SHORT-TERM REAL-WORLD EFFECTIVENESS AND SAFETY OF GRANULOCYTE AND MONOCYTE ADSORPTIVE APHERESIS (GMA) IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: GRACE STUDY

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BACKGROUND

- Inflammatory bowel disease (IBD), including ulcerative colitis (UC) and Crohn's disease (CD), consists in two chronic inflammatory disorders involving the gastrointestinal tract, where an increase in peripheral blood-activated granulocytes and monocyte-macrophages and their intestinal infiltration has been involved in tissue damage [(1)].
- The clinical efficacy and safety of GMA with Adacolumn®, in patients with IBD has been reported in several clinical trials and observational studies, with significant clinical remission rates [(2-7)].
- The ongoing GRACE study aims to assess prospectively the real-world effectiveness of GMA in patients diagnosed with UC or CD.
- The primary aim is to evaluate GMA clinical efficacy, defined as corticosteroid-free clinical remission 6 months after completion of GMA treatment.

METHODS

- GRACE is a multicentric, prospective, and observational study conducted at 31 centers in Spain.
- Eligible patients were aged ≥18 years diagnosed with UC or CD who had been scheduled to receive GMA with Adacolumn® in clinical practice.
- The study consisted of a baseline visit followed by three additional visits 4, 24, and 48 weeks after the last GMA session.
- The estimated sample size was 350 subjects.
- This planned interim analysis (cut-off date: 25 Sept 2023) is mainly focused on the clinical characterization of the patients and their management and clinical outcome 4 weeks after GMA treatment. As this is an interim analysis, the data presented here may be subject to further refinement and updates in subsequent analyses.

RESULTS

- A total of 100 patients were screened, of whom 5 were excluded for non-compliance with eligibility criteria. Thus, 95 evaluable patients were included, whose characteristics are outlined in **Table 1.**

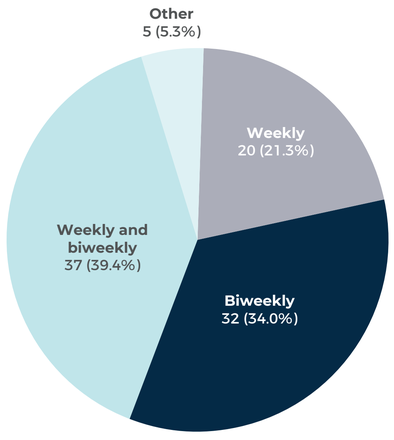
Table 1. Baseline characteristics of evaluable patients (N= 95; diagnosis information from one patient was missing)

Patient characteristics	Value
Age, mean, years (IQR)*	54.0 (40.8-63.0)
Gender, men, n (%)*	47 (50.0)
Smoking habits, n (%)*	
Non-smoker	47 (50.0)
Clinical characteristics	
Outpatients, n (%)▲	74 (81.3)
Ulcerative colitis, n (%)*	84 (89.4)
Disease duration, median (IQR), years*	7.3 (3.5-16.1)
Disease extent, n (%)*	
Proctitis (E1)	6 (7.2)
Left-sided colitis (E2)	29 (34.9)
Pancolitis (E3)	48 (57.8)
Disease severity, n (%)*	
Remission	3 (3.6)
Mild	9 (10.8)
Moderate	48 (57.8)
Severe	23 (27.7)
Mayo index, median score (IQR)▪	5.0 (3.0-6.0)
Crohn's disease, n (%)*	10 (10.6)
Disease duration, median (IQR), years	3.2 (0.8-13.4)
Location, n (%)	
Ileal (L1)	3 (30.0)
Colonic (L2)	4 (40.0)
Ileocolonic (L3)	3 (30.0)
Disease behaviour (B1), n (%)	10 (100.0)
Harvey-Bradshaw Index, median score (IQR)*	5.0 (2.5-10.0)
Immune-mediated inflammatory diseases or cancer, n (%)*	17 (18.1)
Prior IBD-related surgery, n (%)†	3 (3.2)
History of extraintestinal manifestations prior to apheresis, n (%)*	16 (17.0)
Treatments prior to apheresis, n (%)	
Corticosteroids	53 (55.8)
Anti-TNF	50 (52.6)
Thiopurines	36 (37.9)
Anti-integrins	27 (28.4)
IL-12/23	20 (21.1)
JAK inhibitors	16 (16.8)
Apheresis	3 (3.2)

*Missing data, n=1; ‡Missing data, n=14; ▲Missing data, n=4; ▪Missing data, n=6; †Missing data, n=2. Valid percentages are shown. Immune-mediated inflammatory diseases or cancer include psoriasis (3 patients), colonic adenocarcinoma (n=2), breast cancer (n=2), larynx cancer (n=1), oral epidermoid carcinoma (n=1), multiple sclerosis (n=1), gastrointestinal stromal tumor (n=1), systemic vasculitis/pulmonary-renal syndrome (n=1), autoimmune hepatitis (n=1), hypothyroidism (n=1), localized scleroderma (n=1), lung adenocarcinoma (n=1), Sweet's syndrome (n=1). IQR: Interquartile range; n: number of patients; SD: Standard deviation; IL: Interleukins; JAK: Janus Kinase.

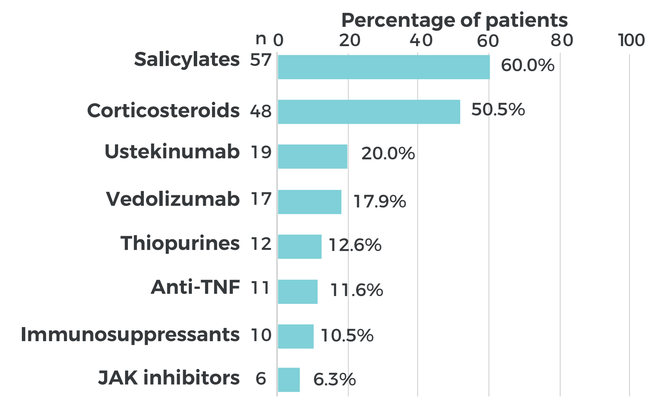
- 71 patients reached the 4-week visit after receiving a median of 10.0 (Interquartile range [IQR], 8.0-10.0; missing data, n=24) GMA sessions. 52 (73.2%) patients had received the prescribed number of GMA sessions (Missing data, n=24). The frequency of apheresis was mostly a combination of weekly and biweekly sessions **(Figure 1)**.
- 81 (87.1%) patients received concomitant treatment along with GMA, including 5-ASA (60%), corticosteroids (51.6%), ustekinumab (20%), and vedolizumab (17.9%) **(Figure 2)**.

Figure 1. Frequency of prescribed GMA sessions at baseline (N=95)



n: number of patients (Missing data, n=1); Weekly: one session a week for 10 weeks. Biweekly: 2 sessions a week for 5 weeks. Weekly and biweekly: 2 sessions a week for 3 weeks and then 1 session a week for 4 weeks until completing 10 sessions.

Figure 2. Concomitant treatments with GMA therapy (N=95)

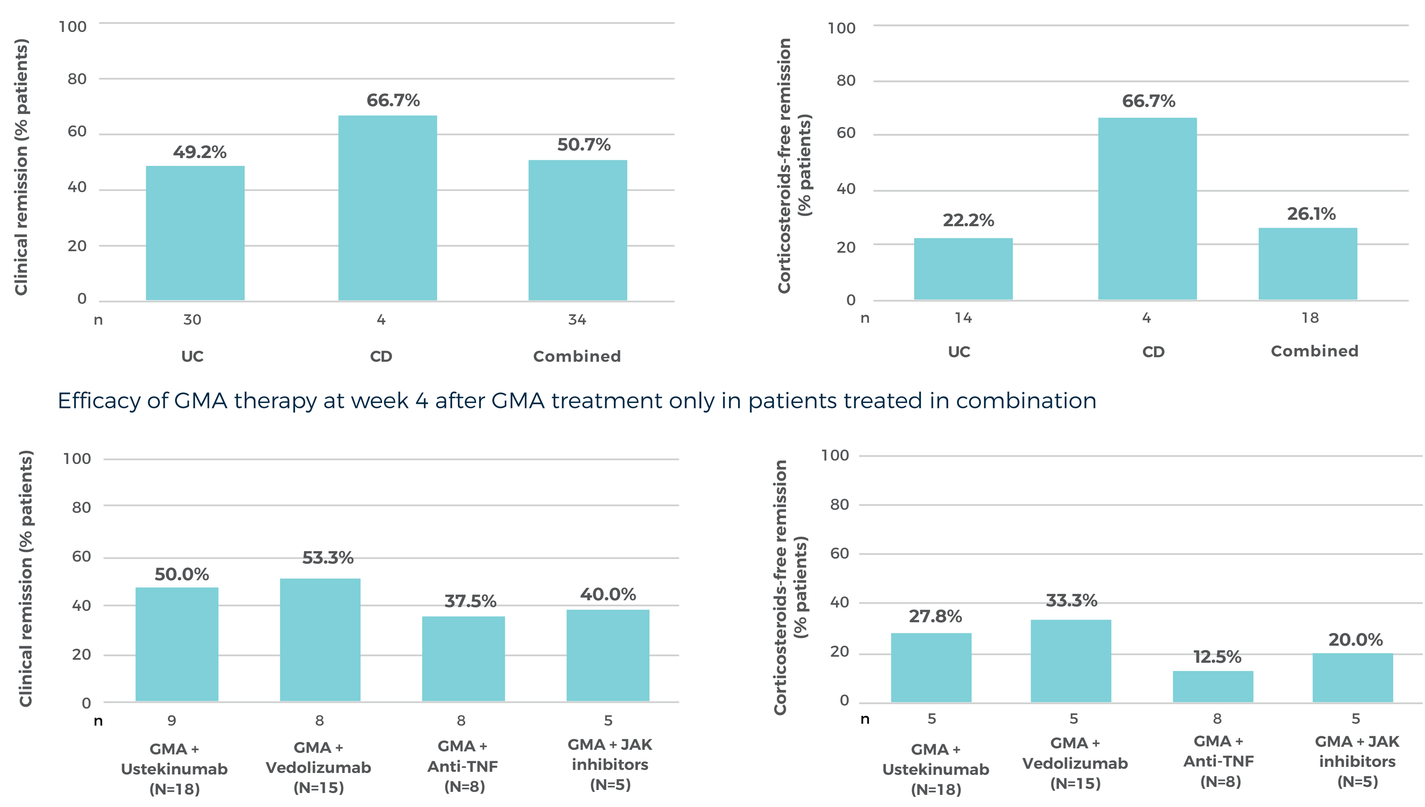


Concomitant treatments overlap with GMA in time. Anti-TNF: infliximab, adalimumab, golimumab; JAK inhibitors: tofacitinib, filgotinib, upadacitinib; Salicylates: mesalazine, sulfasalazine; thiopurines: azathioprine, mercaptopurine; immunosuppressant: cyclosporine, tacrolimus, methotrexate; corticosteroids: low bioavailability oral corticosteroids, intravenous corticosteroids, topical corticosteroids, oral corticosteroids. JAK: Janus Kinase; n: number of patients; TNF: Tumor necrosis factor.

EFFICACY AT WEEK 4 AFTER GMA TREATMENT

- Clinical remission was achieved by 30 (49.2%) patients with UC (missing data, n=3) and 4 (66.7%) patients with CD (missing data, n=1) at week 4 **(Figure 3)**.
- Corticosteroid-free remission rate was 22.2% (missing data, n=1) and 66.7% (missing data, n=1), respectively at week 4.
- None of the patients received IBD-related surgery at week 4.

Figure 3. Efficacy of GMA therapy at week 4 after GMA treatment



N=71 (UC: N=64; CD: N=7). Valid percentages are shown. Clinical remission: for UC: a total Mayo score ≤2, no individual subscore >1, and a rectal bleeding subscore of 0; for CD: a Harvey-Bradshaw Index (HBI) score ≤4. CD: Crohn's disease; GMA: Granulocyte and monocyte adsorptive apheresis; JAK: Janus Kinase; n: number of patients; TNF: Tumor necrosis factor; UC: Ulcerative colitis.

SAFETY

- Overall, 11.2% of patients experienced at least one AE related to GMA, most of them being mild. The most common AEs were headache and asthenia. No SAEs related with the device/procedure were observed.

CONCLUSIONS

- These interim results show the real-world effectiveness and safety of the Adacolumn® treatment in a cohort of refractory IBD patients with previous failure to thiopurines, biologics, and JAK inhibitors.
- Long-term results at week 24 and 48 after GMA are required to confirm these findings.

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CONFLICT OF INTEREST

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