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ORIGINAL RESEARCH

Short-Term Effectiveness of Ustekinumab in Crohn's Disease: Results from a Real-World Retrospective Multicenter Study in China

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Background: There are few data on ustekinumab treatment for Crohn's disease (CD) in a Chinese population. Our study is a real-world retrospective multicenter study aimed at exploring the effectiveness of ustekinumab in CD patients and comparing the effectiveness of first line and second line treatments.

Methods: Laboratory indicators, CD activity index (CDAI) and simple endoscopic score for CD (SES-CD) scores of patients at the 8th, 16th and 24th weeks of treatment were collected, and the clinical remission rate, clinical response rate, endoscopic remission rate and endoscopic response rate were calculated, and the patients were divided into first line group and second line group for comparison.

Results: A total of 102 patients were treated with ustekinumab, and 56 patients with a clinical data integrity rate greater than 70% were ultimately included. The clinical remission rate of the patients gradually increased at the 8th, 16th and 24th weeks of treatment, which were 34 cases (60.7%), 37 cases (66.1%) and 49 cases (87.5%), respectively. The clinical response rates for 8th, 16th and 24th weeks were 38 (67.8%), 42 (0.75%) and 51 (91.1%), respectively, and the endoscopic remission rate was 4% (2/50) at the 24th week. The clinical response rates of the first line group were higher than those of the second line group at the 16th and 24th weeks, with statistically significant differences. The clinical response time of patients receiving first line or second line treatment with ustekinumab was different, and the first line treatment group achieved clinical response more quickly.

Conclusion: Ustekinumab is effective in the short-term treatment of CD patients in China, with first line treatment superior to second line treatment and faster than second line treatment.

Keywords: ustekinumab, Crohn's disease, first line, second line

Introduction

CD is a chronic, progressive inflammatory disease affecting the gastrointestinal tract which requiring long-term therapy.[1] Current treatment options include biologic therapies such as tumor necrosis factor (TNF) inhibitors, integrin inhibitors, and interleukin (IL)-12/23 inhibitors.[2] Ustekinumab specifically binds to the p40 protein subunit shared by human cytokines IL-12 and IL-23, and is a fully human IGG1-κ monoclonal antibody. It is primarily indicated for the treatment of adults with moderate to severe active CD who have inadequate response, loss of response, or intolerance to conventional therapy or TNF-α inhibitors, or are contraindicated to such therapy.[3] In March 2020, the China National Drug Administration approved ustekinumab for the treatment of adult patients with moderate-to-severe active CD. At present, most of the data on the effectiveness and safety of ustekinumab come from Europe and the United States.[3–5] In

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some countries, ustekinumab may be used as first line therapy; there are also sporadic small sample reports in China.[6] Our study is a multicenter, retrospective study aimed at exploring the effectiveness of ustekinumab in CD patients and comparing the effectiveness of first line and second line treatments.

Methods

Study Design and Patient Population

A retrospective, multicenter study was conducted at three hospitals in Anhui Province, China (all are public hospitals).

The subjects of the study were CD patients treated with ustekinumab who were admitted to the First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China, the First Affiliated Hospital of Anhui University of Traditional Chinese Medicine and the First Affiliated Hospital of Wannan Medical College from September 2020 to August 2023.

Inclusion criteria: (1) 18–75 years old; (2) according to the consensus opinion on inflammatory bowel disease in Beijing in 2018,[7] the diagnosis of CD was confirmed by comprehensive clinical manifestations, laboratory, endoscopic, imaging and pathological examinations; (3) ustekinumab treatment.

Exclusion criteria: more than 30% of case data were missing. The missing data were processed through the complete-case analysis, and the last observation was carried forward.

The patients were divided into first line treatment and second line treatment groups. The first line treatment group referred to the first treatment received after the diagnosis of CD was ustekinumab. The second line treatment group referred to other treatment regiments (nutritional therapy, 5-aminosalicylic acid, hormones, immunosuppressants, other biological agents except ustekinumab) before receiving ustekinumab. Hormone therapy referred to in our study included methylprednisolone, prednisone, and hydrocortisone, available in intravenous and oral dosage forms. No patient was treated with ustekinumab and another biological agent simultaneously.

Ustekinumab Treatment

The first dose of the drug is determined by the patient's constitution, dose determination: body weight < 55 kg, the first dose is 260 mg; 55–85 kg, initial dose of 390 mg; >85 kg, the first dose was 520 mg. The follow-up dose was once every 8 weeks, and the second and subsequent maintenance doses were 90 mg. Induction therapy was administered intravenously and maintenance therapy was administered subcutaneously.

Data Collection

Collect the following information from patients: age at diagnosis, sex, course of disease, BMI, presence of perianal lesions, Montreal classification, disease activity, endoscopic severity, whether and how nutritional therapy was used, previous surgical history, previous drug history, laboratory indicators and scores at week 0, 8, 16 and 24 of treatment (albumin, hemoglobin, platelets, lymphocyte count, monocyte count, neutrophil count, fecal calprotectin, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), fecal calprotectin, platelet to lymphocyte ratio (PLR), monocyte to lymphocyte ratio (MLR), neutrophil to lymphocyte ratio (NLR), systemic-inflammatory index (SII), CDAI, SES-CD and other information). The Montreal classification divided the disease into L1, L2, L3, and L4, depending on the degree of involvement of the terminal ileum, colon, ileocolon, and upper gastrointestinal tract. L4 can co-exist with L1, L2, or L3. Disease behavior B1 indicates non-stenogenic non-penetrating type, B2 indicates stenogenic type, and B3 indicates penetrating type.

Evaluation Criteria

Clinical remission was defined as a CDAI score ≤ 150 points, and clinical response was defined as a decrease in CDAI score ≥100 from baseline.[8] SES-CD≤ 2 is classified as endoscopic remission; SES-CD decrease ≥ 50% is classified as endoscopic response.[9] Of the 56 patients, 50 underwent colonoscopy at the 24th week, and only these were evaluated for endoscopic remission and response.

Statistical Analysis

Quantitative variables were represented as mean ± SD or as median with interquartile range and compared using Student's *t*-test or nonparametric tests. The categorical variables were expressed in counts (percentages) and analyzed using the chi-square test or Fisher's exact test. A p-value less than 0.05 (double tailed) was considered significant. All statistical analyses were performed in SPSS version 25.0.

Results

Baseline Population Information

A total of 102 patients were treated with ustekinumab, and 56 patients with a clinical data integrity rate greater than 70% were ultimately included. These 56 patients were divided into a first line ustekinumab treatment group and a second line group for data analysis. Patient demographics and baseline characteristics are summarized in Table 1. The average age was 32.0 (27.3, 38.0) years, and the average course of disease was 4.0 (1.1, 6.8) years. Whether in the first or second line group, the lesion range was more common in L3 type. According to the CDAI score, at baseline, 13 (65.0%) of the first line treatment group were in the active phase, while 23 (63.9%) of the second line treatment group were in the active phase. The SES-CD score of the first line group was lower than that of the second line group, and the difference was statistically significant [(8.7±1.6) vs (9.7±1.7), P 0.025]. A total of 46.6% (26/56) of the patients had previously used

Table 1 Baseline Characteristics of Patients with CD Receiving First Line or Second Line Treatment with Ustekinumab

Parameter	Total (n=56)	Baseline First Line (n=20)	Baseline Second Line (n=36)	p
Age, years	32.0 (27.3, 38.0)	32.0 (24.5, 38.0)	32.5 (28.0, 39.8)	0.355
≤16	4 (7.1%)	1 (5.0%)	3 (8.3%)	0.692
17–40	43 (76.8%)	17 (85.0%)	26 (72.2%)	
≥40	9 (16.1%)	2 (10.0%)	7 (19.4%)	
Sex (female)	12 (21.4%)	4 (20%)	8 (22.2%)	0.846
BMI	18.1 (17.9, 18.2)	18.2 (17.9, 18.3)	18.1 (17.9, 18.2)	0.181
Disease duration, years	4.0 (1.1, 6.8)	1.0 (1.0, 2.4)	6.0 (3.3, 7.8)	<0.001
Location, n (%)				0.181
L1	4 (7.1%)	3 (15.0%)	1 (2.8%)	
L2	2 (3.6%)	1 (5.0%)	1 (2.8%)	
L3	44 (78.6%)	13 (65.0%)	31 (86.1%)	
L3+L4	6 (10.7%)	3 (15.0%)	3 (8.3%)	
Behavior, n (%)				0.058
B1	27 (48.2%)	14 (70.0%)	13 (36.1%)	
B2	23 (41.1%)	5 (25.0%)	18 (50.0%)	
B3	6 (10.7%)	1 (5.0%)	5 (13.9%)	
CDAI	179.1±77.4	195.1±92.0	170.3±67.7	0.253
CDAI (Baseline active), n (%)	36 (64.3%)	13 (65.0%)	23 (63.9%)	0.934
SES-CD	9.3±1.7	8.7±1.6	9.7±1.7	0.025
CRP	17.5±18.0	21.9±26.6	15.4±11.8	0.346
ESR	21.2±17.5	22.4±23.2	20.5±13.4	0.700
Calprotectin	230.0±219.8	189.3±176.4	249.7±238.1	0.373
NLR	2.6±1.4	2.3±1.0	2.9±1.5	0.114
MLR	0.4±0.1	0.3±0.1	0.4±0.2	0.018
PLR	208.0±85.9	193.4±72.2	216.3±92.8	0.348
SII	748.8±505.6	648.0±310.4	806.4±585.5	0.268
Enteral nutrition	23 (41.1%)	9 (45.0%)	14 (38.9%)	0.656
Number of biological agents used in the past				<0.001
0	30 (53.6%)	20 (100.0%)	10 (27.8%)	
1	19 (33.9%)	0 (0.0%)	19 (52.8%)	
2	7 (12.5%)	0 (0.0%)	7 (19.4%)	

biological agents, the most common is infliximab, and some patients received hormone, mesalazine, traditional Chinese medicine and other treatments. In total, there were 41.1% (23/56) cases with a history of abdominal surgery, and 73.2% (41/56) complicated with perianal lesions.

Evaluation of Therapeutic Effects

The overall clinical effectiveness of ustekinumab treatment is presented in Table 2. The clinical remission rate of the patients gradually increased at the 8th, 16th and 24th weeks of treatment, which were 34 cases (60.7%), 37 cases (66.1%) and 49 cases (87.5%), respectively. The clinical response rates for the 8th, 16th, and 24th weeks were 38 (67.8%), 42 (0.75%) and 51 (91.1%), respectively. The average CDAI score, ESR, and CRP gradually decrease with the prolongation of treatment time. At the 24th week, a total of 50 of the 56 patients were re-examined with colonoscopy, of which only 2 cases achieved endoscopic remission, and the rest did not receive endoscopic response, the endoscopic remission rate was 4% (2/50). Treatment response and inflammatory parameters at the 8th, 16th and 24th weeks among patients receiving first line or second line treatment with ustekinumab is shown in Table 3. Overall, the clinical remission rate and response rate were higher in the first line group compared to the second line group at weeks 8, 16, and 24. The clinical response rates for the 8th, 16th, and 24th weeks were 38 (67.8%), 42 (0.75%) and 51 (91.1%), respectively. At the 16th week, the mean ESR and PLR of the first line group were lower than those of the second line group, and at the 24th week, the average NLR of the first line group was lower than that of the second line group; the above differences were statistically significant. At the 24th week, the mean SES-CD score of the first line group was lower than that of the second line group, but the difference was statistically significant (P=0.413). The magnitude of changes in inflammatory parameters and disease activity scores at the 8th, 16th, and 24th weeks in patients receiving first line or second

Table 2 Overall Clinical Effectiveness of Ustekinumab Treatment

Outcome	Baseline	Week 8	Week 16	Week 24
Clinical remission	–	34 (60.7%)	37 (66.1%)	49 (87.5%)
Clinical response	–	38 (67.8%)	42 (0.75%)	51 (91.1%)
Mean CDAI score	179.1±77.4	140.0±56.5	132.5±56.2	114.2±47.2
Mean CRP (mg/L)	17.5±18.0	10.0±9.2	10.6±9.6	9.0±8.2
Mean ESR	21.2±17.5	16.6±12.4	15.9±13.9	15.1±14.2
Mean calprotectin	230.0±219.8	159.1±144.3	188.4±192.1	145.6±179.5
Mean SES-CD score	9.3±1.7	–	–	8.2±1.8

Table 3 Treatment Response and Inflammatory Parameters at the 8th, 16th and 24th Weeks Among Patients Receiving First Line or Second Line Treatment with Ustekinumab

Parameter	8th week			16th week			24th week		
	First Line (n=20)	Second Line (n=36)	p	First Line (n=20)	Second Line (n=36)	p	First Line (n=20)	Second Line (n=36)	p
Clinical remission	11 (55.0%)	23 (63.9%)	0.452	12 (60.0%)	25 (69.4%)	0.429	18 (90.0%)	31 (86.1%)	1.000
Clinical response	3 (15%)	1 (0.03%)	0.234	4 (20%)	1 (0.03%)	0.034	1 (5%)	1 (0.03%)	0.027
Mean CDAI score	142.9±63.4	138.3±53.0	0.775	132.2±56.1	132.7±57.1	0.977	110.2±40.4	116.4±51.0	0.639
Mean CRP (mg/L)	9.3±10.0	10.4±8.9	0.692	8.2±9.5	11.7±9.6	0.235	6.9±7.7	10.0±8.3	0.201
Mean ESR	12.5±10.3	18.8±13.0	0.077	9.9±8.5	19.4±15.3	0.005	12.3±9.5	16.5±16.0	0.308
Mean calprotectin	168.8±169.9	154.4±132.8	0.748	183.2±197.7	191.0±192.3	0.896	104.9±141.3	167.3±195.6	0.266
Mean NLR	2.1±0.9	2.7±1.2	0.061	2.1±1.0	2.8±1.5	0.063	1.9±0.7	2.4±1.0	0.041
Mean MLR	0.3±0.1	0.4±0.1	0.059	0.3±0.1	0.4±0.1	0.103	0.3±0.1	0.3±0.1	0.182
Mean PLR	158.4±68.9	193.6±75.3	0.097	144.2±62.2	180.9±60.0	0.036	141.6±75.5	176.0±78.6	0.126
Mean SII	525.6±294.8	711.4±419.7	0.093	514.4±315.0	677.4±394.5	0.120	461.2±309.8	632.3±358.7	0.086
Mean SES-CD score	–	–	–	–	–	–	7.5±1.9	8.6±1.6	0.413

Table 4 Change of Inflammatory Parameters and Disease Activity Scores at the 8th, 16th and 24th Weeks Among Patients Receiving First Line or Second Line Treatment with Ustekinumab

Parameter	8th week			16th week			24th week		
	First Line	Second Line	p	First Line	Second Line	p	First Line	Second Line	p
Mean CDAI score	52.2±60.2	25.0±34.2	0.075	62.9±72.0	30.6±45.0	0.082	84.9±75.7	53.8±49.9	0.111
Mean CRP (mg/L)	12.6±22.4	5.0±10.2	0.198	14.9±27.1	3.7±10.6	0.130	16.2±28.3	5.3±9.9	0.154
Mean ESR	10.9±17.1	1.7±9.2	0.013	12.5±18.1	1.0±11.2	0.006	12.4±21.7	3.9±13.6	0.091
Mean calprotectin	20.6±194.4	95.3±204.3	0.229	6.1±302.3	58.7±204.5	0.476	84.4±231.7	83.1±219.5	0.985
Mean NLR	0.2±0.8	0.2±1.3	0.939	0.1±0.8	0.0±1.0	0.687	0.4±0.9	0.4±1.1	0.862
Mean MLR	0.0±0.1	0.0±0.1	0.848	0.0±0.2	0.1±0.1	0.434	0.0±0.1	0.1±0.1	0.279
Mean PLR	38.1±85.9	22.7±58.3	0.437	49.3±78.3	35.4±67.9	0.495	41.8±79.4	40.3±86.8	0.949
Mean SII	137.8±338.9	95.0±420.1	0.705	133.7±290.1	129.0±306.4	0.956	152.0±320.9	174.1±445.2	0.849
Mean SES-CD score	–	–	–	–	–	–	1.5±1.9	1.4±0.8	0.759

line ustekinumab is shown in Table 4. The decrease of inflammatory parameters (mean CRP, mean ESR, mean calprotectin, mean NLR, mean MLR, mean PLR, mean SII) and mean CDAI score in first line patients was more significant than that in second line patients at the 8th, 16th and 24th weeks, and the difference of mean ESR between first line and second line patients at the 8th and 16th weeks was statistically significant. Changes in serum levels of inflammatory parameters and disease activity scores during 24 weeks among patients receiving first line or second line treatment with ustekinumab are shown in Figure 1. Serum inflammatory parameter levels and disease activity scores decreased from baseline at the 24th week in the first or second line treatment groups. The clinical response time of

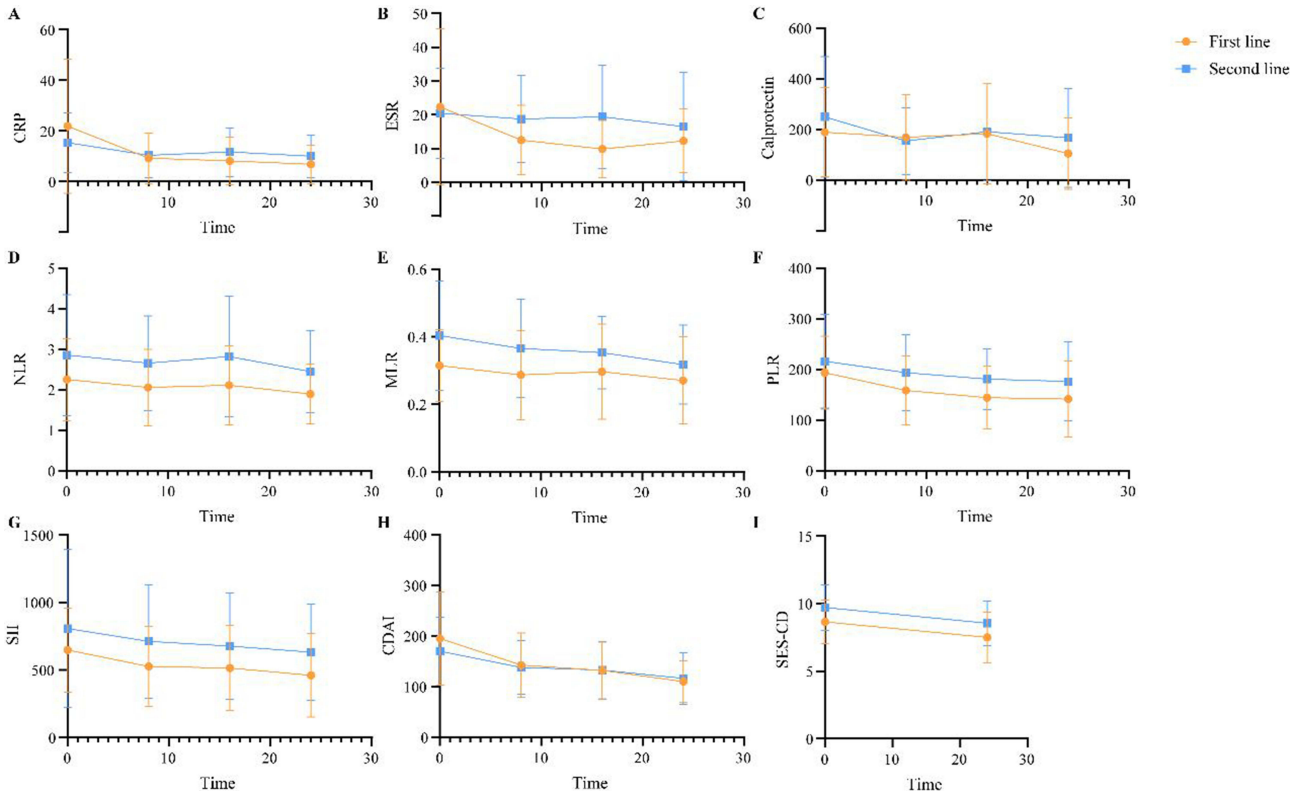

Figure 1 Changes in serum levels of inflammatory parameters and disease activity scores during 24 weeks among patients receiving first line or second line treatment with ustekinumab. (**A**) C-reactive protein (CRP), (**B**) Erythrocyte sedimentation rate (ESR), (**C**) Fecal calprotectin, (**D**) Neutrophil to lymphocyte ratio (NLR), (**E**) Monocyte to lymphocyte ratio (MLR), (**F**) Platelet to lymphocyte ratio (PLR), (**G**) Systemic-inflammatory index (SII), (**H**) CDAI, (**I**) SES-CD.

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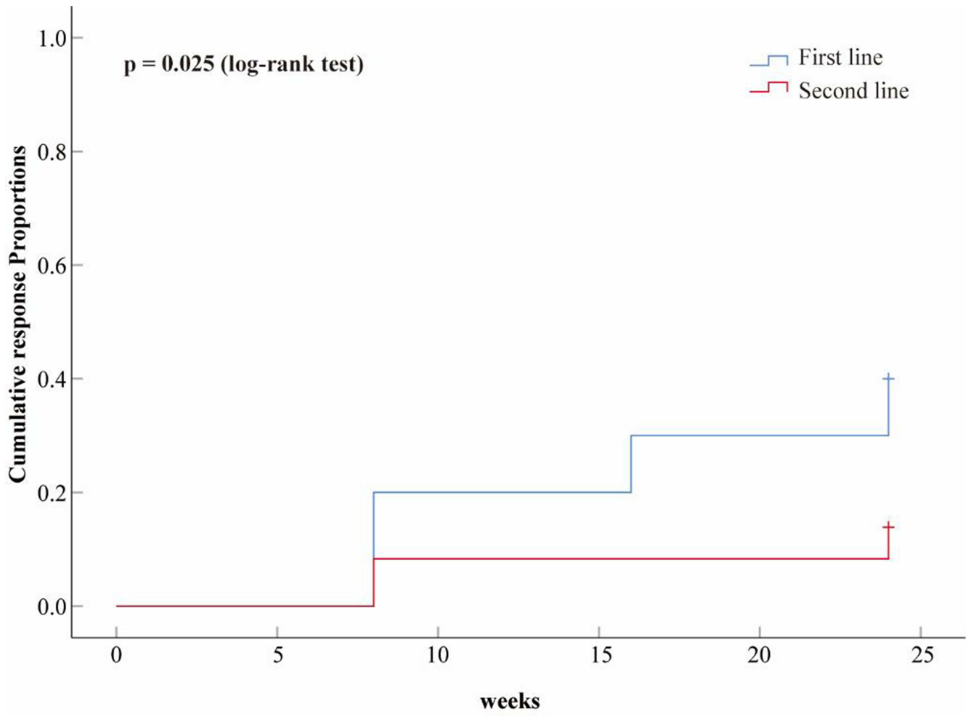

Figure 2 Time to clinical response among patients receiving first line or second line treatment with ustekinumab.

patients receiving first line or second line treatment with ustekinumab was different, and the first line treatment group achieved clinical response more quickly, as shown in Figure 2.

Safety

There were 12 patients with decreased white blood cells, which returned to normal after symptomatic treatment. Five patients developed upper gastrointestinal tract infections within two weeks after treatment and improved after symptomatic treatment. All the above are mild adverse reactions, which have not caused obvious harm to the human body. No moderate to severe adverse reactions such as allergies, rashes, or explosive refractory infections have occurred.

Discussion

Ustekinumab is a monoclonal antibody targeting the IL-12/23p40 subunit, and is a novel biological agent for the treatment of refractory CD. Multiple clinical studies abroad have shown that ustekinumab can effectively induce and maintain CD remission.[10] The results of the UNITI1 study showed that the clinical response rate of the ustekinumab treatment group at the 6th week was 34.3%, the endoscopic mucosal improvement rate at the 8th week was 43.9%, and the endoscopic response rate of the maintenance period is higher with medication every 8 weeks compared to the medication regimen every 12 weeks.[3] A real-world study in Spain reported that the clinical remission rates of ustekinumab treatment for CD at the 8th and 14th weeks were 47% and 58%, respectively.[11] Results from a multicenter prospective study in China showed that the clinical remission rates at the 8th and 20th weeks of ustekinumab treatment was approximately 50–60%, and the clinical response rates was approximately 60–80%.[12] The Department of Gastroenterology at the Sixth Affiliated Hospital of Sun Yat-sen University in China led a multicenter retrospective study to share real-world data on ustekinumab treatment of CD and to analyze and evaluate the short-term effectiveness of ustekinumab treatment of CD. At the 8th week, the clinical response rate was 72.2% (13/18) and the clinical remission rate was 77.8% (14/18). At the 16/20th week, the clinical response rate was 88.9% (16/18) and the clinical remission rate was 94.4% (17/18).[6] Another Chinese study showed that the clinical remission rate and clinical response rate at the 24th and 32th weeks were 81.2% and 93.8%, respectively.[13] A Japanese study showed the clinical

remission rate of ustekinumab is 44.4%.[14] Relevant studies have all confirmed that ustekinumab has good clinical effectiveness and high safety for inflammatory bowel disease, and the research results are similar to the above.[15–17] Our research results show that the clinical remission rate and response rate are similar to those of local and international studies; in our study, the clinical remission rate of the patients gradually increased at the 8th, 16th and 24th weeks of treatment, which were 34 cases (60.7%), 37 cases (66.1%) and 49 cases (87.5%), respectively. The clinical response rates for the 8th, 16th, and 24th weeks were 38 (67.8%), 42 (0.75%) and 51 (91.1%), respectively. The first line treatment group achieved a clinical response and remission more quickly. Our data further confirm that ustekinumab is effective in the treatment of CD, and first line treatment is more effective than second line treatment.

However, there is a significant difference between the endoscopic response rate and endoscopic remission rate compared to existing studies. In our study, the endoscopic response rate and remission rate were extremely low at the 24th week. Our study showed that the endoscopic remission rate at the 24th week was 4% (2/50). Data from Zhongshan Sixth Hospital in China showed that the endoscopic response rate at the 16/20th week was 28.6% (4/14) and the endoscopic response rate was 78.6% (11/14).[6] A Chinese study showed that at the 24th/32th week, the endoscopic remission rate and response rate were 33.3% and 63.9%, respectively. There was no statistically significant difference in endoscopic remission rate and response rate between first line and second line usages of ustekinumab.[13] A number of local and international studies have confirmed that ustekinumab can effectively improve the endoscopic performance of CD patients, but the reported endoscopic remission rate and response rate vary greatly. Post-hoc analysis of three key Phase III studies, including UNITI-1, UNITI-2, and IM-UNITI, showed that the endoscopic response rate and remission rate of patients receiving ustekinumab treatment at the 8th week were 20.6% and 7.7%, respectively. The endoscopic response rate and remission rate at the 44th week were 17.4% and 10.9%, respectively.[18] Verstockt et al included 86 patients with CD who had previously failed treatment with TNF-α antagonists and/or vedrizumab, the endoscopic response rate was 20.5% and the remission rate was 7.1% at the 24th week of ustekinumab treatment.[19] Battat et al included a total of 62 patients with CD in the multicenter study, and the endoscopic response rate and remission rate at the 26th week of ustekinumab treatment were 58.9% and 19.6%, respectively.[20] There are many reasons for the large difference in endoscopic remission or response rate. The possible reasons are as follows: the sample size of each study is different, the time of re-examination colonoscopy is different, the first and second lines are not counted separately, the retrospective and prospective statistical differences, and the endoscopic SES-CD scoring criteria are inconsistent. Some studies used the total score of 3 points, some used the total score of 12 points, and some used other endoscopic scoring systems, which would affect the calculation of endoscopic response/response rate.

A study indicated that ustekinumab is more effective in biologic-naive patients with CD than those who were not responsive to anti-TNF treatment in the past.[12] A long-term real-world study showed that the number of previous biologics used also affects the effectiveness of ustekinumab.[21] Our study showed that the clinical response time of patients receiving first line or second line treatment with ustekinumab was different, and the response time of the first line treatment was faster than that of the second line treatment, and the first line treatment was better than the second line treatment. This conclusion is similar to previous studies and is also consistent with clinical practice. Inflammatory bowel disease brings a heavy burden to patients and families, and even society. This problem needs to be solved urgently. We may start with diagnosis, treatment, follow-up and nursing to solve the problem step by step.[22] Our study has several limitations, firstly, it is a multicenter retrospective study with a short treatment observation period of 24 weeks, which can only evaluate short-term effectiveness, and the observation period needs to be extended to evaluate long-term effectiveness. Secondly, the sample size was too small and the data were incomplete. A total of 102 cases were treated with ustekinumab, and only 56 cases were included in the final statistics. The limited sample size in this study can be attributed to several interrelated factors. Firstly, incomplete data availability significantly reduced the number of eligible cases. Despite 102 patients receiving ustekinumab treatment, nearly half (46 cases) were excluded due to missing critical information in their medical records, such as incomplete clinical assessments, endoscopic findings, or laboratory reports. Retrospective studies inherently rely on pre-existing data, and inconsistencies in documentation across multiple centers further exacerbated this issue. Secondly, strict exclusion criteria were applied to ensure homogeneity in the study population. Patients with comorbid conditions, concurrent use of other biologics or immunomodulators, or insufficient follow-up documentation were systematically excluded. While this enhanced internal validity, it concurrently narrowed

the pool of analyzable cases. Thirdly, loss to follow-up during the 24-week observation period contributed to the reduced sample size. Some patients discontinued participation due to adverse events, perceived lack of effectiveness, or personal reasons (eg, financial constraints, geographic mobility), resulting in fragmented datasets that could not be statistically reconciled. Additionally, the multicenter retrospective design introduced logistical challenges. Lastly, resource constraints, including time and funding, restricted proactive efforts to recruit additional participants or recover excluded cases. Future prospective studies should prioritize centralized data management, harmonized protocols, and extended follow-up durations to mitigate these limitations and improve statistical power.

In summary, our findings show that ustekinumab is effective in the short-term treatment of Chinese patients with CD, first line treatment is superior to and faster than second line treatment, and the effectiveness of ustekinumab on endoscopic outcomes needs to be further studied and evaluated.

Data Sharing Statement

Availability of data and materials: the data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions. All the data come from Zhu Xiuli, Xiaoli Fang, Xiaoping Niu, Song Wang.

Ethics Approval

The present study was approved by the Ethics Committee of The First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China, labeled as 2024KY090.

Informed Consent/ Patient Consent

The medical records or biological specimens used in this study were obtained from previous clinical diagnosis and treatment, and will not cause physical and mental pain to patients, affect the safety and health of patients, increase the economic burden of patients and their families, and exemption from informed consent will not adversely affect the rights and health of patients.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

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References

1. Baumgart DC, Sandborn WJ. Crohn's disease. *Lancet*. 2012;380:1590–1605. doi:10.1016/S0140-6736(12)60026-9
2. Wilson JC, Furlano RI, Jick SS, Meier CR. Inflammatory bowel disease and the risk of autoimmune diseases. *J Crohns Colitis*. 2016;10:186–193. doi:10.1093/ecco-jcc/jjv193
3. Feagan BG, Sandborn WJ, Gasink C, et al. Ustekinumab as induction and maintenance therapy for Crohn's disease. *N Engl J Med*. 2016;375:1946–1960. doi:10.1056/NEJMoa1602773
4. Hanauer SB, Sandborn WJ, Feagan BG, et al. IM-UNITI: three-year effectiveness, safety, and immunogenicity of ustekinumab treatment of Crohn′s disease. *J Crohns Colitis*. 2020;14(1):23–32. doi:10.1093/ecco-jcc/jjz110

5. Biemans VBC, van der Meulen-de Jong AE, van der Woude CJ, et al. Ustekinumab for Crohn′s disease: results of the ICC registry, a nationwide prospective observational cohort study. *J Crohns Colitis*. 2020;14(1):33–45. doi:10.1093/ecco-jcc/jjz119
6. Yao J, Song X, Yu Q, et al. Analysis of the short-term effectiveness of ustekinumab for intractable Crohn′s disease: a multicenter retrospective observational study. *Chin J Inflamm Bowel Dis*. 2021;05(2):151–155.
7. Inflammatory Bowel Disease Group, Chinese Society of Gastroenterology, Chinese Medical Association. Chinese consensus on diagnosis and treatment in inflammatory bowel disease (2018, Beijing). *Chin J Dig*. 2018;38(5):292–311.
8. Best WR, Beckte L, Singleton JW, et al. Development of a Crohn′s disease activity index. National Cooperative Crohn′s Disease Study. *Gastroenterology*. 1976;70(3):439–444. doi:10.1016/S0016-5085(76)80163-1
9. Daperno M, D′Haens G, van Assche G, et al. Development and validation of a new, simplified endoscopic activity score for Crohn′s disease: the SES-CD. *Gastrointest Endosc*. 2004;60(4):505–512. doi:10.1016/S0016-5107(04)01878-4
10. Lichtenstein GR, Loftus EV, Isaacs KL, et al. ACG clinical guideline: management of Crohn′s disease in adults. *Am J Gastroenterol*. 2018;113 (4):481–517. doi:10.1038/ajg.2018.27
11. Iborra M, Beltrán B, Fernández-Clotet A, et al. Real-world short-term effectiveness of ustekinumab in 305 patients with Crohn′s disease: results from the ENEIDA registry. *Aliment Pharmacol Ther*. 2019;50(3):278–288. doi:10.1111/apt.15371
12. Cao Q, Chen C, Gao X, et al. Real-world short-term effectiveness of ustekinumab in Crohn's disease: results from a multicenter prospective study in China. *Inflamm Bowel Dis*. 2022:izac078.
13. Lu J, Xu X, Wang T, et al. Analysis on effectiveness and safety of ustekinumab in Crohn′s disease patients. *Chin J Inflamm Bowel Dis*. 2023;07 (1):37–42.
14. Miyazaki T, Watanabe K, Kojima K, et al. Efficacies and related issues of ustekinumab in Japanese patients with Crohn's disease: a preliminary study. *Digestion*. 2019;A1:1–7.
15. Miranda A, Gravina AG, Cuomo A, et al. effectiveness of ustekinumab in the treatment of patients with Crohn's disease with failure to previous conventional or biologic therapy: a prospective observational real-life study. *J Physiol Pharmacol*. 2021;72(4):537–543. doi:10.26402/jpp.2021.4.05
16. Mocci G, Tursi A, Scaldaferri F, et al. Long-term effectiveness and safety of ustekinumab in Crohn's disease: results from a large real-life cohort study. *J Clin Med*. 2024;13(23):7192. doi:10.3390/jcm13237192
17. Tursi A, Mocci G, Scaldaferri F, et al. Ustekinumab safety and effectiveness in patients with ulcerative colitis: results from a large real-life study. *Expert Opin Biol Ther*. 2024;24(1–2):101–109. doi:10.1080/14712598.2024.2309300
18. Rutgeerts P, Gasink C, Chan D, et al. effectiveness of ustekinumab for inducing endoscopic healing in patients with Crohn′s disease. *Gastroenterology*. 2018;155(4):1045–1058. doi:10.1053/j.gastro.2018.06.035
19. Verstockt B, Dreesen E, Noman M, et al. Ustekinumab exposure-outcome analysis in Crohn′s disease only in part explains limited endoscopic remission rates. *J Crohns Colitis*. 2019;13(7):864–872. doi:10.1093/ecco-jcc/jjz008
20. Battat R, Kopylov U, Bessissow T, et al. Association between ustekinumab trough concentrations and clinical, biomarker, and endoscopic outcomes in patients with Crohn′s disease. *Clin Gastroenterol Hepatol*. 2017;15(9):1427–1434.e2. doi:10.1016/j.cgh.2017.03.032
21. Chaparro M, Baston-Rey I, Fernández-Salgado E, et al. Long-term real-world effectiveness and safety of ustekinumab in Crohn's disease patients: the SUSTAIN Study. *Inflamm Bowel Dis*. 2022;28(11):1725–1736. doi:10.1093/ibd/izab357
22. Wang S, Dong Z, Wan X. Global, regional, and national burden of inflammatory bowel disease and its associated anemia, 1990 to 2019 and predictions to 2050: an analysis of the global burden of disease study 2019. *Autoimmun Rev*. 2023;23:103498. doi:10.1016/j.autrev.2023.103498