A Randomized, Double-Blind, Multicenter, Open Phase IV Clinical Trial to Evaluate The Efficacy and Safety of A Chinese Patent Medicine Combined With Mesalazine for Ulcerative Colitis

Lei Zhu
Jiangsu Province Hospital of Chinese Medicine
Naizhong Hu
The First Hospital of Anhui Medical University
Shunping Ren
The hospital of Shanxi University of TCM
Hongpu Sun
Luoyang Second Hospital
Shaofeng Wang
Shanxi Province Changzhi People's Hospital
Xianmei Meng
The second Affiliated Hospital of Baotou medical College
Peimin Feng
Teaching Hospital of Chengdu University of TCM
Suyun Zhang
Chifeng Municipal Hospital
Jieqiong Wu
The second Affiliated Hospital of shaanxi University of TCM
Yangqian Hu
Dongfeng Motor Corporation General Hospital
Baisui Zhao
Affiliated Hospital of Inner Mongolia University for the Nationalities
Wenxi Chen
Ezhou Central Hospital
Sumin Zhang
Nanjing Hospital of Traditional Chinese Medicine
Min Wang
The Second People's Hospital of Yunnan Province
Yaozhou Tian
Jiangsu Province Hospital on Integration of Chinese and Western Medicine

Jianguo Xiao
Taizhou Hospital of TCM
Qi Wang
Second Hospital of Shanxi Medical University
Xiaojun Yang
Chongqing Traditional Chinese Medicine Hospital
Hong Shen (shenhong999@163.com)
Jiangsu Province Hospital of Chinese Medicine, Gastroenterology Department

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Research

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Abstract

Background: Enteric-coated HuDi capsules（HuDi）have been approved for the treatment of ulcerative colitis (UC) in China. In this clinical trial, we objectively evaluated the clinical efficacy and safety of HuDi combined with enteric-coated mesalazine tablets in the treatment of active UC.

Methods: A total of 355 patients from 18 hospitals in China were randomly divided into the HuDi group, enteric-coated mesalazine tablet group (mesalazine group) or combined group with randomized, controlled double-blinding and double-modeling methods. The patients were followed every two weeks and reexamined by endoscopy at the end of six weeks of treatment. The clinical response; clinical remission rate; endoscopic response rate; mucosal healing rate; erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP); and safety indicators were evaluated after treatment.

Results: The clinical response rate was 58% in the HuDi group and 58.82% in the mesalazine group, while the clinical effective rate in the combined group was 82.46%. A total of 32% of the patients receiving the enteric-coated HuDi capsules and 29.41% of the patients receiving the enteric-coated mesalazine tablets achieved clinical remission. The clinical remission rate in the combined group was 52.63%, which was better than that in the mesalazine group (P = 0.0145)and HuDi group(P = 0.0315). Moreover, the endoscopic response rates were 50% in the HuDi group, 47.06% in the mesalazine group and 64.91% in the combined group, with no significant difference among the three groups (P > 0.05). Further, the mucosal healing rates in the three groups were 44%, 41.18% and 63.16%, respectively, the combined group was better than that in the HuDi group(P=0.0472) and mesalazine group (P=0.0223). Finally, there was no significant difference in the normalization rates of the ESR and CRP among the three groups (P > 0.05).There were no serious adverse events in the combined drug group.

Conclusions: In patients with mild and moderate active UC, combined treatment with enteric-coated mesalazine tablets and enteric-coated HuDi capsules improved the Clinical response and induced clinical remission. However, further studies need extended follow-up periods to determine the efficacy.

Trial registration: Chinese It was registered in Clinical Trial Registry on 2015-01-14.

Background

Ulcerative colitis (UC) is a chronic intestinal inflammatory disease with a high recurrence rate [1]. In recent years, the incidence and morbidity of UC worldwide have increased, including in China [2, 3]. At present, it is believed that the treatment of UC is based on the control of intestinal inflammation, and the primary aim of treatment is to induce and maintain clinical remission, promote mucosal healing and maintain normal intestinal function. Medical treatment is still the main means of UC therapy. For mild to moderate UC patients, 5-aminosalicylic acid preparation is the first-line treatment drug; however, in some patients, the illness is not alleviated a step-up treatment program is required. If there is no reduction in hormones after treatment, patients will start a moderate to severe treatment program involving immunosuppressive

agents, biological agents or both for management [4]. The UC disease burden is heavy for patients, so it is necessary to improve the clinical efficacy of therapeutic drugs or treatment programs.

As a holistic treatment, the therapeutic effect of traditional Chinese medicine or Chinese patent medicine for UC has gradually become prominent. Treatment of UC with traditional Chinese medicine is a characteristic in China. Enteric-coated HuDi capsules is a Chinese patent medicine with indications for UC; it consists of Polygonum cillinerve, Rhizoma Polygoni Cuspidati,Hedyotis diffusa,Dahurian Patrinia Herb,Limonium bicolor,Radix Sanguisorbae,Rhizoma Bletillae,Radix Glycyrrhizae,which has been approved by State Food and Drug Administration (Z20020035). Enteric-coated HuDi capsules have been used in clinical practice for many years in China.

Methods

Study design

The trial was a randomized, double-blind, positive drug-controlled, multicenter clinical trial with double modeling methods; it was conducted in 18 hospitals in China, and the start and end dates of the trial were March 2015 and November 2017. The Research Institutions Examination Committee approved each participating research center (ClinicalTrials.gov, Registration number: ChiCTR1800016668). Considering the Declaration of Helsinki and the relevant rules and regulations of clinical trial research in China, the experimental scheme was approved by the Institutional Review Board of Affiliate Hospital of Nanjing University of Chinese Medicine and the Sub-Center Ethics Committee. Further, all subjects signed a written informed consent form.

The participating units included the Jiangsu Province Hospital of Chinese Medicine, First Affiliated Hospital of Anliui Medical University, Second Hospital of Shanxi Medical University, Affiliated Hospital of Shanxi College of Traditional Chinese Medicine Changzhi People's Hospital, Luoyang No.2 Hospital of Traditional Chinese Medicine, General Hospital of Dongfeng Motor Company, The Second Affiliated Hospital of Baotou Medical College, Chongqing Traditional Chinese Medicine Hospital, Second Affiliated Hospital of Shaanxi College of Traditional Chinese Medicine, Taizhou Hospital of Traditional Chinese Medicine, Nanjing Hospital of Traditional Chinese Medicine, Jiangsu Province Hospital on Integration of Chinese and Western Medicine, Affiliated Hospital of Inner Mongolia University for Nationalities, Ezhou Central Hospital, Chifeng Municipal Hospital, The Second People's Hospital of Hunan Province and Affiliated Hospital of Chengdu University of Traditional Chinese Medicine.

Inclusion and exclusion criteria

Inclusion criteria: Patients aged 18 to 65 years, regardless of sex, who had mild to moderate UC in the active stage (Mayo score > 2, mild to moderate Truelove-Witts evaluation), volunteered to participate in this clinical trial and signed the informed consent form were included.

Exclusion criteria: Patients who were in remission or the severe active phase, pregnant, lactating, or had recently given birth; patients with a severe allergic constitution or who were allergic to known components in the enteric-coated HuDi capsules or enteric-coated mesalazine tablets; patients complicated with severe cardiovascular and cerebrovascular diseases or severe primary diseases involving the liver, kidney or hematopoietic system and in whom blood alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were above the normal upper limit and blood creatinine (Cr) was above normal upper limit; patients with UC who had serious complications, such as local stenosis, intestinal obstruction, intestinal perforation, multiple intestinal polyps, toxic megacolon, and rectal cancer; and patients with mental disorders or intellectual disability were excluded.

Randomization and masking

Given the number of seeds according to SAS v9.4 statistical software, a random arrangement of subjects (random coding table) was generated. Personnel unrelated to clinical observation, monitoring and statistical analysis in this clinical trial placed the corresponding drug number in a conspicuous location on the external packaging of the drug according to an established processing code and sent the packed test medicine boxes to the test centers. Secondary blinding was used in this experiment.

The random coding table was established by the data management and statistical units involved in the clinical trial. Two copies were sealed; one was submitted to the applicant, and the other was submitted the lead unit for proper preservation.

Patients who met the inclusion criteria and did not meet the exclusion criteria were randomly divided into three groups: an enteric-coated HuDi capsules group who received enteric-coated HuDi capsules and enteric-coated mesalazine tablet simulators, an enteric-coated mesalazine tablet group who received enteric-coated HuDi capsule simulators and enteric-coated mesalazine tablets and a combined drug group who received enteric-coated HuDi capsules and enteric-coated mesalazine tablets. The enteric-coated HuDi capsules and enteric-coated HuDi capsule simulators were taken 4 capsules at a time, 3 times a day, at 1 h before breakfast, midday and dinner, respectively. The enteric-coated mesalazine tablets and enteric-coated mesalazine tablet simulators were taken 1 g at a time, 3 times a day, in the morning, afternoon, and night, respectively. Before the participants were formally enrolled in the group, a two-week screening period was established, and medicines for UC were discontinued. During the treatment period, spicy food, seafood, milk and other foods that can aggravate the disease were avoided. Moreover, medicines with the same efficacy as the experimental drugs were also forbidden.

Clinical and mucosalmeasurements

The subjects were assessed to establish their Mayo scores and identify symptoms of abdominal pain, diarrhea, or visible mucus or blood in the stool at the time of admission and at 2, 4 and 6 weeks after treatment and were examined by colonoscopy at 0 weeks before treatment (within 6 weeks before admission) and 6 weeks after treatment (within 2 weeks after treatment). Routine blood tests were conducted and liver function (ALT, AST, r-GT, TBil, ALP) and renal function (blood urea nitrogen (BUN), Cr)

were examined at 0, 2 and 6 weeks before treatment. Electrocardiogram results were examined before and 6 weeks after treatment. The type, degree and incidence of adverse events were recorded. The primary endpoint was clinical efficacy and remission after 6 weeks of treatment, and the secondary endpoints were endoscopic response, mucosal healing rate, and improvement of chemical parameters (ESR, CRP).

Clinical efficacy criteria: The total Mayo score decreased from baseline by more than 30% or more than 3 points, and the absolute score of the stool subscale decreased by more than 1 point or was 0 or 1 point.

Clinical remission criteria: The total Mayo score was < 2 and no single score was > 1.

Endoscopic response criteria: The Mayo score and endoscopy subscore decreased by at least 1 point relative to baseline.

Standard of mucosal healing: The absolute score of the Mayo endoscopy subscore was 0 or 1.

Statistical analysis

After the test plan was determined, the statistical professionals were responsible for formulating the statistical analysis plan in consultation with the main researchers. SAS 9.4 statistical software was used for the descriptive statistical analysis. Qualitative indicators are described by frequencies, percentages or composition ratios, and quantitative indicators are described in terms of means and standard deviations or medians, lower quartiles (Q1), upper quartiles (Q3), or minimum and maximum values. Regarding the comparative analysis of two groups, qualitative data were analyzed using chi-square tests, Fisher's exact tests, Wilcoxon rank sum tests, Cochran-Mantel-Haenszel (CMH) 2 tests, and weighted least squares (WLS) covariance. Quantitative data conforming to a normal distribution were analyzed using the t-test (homogeneity test of variance was conducted among groups, 0.05 was used as the test level, and a t-test considering the Satterthwaite method was used for correction when the variance was uneven). Wilcoxon rank sum tests and general linear model (GLM) covariance were used for non-normally distributed data. The hypothesis test employed the bilateral test and provided the test statistics and corresponding *P* values. Statistical significance was considered at $P < 0.05$ and $P < 0.01$.

Results

Analysis of the subject population

In this clinical trial involving 18 centers, 355 subjects were randomized; 118 patients were included in the enteric-coated HuDi capsule group.15 patients dropped out, 2 patients violated the experimental scheme and 101 patients completed treatment, of which 51 patients were reexamined by colonoscopy. The enteric-coated mesalazine tablet group included 118 patients; 9 patients dropped out, 5 patients violated the test plan, and 104 patients completed treatment, of which 51 patients were reexamined by colonoscopy. In the combined drug group, 119 patients were enrolled, 5 patients dropped out, 1 patient violated the test plan, and 57 patients were reexamined by colonoscopy (Figure 1).

Baseline characteristics

There was no significant difference ($P > 0.05$) among the three groups in demographic characteristics (age, weight, body mass index (BMI)), vital signs (temperature, pulse, respiratory rate, systolic blood pressure (SBP), diastolic blood pressure (DPB)), Clinical data (course of disease, previous medication history, mayo score,partial Mayo score), indicating that there was comparability among the three groups (Table 1).

Efficacy

Clinical response

After 6 weeks of treatment, 29 out of 50 (58%) patients in the enteric-coated HuDi capsule group showed clinically effecicacy, 30 out of 51 (58.82%) patients in the enteric-coated mesalazine tablet group showed clinical efficacy, and 47 out of 57 (82.46%) patients in the combined drug group showed clinical efficacy. The combined treatment was more effective than the enteric-coated HuDi capsules ($P = 0.0054$) and the enteric-coated mesalazine tablets ($P=0.0067$) alone. There was no significant difference between the enteric-coated HuDi capsule group and the enteric-coated mesalazine tablet group ($P = 0.9331$) (Table 2) (Figure 2).

Clinical remission

After 6 weeks of treatment, according to the colonoscopy reexamination results, clinical remission occurred in 16 of 50 patients in the enteric-coated HuDi capsules group (32%), 15 of 51 patients in the enteric-coated mesalazine tablet group (29.41%) and 30 of 57 patients in the combined drug group (52.63%). The combined drug group showed a greater rate of remission than the enteric-coated HuDi capsules (P=0.0315) and the enteric-coated mesalazine tablet group (P=0.0145). There was no significant difference between the enteric-coated HuDi capsule group and the enteric-coated mesalazine tablet group or the enteric-coated HuDi capsule group and the combined drug group ($P = 0.7780$) (Figure 3).

Mucosal response

Six weeks after treatment, an endoscopic response was found in 25 of 50 subjects in the enteric-coated HuDi capsule group (50%), 24 of 51 patients in the enteric-coated mesalazine tablet group (47.06%) and 37 of 57 patients in the combined drug group (64.91%). There was no significant difference among the three groups ($P > 0.05$) (Figure 4).

Mucosal healing

Six weeks after treatment, 22 of 50 subjects in the enteric-coated HuDi capsule group presented healed mucosa (44%), 21 of 51 patients in the enteric-coated mesalazine tablet group presented healed mucosa (41.18%), and 36 of 57 patients in the combined drug group presented healed mucosa (63.16%). The

combined group was better than that in the mesalazine group (P = 0.0223) and HuDi group(P = 0.0472). (Figure 5).

ESR and CRP

After 6 weeks of treatment, there was no significant difference in the normalization rates of ESR and CRP among the three groups ($P > 0.05$) (Table 2).

Safety

A total of 37 patients, including 13 patients in the enteric-coated HuDi capsule group (14 adverse events), 13 patients in the enteric-coated mesalazine tablet group (18 adverse events) and 11 patients in the combination group (15 adverse events), had 47 adverse events during the trial. There was no significant difference among the three groups ($P > 0.05$).Among them, 5 patients (6 cases) were judged to have adverse reactions. No adverse reactions occurred in the enteric-coated HuDi capsule group; 4 patients (5 cases) had adverse reactions in the enteric-coated mesalazine tablet group, and 1 patient (1 case) had an adverse reaction in the combined drug group. There was no significant difference among the three groups ($P > 0.05$).

There were 4 serious adverse events in 3 patients during the experiment, including 1 patient (1 case) in the enteric-coated HuDi capsule group who developed diarrhea with nausea and vomiting, which was aggravated by UC, and 2 patients (3 cases) in the enteric-coated mesalazine tablet group, including 1 case of UC with infection and 1 case of urinary protein. There were no serious adverse events in the combined drug group. There was no significant difference among the three groups ($P > 0.05$).

Discussion

In recent years, with the increase in the incidence of UC, the prolongation of the course of the disease, and the deepening of the understanding of UC, an increasing number of patients with refractory UC have been identified. Ultimately, it is difficult to avoid the outcome of total colectomy. Therefore, the treatment goal of UC has been transformed from simple symptom control to altering the natural course of the disease. Defining the type and severity of the disease, choosing the appropriate treatment plan and inducing rapid remission play important roles in the treatment of the disease. Mesalazine (5-aminosalicylic acid, 5-ASA) is recommended for the induction of remission and maintenance of most mild to moderate diseases [5, 6]. Oral mesalazine at 2.4-4.0 grams per day is usually used to induce remission; its efficacy is dose-dependent, and the effective dose (> 2 g/day) is associated with better results than the low dose [7, 8]. Although 5-aminosalicylic acid has good efficacy and safety, it is still ineffective in some patients. Some studies showed that the clinical effective rate was 60–70% and the clinical remission rate was 40–70% [9, 10]. Patients who fail to respond need to be treated with glucocorticoids. The main causes of poor therapeutic effects are starting treatment too late, choosing a poor treatment method, not identifying the correct cause of the disease, a poor degree of symptom improvement, and so on. Therefore, it is necessary to find appropriate treatments to improve the clinical remission rate of mild to moderate UC.

The medicinal ingredients of enteric-coated HuDi capsules include Polygonum cillinerve, Rhizoma Polygoni Cuspidati,Hedyotis diffusa,Dahurian Patrinia Herb,Limonium bicolor,Radix Sanguisorbae,Rhizoma Bletillae,Radix Glycyrrhizae,Pharmacodynamic studies suggest that enteric-coated HuDi capsules have positive analgesic activity and an antagonistic effect on excitation of the intestinal tract, reducing the prevalence of diarrhea in UC patients.In this study involving 18 centers in China, 355 subjects were analyzed with a randomized, double-blind, positive drug-controlled, multicenter clinical trial with a double modeling method. However, due to two enteroscopic examinations in a short time, the subjects' compliance was poor. There were 51 patients in the enteric-coated HuDi capsule group, 56 patients in the enteric-coated mesalazine tablet group and 58 patients in the combination group that underwent colonoscopy before and after treatment. After 6 weeks of treatment, the enteric-coated HuDi capsules and enteric-coated mesalazine tablets showed the same efficacy, but the combined treatment was better than the two treatments alone. There was no significant difference in the endoscopic response rate and mucosal healing rate among the three groups, indicating that enteric-coated HuDi capsules had similar efficacy in promoting mucosal recovery as enteric-coated mesalazine tablets, and the effect of the combination of the two drugs showed no significant improvement. Because of the sample size, this study had some limitations. It is suggested that further research should be carried out to confirm these results.

There were 5 patients (6 cases) with adverse reactions. There were no adverse reactions in the enteric-coated HuDi capsule group; 4 patients (5 cases) had adverse reactions in the enteric-coated mesalazine tablet group, and 1 patient (1 case) had an adverse reaction in the combined drug group. There was no significant difference among the three groups ($P > 0.05$).

The data of this large-scale clinical trial showed that enteric-coated HuDi capsules combined with enteric-coated mesalazine tablets were safe and effective in the treatment of mild to moderate UC and improved its clinical efficacy. Nevertheless, the limitation of this study was that the 6-week trial was relatively short. In the future, researchers should follow patients for an extended period of time to evaluate its safety and effectiveness. In addition, although there were many randomized patients in this study, few patients underwent reexamination by colonoscopy; thus, large-sample data are needed to evaluate its effect on mucosal healing.

Conclusions

In patients with mild and moderate active UC, combined treatment with enteric-coated mesalazine tablets and enteric-coated HuDi capsules improved the Clinical response and induced clinical remission. However, further studies need extended follow-up periods to determine the efficacy.

Abbreviations

Ulcerative colitis (UC)

Alanine aminotransferase (ALT)

Aspartate aminotransferase (AST)

Blood urea nitrogen (BUN)

Cochran-Mantel-Haenszel (CMH)

Declarations

Ethics approval and consent to participate

The experimental protocol was established, according to the ethical guidelines of the Helsinki Declaration and was approved by the Human Ethics Committee of Institutional Review Board of Affiliate Hospital of Nanjing University of Chinese Medicine and the Sub-Center Ethics Committee. Written informed consent was obtained from individual or guardian participants.

Consent for publication

All data generated or analyzed during this study are included in this published article

Availability of data and materials

All data generated or analyzed during this study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

Not applicable.

Authors' contributions

LeZ and HS designed the study and wrote the manuscript. NzH, SpR, HpS, SfW, XmM, PmF, SyZ, JqW, YqH, BsZ, WxC, SmZ, MW, YzT, JgX, QWang, XjY performed the experiments. LeZ analyzed the data. All authors read and approved the final manuscript.

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References

1. Ordás I, Eckmann L, Talamini M. et al. Ulcerative colitis. Lancet. 2012;380(9853):1606–19.

2. 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(10114):2769–78.
3. Kamm MA. Rapid changes in epidemiology of inflammatory bowel disease. Lancet. 2018;390(10114):2741–2.
4. Magro F, Gionchetti P, Eliakim R. et al. Third European Evidence-based Consensus on Diagnosis and Management of Ulcerative Colitis. Part 1: Definitions, Diagnosis, Extra-intestinal Manifestations, Pregnancy, Cancer Surveillance, Surgery, and Ileo-anal Pouch Disorders. J Crohns Colitis. 2017;11(6):649–70.
5. Mowat C, Cole A, Windsor A. et al. Guidelines for the management of inflammatory bowel disease in adults. Gut. 2011;60(5):571–607.
6. Schroeder KW, Tremaine WJ, Ilstrup DM. Coated oral 5-aminosalicylic acid therapy for mildly to moderately active UC. A randomized study. N Engl J Med. 1987;317(26):1625–9.
7. Vecchi M, Meucci G, Gionchetti P. et al. Oral versus combination mesalazine therapy in active ulcerative colitis: a double-blind, double-dummy, randomized multicenter study. Aliment Pharmacol Ther. 2001;15(2):251–6.
8. Flourié B, Hagège H, Tucat G. et al. Randomised clinical trial: once- vs. twice-daily prolonged-release mesalazine for active ulcerative colitis. Aliment Pharmacol Ther. 2013;37(8):767–75.
9. Marteau P, Probert CS, Lindgren S. et al. Combined oral and enema treatment with Pentasa (mesalazine) is superior to oral therapy alonein patients with extensive mild/moderate active ulcerative colitis: a randomised, double blind, placebo controlled study. Gut. 2005;54(7):960–5.
10. Ford AC, Achkar JP, Khan KJ. et al. Efficacy of 5-aminosalicylates in ulcerative colitis: systematic review and meta-analysis. Am J Gastroenterol. 2011;106(4):601–16.

Tables

Table 1
Baseline demographic and clinical characteristics of the groups.

Characteristics	HuDi group (n = 101)	Mesalazine group (n = 104)	Combined group (n = 113)	*P* value
Demographic data				
Age (y)	45.80 ± 12.08	45.55 ± 11.18	45.03 ± 11.93	0.8837
Weight (kg)	63.48 ± 11.09	61.82 ± 10.25	63.75 ± 11.37	0.4612
BMI (kg/m^2)	22.88 ± 3.32	22.87 ± 2.98	22.71 ± 3.17	0.9306
temperature(℃)	36.44 ± 0.23	36.45 ± 0.20	36.47 ± 0.25	0.7262
Pulse	70.86 ± 9.31	72.43 ± 9.23	73.68 ± 8.55	0.0751
Respiratory rate (breaths/min)	18.84 ± 1.82	18.88 ± 1.59	18.88 ± 1.59	0.9030
SBP (mmHg)	121.81 ± 7.29	121.02 ± 7.99	120.66 ± 10.21	0.3728
DBP (mmHg)	77.46 ± 5.59	77.70 ± 5.89	76.93 ± 6.97	0.5203
Clinical data				
Course (month)	33.60 ± 55.98	32.29 ± 46.24	31.01 ± 46.79	0.7999
Previous medication history (%)	54 (53.47)	47 (45.19)	57 (50.44)	0.4860
Mayo score	6.08 ± 1.72	5.80 ± 1.67	6.09 ± 1.68	0.6166
Partial Mayo score	4.07 ± 1.29	4.02 ± 1.22	4.13 ± 1.35	0.8259

Table 2
Normalization rates of ESR and CRP (%)

Characteristics	HuDi group (n = 101)	Mesalazine group (n = 104)	Combined group (n = 113)	*P* value
ESR	43.48	50.00	61.90	0.4689
CRP	42.86	47.37	63.64	0.5609

Figures

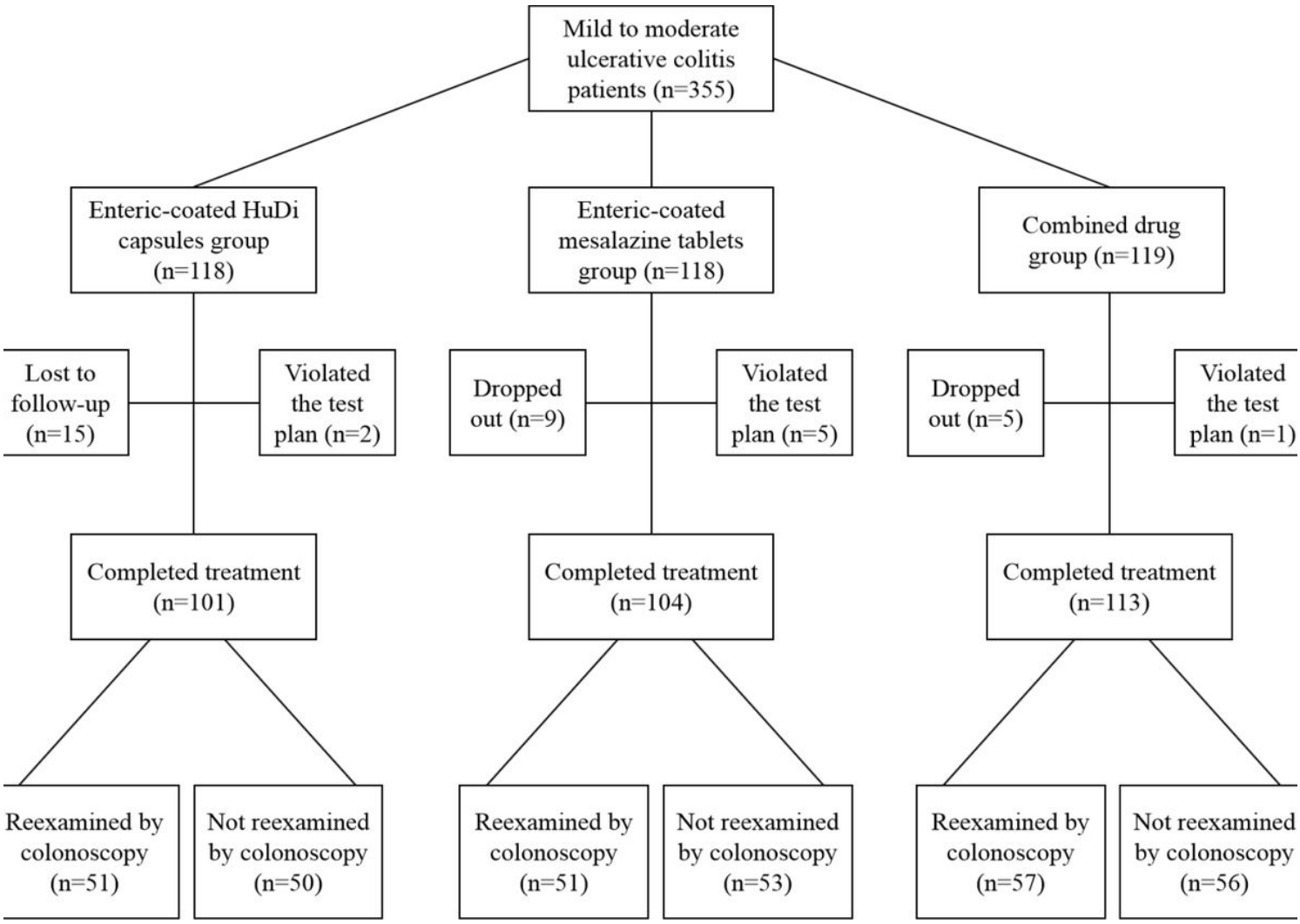

Figure 1

Analysis of the subject population.

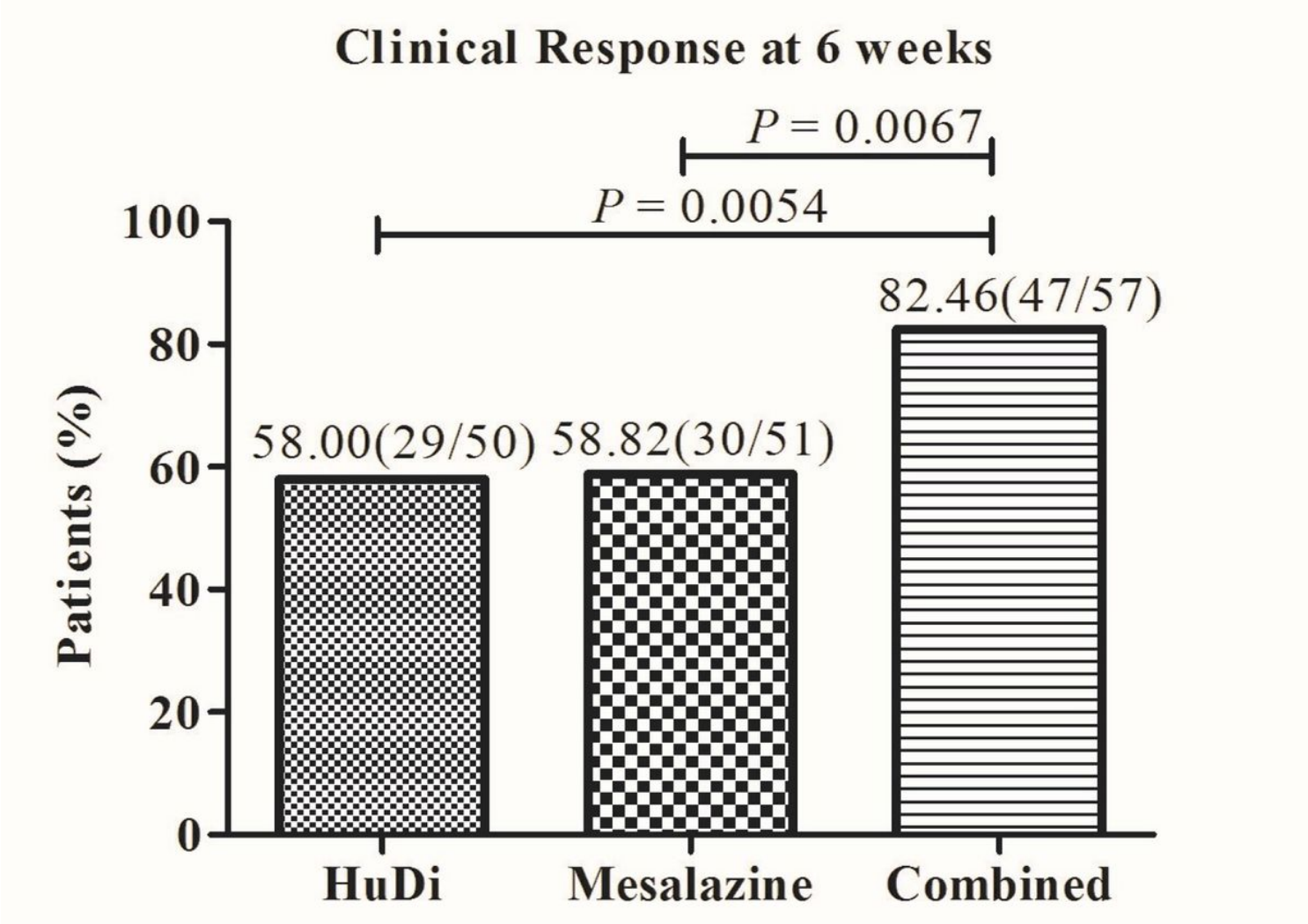

Figure 2

Clinical response at 6 weeks.

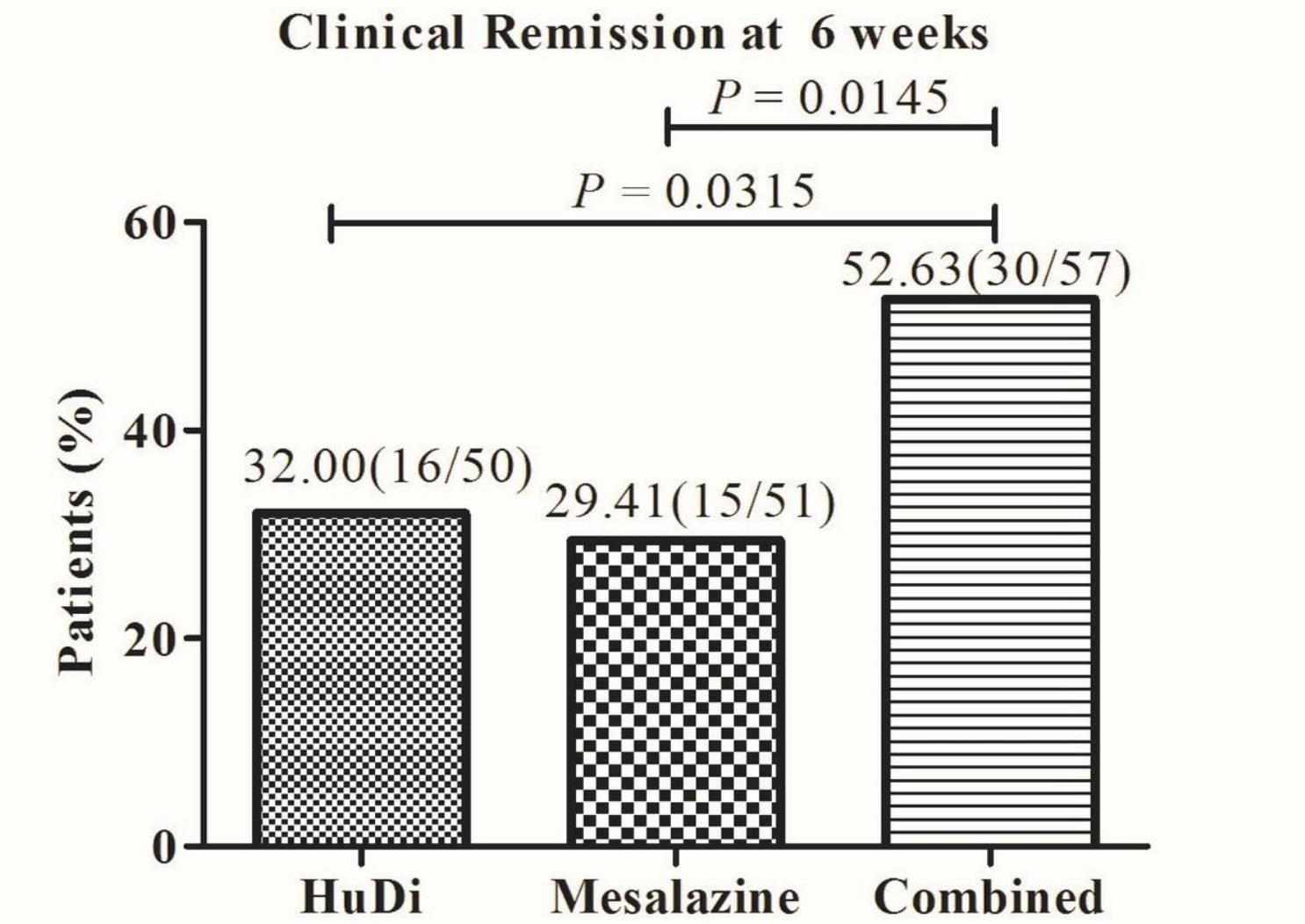

Figure 3

Clinical remission at 6 weeks.

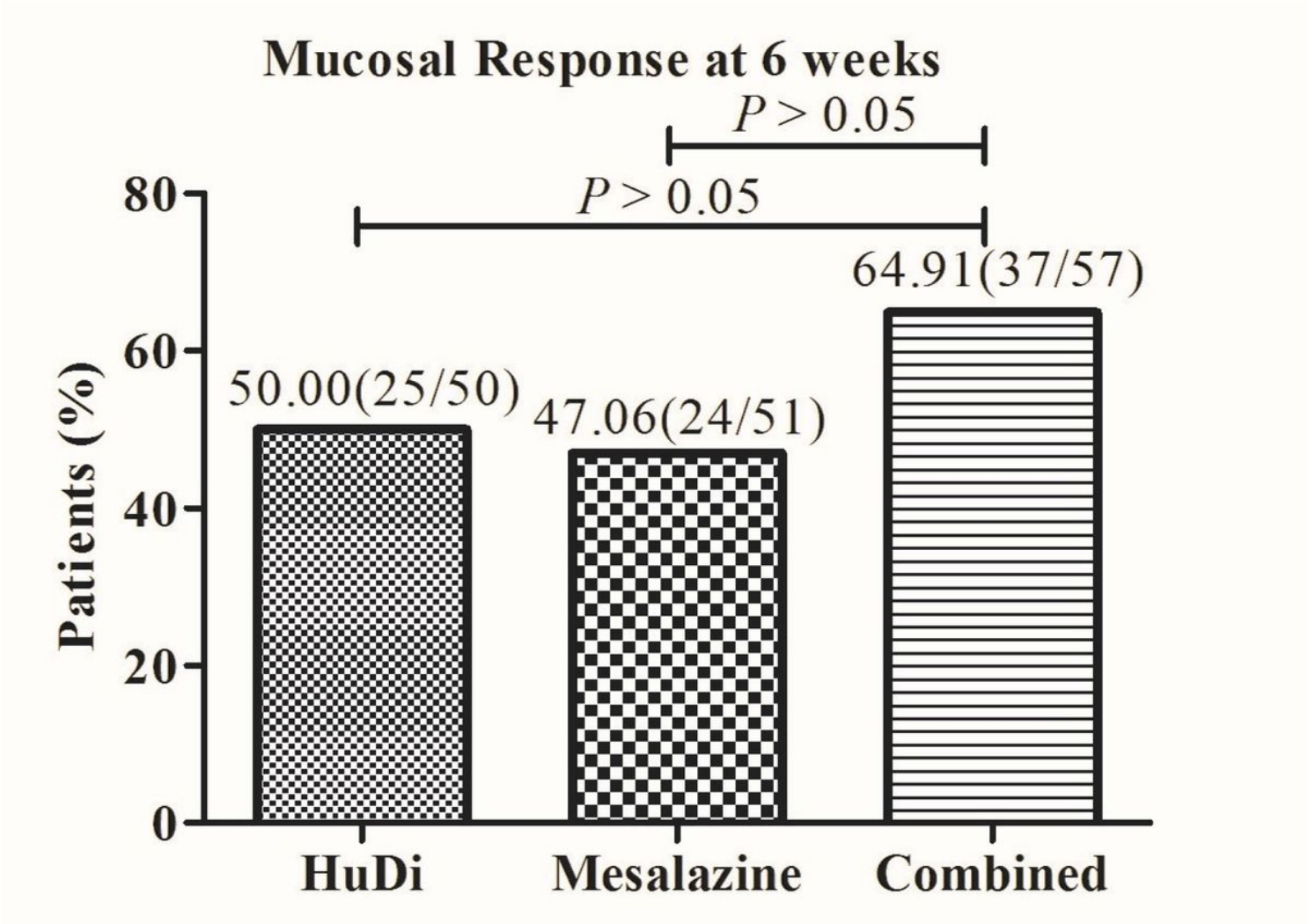

Figure 4

Mucosal response at 6 weeks.

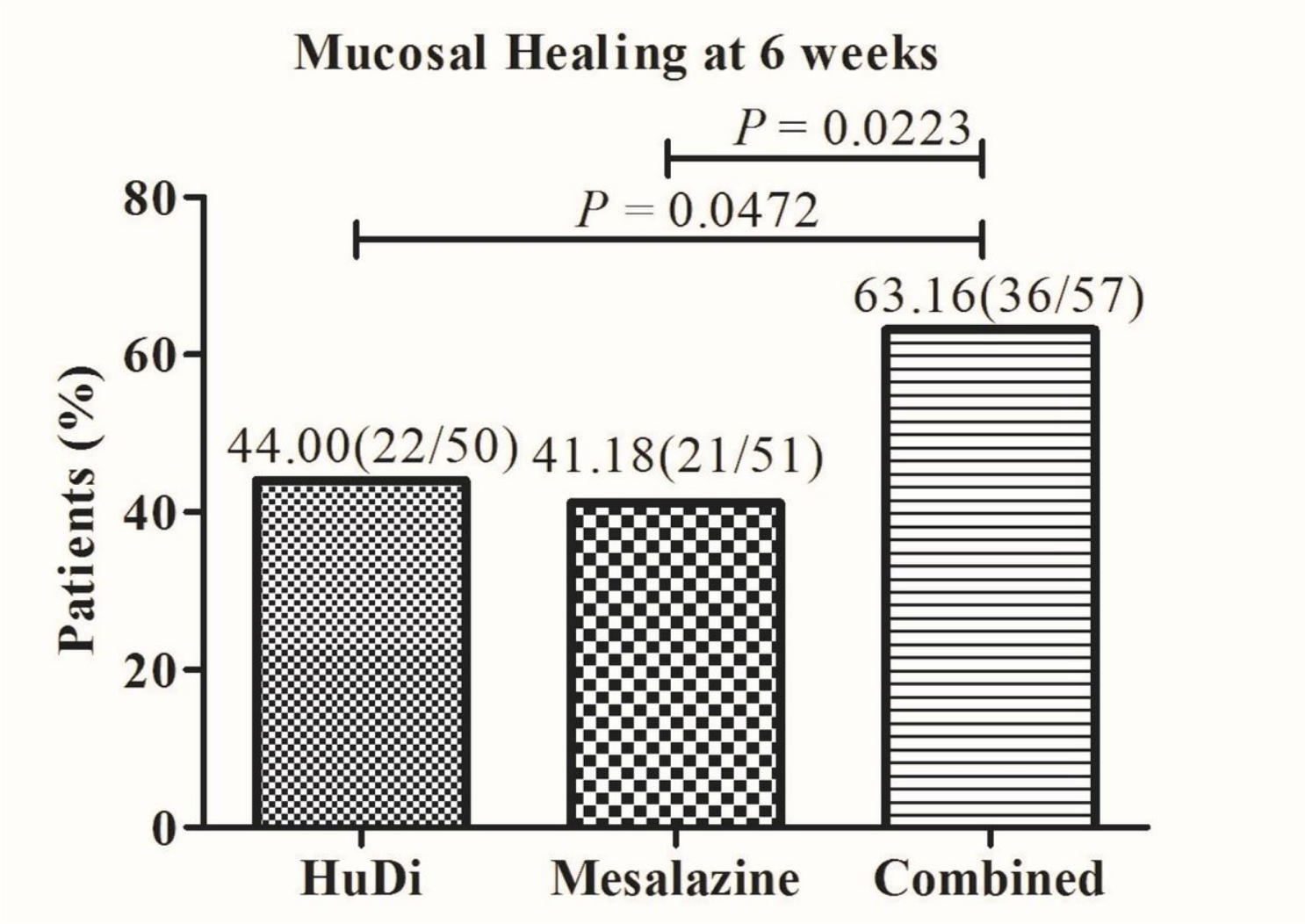

Figure 5

Mucosal healing at 6 weeks.