected to continue serving as a valuable component of the therapeutic arsenal in clinical practice. A clearer definition of its optimal clinical niche, supported by standardized protocols and international studies, will determine the future role of GMA in UC management. Nevertheless, current evidence remains limited by the scarcity of large multinational randomized controlled trials and the heterogeneity of existing studies. Further international collaborative research will be necessary to better define the optimal role of GMA in modern UC management.

Acknowledgment

AI-assisted tools were used to support early drafting and language refinement of this manuscript. All content was subsequently reviewed, substantially revised, and approved by the authors to ensure accuracy, originality, and appropriate scientific interpretation

References

1. Ng SC, Shi HY, Hamidi N, et al. Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: a systematic review of population-based studies. *Lancet* 2018;**390**:2769-2778.
2. Thanaraj S, Hamlin PJ, Ford AC. Systematic review: granulocyte/monocyte adsorptive apheresis for ulcerative colitis. *Aliment Pharmacol Ther* 2010;**32**:1297-1306.
3. Sands BE, Sandborn WJ, Panaccione R, et al; UNIFI Study Group. Ustekinumab as induction and maintenance therapy for ulcerative colitis. *N Engl J Med* 2019;**381**:1201-1214.
4. Feagan BG, Rutgeerts P, Sands BE, et al; GEMINI 1 Study Group. Vedolizumab as induction and maintenance therapy for ulcerative colitis. *N Engl J Med* 2013;**369**:699-710.
5. Danese S, Vermeire S, Zhou W, et al. Upadacitinib as induction and maintenance therapy for moderately to severely active ulcerative colitis: results from three phase 3, multicentre, double-blind, randomised trials. *Lancet* 2022;**399**:2113-2128.
6. Saniabadi AR, Tanaka T, Ohmori T, Sawada K, Yamamoto T, Hanai H. Treating inflammatory bowel disease by adsorptive leucocytapheresis: a desire to treat without drugs. *World J Gastroenterol* 2014;**20**:9699-9715.
7. Sands BE, Sandborn WJ, Feagan BG, et al. A randomized, double-blind, sham-controlled study of granulocyte/monocyte adsorptive apheresis in patients with moderate-to-severe ulcerative colitis. *Gastroenterology* 2008;**135**:400-409.