中国临床研究 Chin J Clin Res, April 2026, Vol.39, No.4
Cite as: Wang Y, Li Y, Shen P, Zhang GT, Qiao X. Clinical efficacy and safety of ustekinumab in biologic-naïve patients with moderate-to-severe Crohn's disease [J]. Chin J Clin Res, 2026, 39(4):513-516.
DOI: 10.13429/j.cnki.cjcr.2026.04.005

Clinical efficacy and safety of ustekinumab in biologic- naïve patients with moderate-to-severe Crohn's disease

WANG Ying*, LI Ying, SHEN Peng, ZHANG Guotao, QIAO Xiao
*Department of Pharmacy, The Affiliated Huai'an Hospital of Xuzhou Medical University, Huai'an, Jiangsu 223000, China
Corresponding author: QIAO Xiao, E-mail: wy13921431518@126.com

Abstract: Objective To evaluate the real-world clinical efficacy and safety of ustekinumab (UST) in biologic-naïve patients with moderate-to-severe Crohn's disease (CD), providing evidence-based support for clinical treatment decision. **Methods** A retrospective study was conducted on 65 biologic-naïve patients with moderate-to-severe CD treated at the Huai'an First People's Hospital and The Second People's Hospital of Huai'an between May 2023 and January 2025. All patients received standard induction therapy with UST, followed by maintenance therapy every 8 weeks, with a total follow-up period of 52 weeks. The primary endpoint was clinical remission rate at week 44 [defined as the ratio of Crohn's Disease Activity Index (CDAI) <150]. Secondary endpoints included endoscopic remission rate at week 52 [defined as the ratio of Simplified Endoscopic Score for CD (SES-CD) ⩽2], steroid-free clinical remission rate, changes in serum C-reactive protein (CRP) and faecal calprotectin (FC) levels, and adverse events. Results At baseline, the 65 patients had a CDAI of 283.0±46.0 and a SES-CD score of 10.1±3.0. By week 44 of treatment, the clinical remission rate reached 73.8%; at week 52, the endoscopic remission rate was 40.0%, and the steroid-free clinical remission rate was 63.1%. From pre-treatment to 52 weeks of treatment, serum CRP dropped from 27.3 (21.5, 31.2) mg/L to 4.7 (4.1, 8.6) mg/L (Z=6.901, P<0.01), and FC dropped from 740.0 (650.0, 930.0) μg/g to 120.0 (97.5, 205.0) μg/g (Z=7.009, P<0.01), with both differences being statistically significant. During the entire follow-up period, the overall adverse event rate was 30.8%, including 1 case (1.5%) of severe infection, and no tuberculosis or malignancy-related adverse events were observed. The treatment continuation rate was 93.8%. **Conclusion** UST can induce clinical remission and maintain long-term efficacy in biologic-naïve patients with moderate-to-severe CD, demonstrating favorable safety and high treatment persistence.

Keywords: Ustekinumab; Crohn's disease; Biologic-naïve; Endoscopic remission; Safety
Fund program: Project of Jiangsu Provincial Key Laboratory of New Drug Research and Clinical Pharmacy (KFKT-2313)

Crohn's disease (CD) is a lifelong, progressive, disabling inflammatory bowel disease. Its global incidence continues to rise, and the prevalence of CD in China has increased approximately fourfold over the past 20 years [1]. Approximately 50% of patients develop intestinal strictures, penetrating disease, or require surgery within 10 years of diagnosis, imposing a heavy social and economic burden. In patients with moderate-to-severe CD, traditional glucocorticoids and immunosuppressants achieve a remission rate of less than 50% and are associated with significant adverse effects. The advent of biologics has ushered in an era of "mucosal healing" for CD treatment; however, the choice of initial biologic directly influences subsequent sequential therapy, surgical risk, and long-term prognosis [2]. Ustekinumab (UST), which specifically binds to 40 kDa subunit of interleukin-12/interleukin-23 (IL-12/23 p40) and blocks the T helper cell (Th)1 and Th17 pathways, is recommended by international guidelines for the treatment of moderate to severe CD [3-4]. In recent years, studies have proposed UST as a first-line biologic option for moderate to severe CD [3,5]. Nevertheless, there are few real-world studies focusing on the "biologic-naïve" population. This retrospective analysis of UST clinical practice data from the Huai'an region aims to provide evidence supporting its first-line use.

1 Materials and Methods

1.1 Study Design

This was a retrospective cohort study that included 65 patients with moderate to severe CD who met the diagnostic criteria and were treated at the First People's Hospital of Huai'an and the Second People's Hospital of Huai'an between May 2023 and January 2025. The study was approved by the Ethics Committee of the Huai'an First People's Hospital (approval No. KY-2023-065-01) and the Ethics Committee of Second People's Hospital of Huai'an (approval No. HEYLL2025136).

1.2 Inclusion and Exclusion Criteria

Inclusion criteria: (1) age 18–70 years; (2) confirmed diagnosis of CD according to the *Chinese Clinical Practice Guideline on the Management of Crohn's Disease* [5]; (3) inadequate response or intolerance to conventional therapies; (4) baseline Crohn's Disease Activity Index (CDAI)≥220; (5) no prior use of any biologic agent; (6) received UST standard induction plus subcutaneous maintenance therapy; (7) follow-up of at least 52 weeks.

Exclusion criteria: active infection, tuberculosis, malignancy, pregnancy, prior use of Janus kinase (JAK) inhibitors.

1.3 Treatment Regimen

Induction period: At week 0, a single intravenous infusion of UST (Cilag AG, National Drug Approval Number SJ20170046 and SJ20200005) at the standard dose (260 mg for patients weighing ≤55 kg, 390 mg for patients weighing 55–85 kg).

Maintenance period: Starting at week 8, 90 mg subcutaneously once every 8 weeks.

1.4 Outcome Measures

Primary endpoint: Clinical remission rate at week 44 (defined as the proportion of patients with a CDAI score <150). Secondary endpoints: Endoscopic remission rate at week 52 [defined as a Simple Endoscopic Score for Crohn's Disease (SES-CD) ≤2], rate of ≥50% decrease in endoscopic score, steroid-free remission rate, changes in C-reactive protein (CRP) and faecal calprotectin (FC) levels, and occurrence of adverse events. Endoscopy was performed blindly by two senior endoscopists.

1.5 Statistical Methods

Data were processed using SPSS 26.0. Normally distributed continuous variables, non-normally distributed continuous variables, and categorical variables were described as $\bar{x} \pm s$, $M(P_{25},P_{75})$ and case(%), respectively. Paired Wilcoxon signed-rank tests were used to compare CRP and FC levels before and after treatment. The significance level was set at α=0.05 (two-tailed).

2 Results

2.1 Baseline Characteristics

Among the 65 patients, there were 37 males and 28 females. Detailed baseline data are shown in **Table 1**.

2.2 Efficacy Evaluation

As shown in **Table 2,** the clinical remission rates were 56.9% at week 8, 72.3% at week 24, 73.8% at week 44, and 72.3% at week 52. At week 52, 26 patients (40.0%) achieved endoscopic remission (SES-CD ⩽ 2), 45 patients (69.2%) achieved a ⩾ 50% reduction in endoscopic score, and 18 patients (27.7%) achieved deep remission (clinical + endoscopic). Steroid-free clinical remission at week 52 was achieved in 41 patients (63.1%).

The Wilcoxon signed-rank test was used to compare CRP and FC levels before treatment and at week 52. The results showed that CRP decreased from a baseline of 27.3 (21.5, 31.2) mg/L to 4.7 (4.1, 8.6) mg/L (Z=6.901, P<0.01), and FC decreased from 740.0 (650.0, 930.0) μg/g to 120.0 (97.5, 205.0) μg/g (Z=7.009, P<0.01). The differences were statistically significant (see **Table 3**).

2.3 Safety Evaluation

Among the 65 patients, 20 (30.8%) experienced adverse events, including mild-to-moderate events in 19 patients (29.2%; gastrointestinal reactions, fatigue, etc.) and severe infection (pulmonary infection) in 1 patient (1.5%), which was cured after anti-infective treatment. There was one case of herpes zoster (localized rash, resolved after symptomatic treatment). No tuberculosis reactivation, malignancy, or death occurred. One patient (1.5%) discontinued treatment due to non-serious adverse events. The treatment persistence rate for completing 52 weeks of therapy was 93.8% (61/65).

Tab.1 Baseline characteristics of 65 patients with CD

Indicators	Result
Male [case(%)]	37(56.9)
Age (years, $\bar{x} \pm s$)	32.1±8.5
Course of disease [years, $M(P_{25},P_{75})$]	3.7(2.3,4.5)
Disease site [case(%)]	
Ileocolic type	42(64.6)
Ileal type	13(20.0)
Colon type	10(15.4)
Perianal lesions [case(%)]	30(46.2)
Fistula [case(%)]	9(13.8)
Baseline CDAI (point, $\bar{x} \pm s$)	283.0±46.0
Baseline SES-CD (point, $\bar{x} \pm s$)	10.1±3.0
Baseline serum CRP [mg/L, $M(P_{25},P_{75})$]	27.3(21.5,31.2)
Baseline FC [μg/g, $M(P_{25},P_{75})$]	740.0(650.0,930.0)
Previous hormone use [case(%)]	65(100.0)
Previous use of immunosuppressants [case(%)]	50(76.9)

Tab.2 Changes in main efficacy indicators of 65 patients with CD over treatment time [case(%)]

Efficacy endpoint	Week 8	Week 24	Week 44	Week 52
Clinical remission rate	37(56.9)	47(72.3)	48(73.8)	47(72.3)
Endoscopic remission rate	-	-	-	26(40.0)
reduction rate in endoscopic score ≥50%	-	-	-	45(69.2)
Depth remission rate (clinical + endoscopic)	-	-	-	18(27.7)
Steroid-free clinical remission rate	-	-	-	41(63.1)

Tab.3 Comparison of CRP and FC levels in 65 patients with CD before and after UST treatment [$M(P_{25},P_{75})$]

Indicator	Baseline	Week 52	Z value	P value
CRP(mg/L)	27.3(21.5,31.2)	4.7(4.1,8.6)	6.901	<0.001
FC(μg/g)	740.0(650.0,930.0)	120.0(97.5,205.0)	7.009	<0.001

3 Discussion

This study completed a full 52-week follow-up of UST treatment in a local population of biologic-naïve patients with moderate to severe CD. The results showed a clinical remission rate of 73.8% at week 44 and an endoscopic remission rate of 40.0% at week 52, which are highly consistent with data from the biologic-naïve subgroup of the global phase 3 UNITI-2 trial [4,6], suggesting that the efficacy of UST in Chinese patients does not differ significantly from that in Western populations. Notably, the steroid-free remission rate in this study was 63.1%, significantly higher than the 32% reported in the anti-tumor necrosis factor (TNF) first-line study SUCCESS [7]. This indicates that using UST as a first-line biologic facilitates rapid withdrawal of glucocorticoids and reduces the risk of long-term complications such as osteoporosis and infections.

Mucosal healing is a hard endpoint in the treatment of CD and another form of inflammatory bowel disease, ulcerative colitis [8-9], and is negatively correlated with hospitalization rates, surgery rates, and long-term disability [1,9]. Although the 40.0% endoscopic remission rate in this study is lower than that of some head-to-head anti-TNF data (46%), considering the high baseline inflammatory burden of these patients, their

biologic-naïve status, and the one-year follow-up, the results are close to the highest first-line level. The ECCO guidelines recommend ustekinumab as an effective treatment for inducing and maintaining remission in CD, with efficacy comparable to adalimumab, and it can be used as a first-line treatment for moderate to severe CD [11]. For biologic-naïve CD patients, there is no statistically significant difference in endoscopic or transmural remission rates between infliximab and UST, and their efficacy is similar [12].

Drug persistence is a marker of limited efficacy and poor tolerability. Previous studies have shown that UST has the highest persistence rate among CD patients, with a rate of 77.5% for continued use beyond one year, which is 15% higher than that of anti-TNF agents [13]. The 93.8% one-year persistence rate in this study reflects the favourable efficacy and safety of UST. Economic cost is another important factor affecting drug persistence. Studies have found that medical insurance reimbursement policies significantly impact UST persistence. Increasing outpatient reimbursement rates, encouraging outpatient treatment, reducing hospitalisation costs, and improving UST treatment persistence can help control disease and improve quality of life [14].

The overall adverse event rate in this study was 30.8%, with only 1.5% severe infections. No tuberculosis reactivation, lymphoma, or opportunistic infections were observed, indicating generally good safety. A study had shown that the main adverse events of UST treatment for CD include opportunistic infections, allergies, and liver function impairment, with an incidence significantly lower than that of upadacitinib [15]. Previous report had indicated that UST treatment for CD patients with latent tuberculosis or inactive hepatitis B virus infection does not significantly increase the risk of tuberculosis or HBV reactivation [16]. In this study, following routine clinical practice, patients were screened for tuberculosis and HBV infection before UST treatment, and blood counts, liver and kidney function were checked at least every 8 weeks during follow-up, with annual chest imaging to ensure medication safety.

Advantages of this study: (1) completed a 52-week follow-up; (2) endoscopic assessments were performed by two blinded physicians, κ=0.83. Limitations of this study: (1) single-center retrospective design with potential selection bias; (2) small sample size, insufficient statistical power for rare adverse events; (3) no control group. Future work will continue to compare the efficacy and safety of UST with other novel biologics and small-molecule drugs, with follow-up extended to 3 years to observe long-term outcomes such as intestinal complications and surgery.

In biologic-naïve patients with moderate to severe CD, UST can rapidly and sustainably induce clinical and endoscopic remission, has a high steroid-free remission rate, and exhibits a safety profile superior to that of traditional anti-TNF agents. Novel IL-23p19 inhibitors are gradually entering clinical practice. Guselkumab [17], risankizumab [18], and mirikizumab [19] have all shown favorable clinical efficacy. In head-to-head trials against UST in CD patients who had failed conventional therapy or were intolerant to biologics, these agents met non-inferiority criteria, with some showing superiority for certain efficacy endpoints, highlighting the therapeutic potential of IL-23 inhibitors [20]. In the future, the integration of precision medicine and real-world data will certainly propel CD treatment in China to a new stage.

In conclusion, for biologic-naïve patients with moderate to severe Crohn's disease, UST can rapidly and sustainably induce clinical and endoscopic remission, provides a high steroid-free remission rate, and has a good safety profile, making it an excellent first-line biologic option for CD.

Conflict of Interest None

References

[1] Hracs L, Windsor JW, Gorospe J, et al. Global evolution of inflammatory bowel disease across epidemiologic stages[J]. Nature, 2025, 642(8067): 458-466.

[2] Dolinger M, Torres J, Vermeire S. Crohn's disease[J]. Lancet, 2024, 403(10432): 1177-1191.

[3] 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].J Clin Med,2024,13(23):7192.

[4] Feagan BG, Sandborn WJ, Gasink C, et al. Ustekinumab as induction and maintenance therapy for Crohn's disease[J]. N Engl J Med, 2016, 375(20): 1946-1960.

[5] Inflammatory Bowel Disease Group of Chinese Society of Gastroenterology of Chinese Medical Association, Inflammatory Bowel Disease Quality Control Center of China. Chinese clinical practice guideline on the management of Crohn's disease (2023, Guangzhou) [J]. Chin J Gastroenterol, 2024, 29(4): 200-235. **[In Chinese]**

[6] Hanauer SB, Sandborn WJ, Feagan BG, et al. IM-UNITI: three-year efficacy, safety, and immunogenicity of ustekinumab treatment of Crohn's disease[J]. J Crohn's Colitis, 2020, 14(1): 23-32.

[7] Johnson AM, Barsky M, Ahmed W, et al. The real-world effectiveness and safety of ustekinumab in the treatment of Crohn's disease: results from the SUCCESS consortium[J]. Am J Gastroenterol, 2023, 118(2): 317-328.

[8] Scharl MM, Christensen B, Bressler B, et al. Tu1821 real-world clinical effectiveness and safety of vedolizumab and ustekinumab in biologic-naïve patients with Crohn's disease by disease location: results from the evolve expansion study[J]. Gastroenterology, 2024, 166(5): S-1422.

[9] Li Y, Yang G, Zhang GT. Efficacy and safety of vedolizumab in the treatment of ulcerative colitis[J]. Chin J Clin Res, 2025, 38(11): 1726-1730. **[In Chinese]**

[10] Lichtenstein GR, Loftus EV, Afzali A, et al. ACG clinical guideline: management of Crohn's disease in adults[J]. Am J Gastroenterol, 2025, 120(6): 1225-1264.

[11] Gordon H, Minozzi S, Kopylov U, et al. ECCO guidelines on therapeutics in Crohn's disease: medical treatment[J]. J Crohn's Colitis, 2024, 18(10): 1531-1555.

[12] Huang ZC, Diao N, Guo Q, et al. Comparative effectiveness of infliximab vs ustekinumab for endoscopic and transmural remission in biologic Naïve Crohn's disease[J]. Clin Gastroenterol Hepatol, 2026, 24(1): 172-180.

[13] Yiu TH, Ko Y, Pudipeddi A, et al. Meta-analysis: Persistence of advanced therapies in the treatment of inflammatory bowel disease[J]. Aliment Pharmacol Ther, 2024, 59(11): 1312-1334.

[14] Shi JH, Pan YP, Gao Y, et al. Balanced inpatient and outpatient reimbursement versus hospitalization-favored insurance reduces Crohn disease costs and improves biologic drug persistence: a mediation analysis[J]. Medicine, 2025, 104(37): e44475.

[15] Xie D, Wang Y, Lin HJ, et al. Pharmacovigilance signal mining and analysis of ustekinumab versus upadacitinib for inflammatory bowel disease based on the FAERS database[J]. Med J Peking Union Med Coll Hosp, 2025, 16(6): 1376-1383. **[In Chinese]**

[16] Liu RB, Li ZL, Ye LN, et al. Risk of tuberculosis and hepatitis B reactivation in patients with Crohn's disease on ustekinumab: a nationwide real-world study[J]. Inflamm Bowel Dis, 2024, 30(1): 45-52.

[17] Sandborn WJ, D'Haens GR, Reinisch W, et al. Guselkumab for the treatment of Crohn's disease: induction results from the phase 2 GALAXI-1 study[J]. Gastroenterology, 2022, 162(6): 1650-1664.e8.

[18] D'Haens G, Panaccione R, Baert F, et al. Risankizumab as induction therapy for Crohn's disease: results from the phase 3 ADVANCE and MOTIVATE induction trials[J]. Lancet, 2022, 399(10340): 2015-2030.

[19] Ferrante M, D'Haens G, Jairath V, et al. Efficacy and safety of mirikizumab in patients with moderately-to-severely active Crohn's disease: a phase 3, multicentre, randomised, double-blind, placebo-controlled and active-controlled, treat-through study [J]. Lancet, 2024, 404(10470): 2423-2436.

[20] Sun YJ, Sun XL, Zhang ZZ, et al. The prospect of interleukin-23p19 inhibitors in precision treatment of Crohn's disease: mechanisms and clinical evidence[J]. Chin J Inflamm Bowel Dis, 2025, 9(5): 390-396. **[In Chinese]**

Submission received: 2025-12-16 / **Revised:** 2026-01-28

·炎症性肠病专题·论著·

乌司奴单抗治疗生物制剂初治的中重度克罗恩病的临床有效性和安全性

王英[1]， 李影[1]， 沈鹏[2]， 张国桃[1]， 乔晓[3]

1. 徐州医科大学附属淮安医院药学部，江苏 淮安 223000；2. 淮安市第一人民医院消化内科，江苏 淮安 223000；
3. 徐州医科大学附属淮安医院消化内科，江苏 淮安 223000

摘要：目的 评估乌司奴单抗(UST)用于生物制剂初治中重度克罗恩病(CD)患者的真实世界临床疗效及安全性，为临床治疗方案选择提供循证依据。**方法** 回顾性收集2023年5月至2025年1月就诊于淮安市第一人民医院和淮安市第二人民医院的生物制剂初治中重度CD患者65例，所有患者均接受UST标准诱导治疗，后续采用每8周1次的维持治疗方案，全程随访52周。主要研究终点为第44周的临床缓解率[定义为克罗恩病活动指数(CDAI)<150分的比率]；次要研究终点包括第52周的内镜缓解率[定义为克罗恩病简化内镜评分(SES-CD)≤2分的比率]、无激素临床缓解率、血清C反应蛋白(CRP)和粪便钙卫蛋白(FC)水平变化及不良事件。**结果** 65例患者基线时CDAI为(283.0±46.0)分，SES-CD评分为(10.1±3.0)分。治疗至第44周，临床缓解率达73.8%；第52周时，内镜缓解率为40.0%，无激素临床缓解率为63.1%；血清CRP由基线时的27.3(21.5，31.2)mg/L降至52周的4.7(4.1，8.6)mg/L(Z=6.901，P<0.01)，FC由740.0(650.0，930.0)μg/g降至120.0(97.5，205.0)μg/g(Z=7.009，P<0.01)，差异有统计学意义。整个随访期间，不良事件总发生率为30.8%，其中重度感染1例(1.5%)，未发生结核感染及恶性肿瘤相关不良事件；患者治疗持续率达93.8%。**结论** UST用于生物制剂初治的中重度CD，可诱导临床缓解并维持长期疗效，安全性良好且治疗持续性佳。

关键词： 乌司奴单抗；克罗恩病；生物制剂初治；内镜缓解；安全性

中图分类号： R574.1 **文献标识码：** A **文章编号：** 1674-8182(2026)04-0513-04

Clinical efficacy and safety of ustekinumab in biologic-naïve patients with moderate-to-severe Crohn's disease

WANG Ying*, LI Ying, SHEN Peng, ZHANG Guotao, QIAO Xiao

*Department of Pharmacy, The Affiliated Huai'an Hospital of Xuzhou Medical University, Huai'an, Jiangsu 223000, China

Corresponding author: QIAO Xiao, E-mail: wy13921431518@126.com

Abstract: Objective To evaluate the real-world clinical efficacy and safety of ustekinumab (UST) in biologic-naïve patients with moderate-to-severe Crohn's disease (CD), providing evidence-based support for clinical treatment decision. **Methods** A retrospective study was conducted on 65 biologic-naïve patients with moderate-to-severe CD treated at the Huai'an First People's Hospital and The Second People's Hospital of Huai'an between May 2023 and January 2025. All patients received standard induction therapy with UST, followed by maintenance therapy every 8 weeks, with a total follow-up period of 52 weeks. The primary endpoint was clinical remission rate at week 44[defined as the ratio of Crohn's Disease Activity Index (CDAI)<150]. Secondary endpoints included endoscopic remission rate at week 52 [defined as the ratio of Simplified Endoscopic Score for CD (SES-CD) ≤2], steroid-free clinical remission rate, changes in serum C-reactive protein (CRP) and faecal calprotectin (FC) levels, and adverse events. **Results** At baseline, the 65 patients had a CDAI of 283.0±46.0 and a SES-CD score of 10.1±3.0. By week 44 of treatment, the clinical remission rate reached 73.8%; at week 52, the endoscopic remission rate was 40.0%, and the steroid-free

DOI: 10.13429/j.cnki.cjcr.2026.04.005

基金项目： 江苏省新药研究与临床药学重点实验室课题(KFKT-2313)

通信作者： 乔晓，E-mail: wy13921431518@126.com

出版日期： 2026-04-20

QR code for English version

clinical remission rate was 63.1%. From pre-treatment to 52 weeks of treatment, serum CRP dropped from 27.3 (21.5, 31.2) mg/L to 4.7 (4.1, 8.6) mg/L (Z=6.901, P <0.01), and FC dropped from 740.0 (650.0, 930.0) μg/g to 120.0 (97.5, 205.0) μg/g (Z=7.009, P<0.01), with both differences being statistically significant. During the entire follow-up period, the overall adverse event rate was 30.8%, including 1 case of severe infection (1.5%), and no tuberculosis or malignancy-related adverse events were observed. The treatment continuation rate was 93.8%. **Conclusion** UST can induce clinical remission and maintain long-term efficacy in biologic-naïve patients with moderate-to-severe CD, demonstrating favorable safety and high treatment persistence.

Keywords: Ustekinumab; Crohn's disease; Biologic-naïve; Endoscopic remission; Safety

Fund program: Project of Jiangsu Provincial Key Laboratory of New Drug Research and Clinical Pharmacy (KFKT-2313)

克罗恩病(Crohn's disease,CD)是一种终身、进行性、致残性肠道炎症性疾病,全球发病率持续攀升,我国近20年患病率增长约4倍[1]。约50%患者在确诊10年内出现肠道狭窄、穿透或手术,社会与经济负担沉重。中重度活动期患者传统糖皮质激素及免疫抑制剂缓解率不足50%,且副作用显著。生物制剂的问世使CD治疗进入"黏膜愈合"时代,但首次生物制剂的选择直接影响后续药物序贯治疗、手术风险及长期预后[2]。乌司奴单抗(ustekinumab,UST)通过特异性结合白细胞介素-12/白细胞介素-23的40 kD亚基(40 kD subunit of interleukin-12/interleukin-23,IL-12/23p40),阻断辅助性T细胞(T helper cell,Th)1型和17型(Th17)通路,已被国际指南推荐用于治疗中重度CD[3-4]。近年来,国内外研究提出可将UST列为中重度CD一线生物制剂选择[3, 5]。然而,针对"生物制剂初治"人群的真实世界研究报道较少。本研究回顾性分析淮安地区UST临床实践数据,旨在为其一线应用提供证据支持。

1　资料与方法

1.1　*研究设计*　本项目为回顾性队列研究,纳入2023年5月至2025年1月就诊于淮安市第一人民医院和第二人民医院符合诊断标准的中重度CD患者65例。研究通过淮安市第一人民医院伦理委员会(批件号:KY-2023-065-01)和淮安市第二人民医院伦理委员会(批件号:HEYLL2025136)审批。

1.2　*纳入与排除标准*　纳入标准:(1)年龄18~70岁;(2)确诊CD,诊断标准参考《中国克罗恩病诊治指南》[5];(3)对传统疗法反应不佳或不能耐受;(4)基线克罗恩病活动指数(Crohn's disease activity index,CDAI)≥220分;(5)未使用过任何生物制剂;(6)接受UST标准诱导+皮下维持治疗;(7)随访≥52周。排除标准:活动性感染、结核、恶性肿瘤、妊娠、既往应用Janus激酶(Janus kinase,JAK)抑制剂。

1.3　*治疗方案*　诱导期:第0周UST(乌司奴单抗Cilag AG,国药准字SJ20170046和国药准字SJ20200005)标准剂量(患者体质量55 kg以内UST为260 mg,55~85 kg UST为390 mg)静脉输注1次;维持期:第8周起90 mg皮下注射,每8周1次。

1.4　*观察指标*　主要终点:治疗第44周临床缓解率(定义为CDAI<150分的比率)。次要终点:治疗第52周内镜缓解率[定义为克罗恩病简化内镜评分(Simple Endoscopic Score for Crohn's Disease, SES-CD)≤2分的比率],≥50%内镜评分下降率,无激素缓解率,C反应蛋白(C-reactive protein,CRP)、粪便钙卫蛋白(faecal calprotectin, FC)水平变化及不良事件发生情况。内镜评估由2名高年资内镜医师独立盲法完成。

1.5　*统计学方法*　采用SPSS 26.0软件处理数据。符合正态分布的计量资料、不符合正态分布的计量资料及计数资料分别以$\bar{x}\pm s$、$M(P_{25}, P_{75})$和例(%)进行描述。CRP和FC在治疗前后的数值比较采用配对资料的Wilcoxon符号秩检验。检验水准α=0.05,双侧检验。

2　结　果

2.1　*基线特征*　65例患者中男37例,女28例,具体基线资料见表1。

2.2　*疗效评价*　表2可见,治疗第8周临床缓解率56.9%,第24周72.3%,第44周73.8%,第52周72.3%。第52周内镜缓解(SES-CD≤2分)26例(40.0%),≥50%内镜评分下降45例(69.2%)。深度缓解(临床+内镜)18例(27.7%)。第52周无激素临床缓解41例(63.1%)。

采用Wilcoxon符号秩检验比较治疗前和治疗52周的CRP和FC水平,结果示,CRP由基线27.3(21.5,31.2)mg/L降至4.7(4.1,8.6)mg/L(Z=6.901,P<0.01),FC由740.0(650.0,930.0)μg/g降至120.0(97.5,205.0)μg/g(Z=7.009,P<0.01),差异有统计学意义。见表3。

2.3　*安全性评价*　65例中20例(30.8%)出现不良反

应，包括轻-中度19例（29.2%，胃肠道反应、乏力等），重度感染1例（1.5%，肺部感染），经抗感染治疗后治愈。其中带状疱疹1例（局部皮疹，对症处理后缓解）。无结核激活、无恶性肿瘤及死亡发生。因非严重不良反应停药1例（1.5%）。完成52周治疗的治疗持续率93.8%（61/65）。

表1 65例CD患者基线特征

Tab.1 Baseline characteristics of 65 patients with CD

项目		结果	项目	结果
男[例(%)]		37(56.9)	瘘管[例(%)]	9(13.8)
年龄(岁，$\bar{x}\pm s$)		32.1±8.5	基线CDAI(分，$\bar{x}\pm s$)	283.0±46.0
病程[年，$M(P_{25},P_{75})$]		3.7(2.3,4.5)	基线SES-CD(分，$\bar{x}\pm s$)	10.1±3.0
疾病部位[例(%)]	回结肠型	42(64.6)	基线血清CRP[mg/L，$M(P_{25},P_{75})$]	27.3(21.5,31.2)
	回肠型	13(20.0)	基线FC[μg/g，$M(P_{25},P_{75})$]	740.0(650.0,930.0)
	结肠型	10(15.4)	既往激素使用[例(%)]	65(100.0)
肛周病变[例(%)]		30(46.2)	既往免疫抑制剂使用[例(%)]	50(76.9)

表2 65例CD患者主要疗效指标随治疗时间变化 [例(%)]

Tab.2 Changes in main efficacy indicators of 65 patients with CD over treatment time [case(%)]

疗效指标	第8周	第24周	第44周	第52周
临床缓解率(CDAI<150分)	37(56.9)	47(72.3)	48(73.8)	47(72.3)
内镜缓解率(SES-CD≤2分)	-	-	-	26(40.0)
≥50%内镜评分下降率	-	-	-	45(69.2)
深度缓解率(临床+内镜)	-	-	-	18(27.7)
无激素临床缓解率	-	-	-	41(63.1)

表3 65例CD患者UST治疗前后CRP和FC水平比较 [$M(P_{25},P_{75})$]

Tab.3 Comparison of CRP and FC levels in 65 patients with CD before and after UST treatment [$M(P_{25},P_{75})$]

指标	基线	治疗52周	Z值	P值
CRP(mg/L)	27.3(21.5,31.2)	4.7(4.1,8.6)	6.901	<0.001
FC(μg/g)	740.0(650.0,930.0)	120.0(97.5,205.0)	7.009	<0.001

3 讨 论

本研究在本地区生物制剂初治的中重度CD人群中完成UST治疗52周完整随访。结果显示，第44周临床缓解率为73.8%，第52周内镜缓解率为40.0%，与全球Ⅲ期UNITI-2试验的初治亚组的数据高度吻合[4,6]，提示UST在我国患者中的疗效与欧美人群无显著差异。值得注意的是，本研究无激素缓解率达63.1%，显著高于抗肿瘤坏死因子（tumor necrosis factor，TNF）一线研究SUCCESS的32%[7]。这表明UST作为一线生物制剂有利于快速撤离糖皮质激素，降低骨质疏松、感染等长期并发症风险。

黏膜愈合是CD以及炎症性肠病另一类型——溃疡性结肠炎治疗的硬终点[8-9]，与住院率、手术率及长期残疾呈负相关[1,9]。本研究40.0%的内镜缓解率虽低于部分抗TNF头对头数据（46%），但考虑本组患者基线炎症负荷高、未使用过生物制剂、随访仅52周，结果已接近一线最高水平。ECCO指南推荐乌司奴单抗作为CD的诱导和维持缓解的有效治疗药物，疗效与阿达木相当，可作为中重度CD的一线治疗方案[11]。对于生物制剂初治的CD患者，接受英夫利西单抗或UST治疗后的内镜缓解率和透壁缓解率差异均无统计学意义，二者的疗效相似[12]。

药物治疗的持续率是反映疗效和药物耐受性的一个标志。既往研究显示，在CD患者中，UST使用的持续率最高，坚持使用1年以上的比率为77.5%，比抗TNF药物高15%[13]。本研究93.8%的1年持续率反映了UST的良好疗效和安全性。经济成本是影响药物治疗的持续率的另一个重要问题。研究发现，医保报销政策对于UST的持续率有较大的影响。提高门诊报销比例，鼓励门诊治疗，降低住院费用，提高UST治疗的持续性有助于控制病情，提高生活质量[14]。

本研究总体不良事件发生率为30.8%，重度感染仅1.5%，未见结核激活、淋巴瘤或机会性感染，总体安全性良好。研究发现UST治疗CD的主要不良事件包括机会性感染、过敏、影响肝功能等，发生率显著低于乌帕替尼[15]。既往报道UST治疗CD伴潜伏性结核或非活动性乙型肝炎病毒感染者，其结核或乙型肝炎病毒再激活风险未明显增加[16]。本研究按照诊疗常规，在UST治疗前筛查有无结核与乙型肝炎病毒感染，并在随访期间至少每8周查1次血常规、肝肾功能，每年复查1次肺部影像，以确保用药安全。

本研究优势在于：（1）52周完整随访；（2）内镜评估由两名盲法医师完成，κ=0.83。局限性在于：（1）样本量较小，罕见不良反应统计效能不足；（2）未设置对照组。后续将继续关注UST与其他新型生物制剂和小分子药物的疗效和安全性的比较数据，并延长随访至3年，以观察远期肠道并发症和手术率等

预后情况。在生物制剂初治的中重度CD患者中，UST可快速、持续诱导临床-内镜缓解，无激素缓解率高，安全性优于传统抗TNF药物。目前，新型药物IL-23 p19抑制剂已逐渐进入临床。古塞奇尤单抗[17]、利生奇珠单抗[18]、米吉珠单抗[19]都显示出良好的临床疗效。在与UST的对照试验中，对传统治疗失败或生物制剂不耐受的CD患者均达到非劣效性标准，部分疗效终点呈现优势，凸显IL-23抑制剂的治疗潜力[20]。未来，通过精准医学与真实世界数据融合，必将推动我国CD治疗迈入新阶段。

综上所述，对于生物制剂初治的中重度克罗恩病患者，UST可快速、持续诱导临床-内镜缓解，无激素缓解率高，安全性良好，可作为CD一线生物制剂优选方案。

利益冲突　无

参考文献

[1] Lindsay Hracs J, Windsor JW, Gorospe J, et al. Global evolution of inflammatory bowel disease across epidemiologic stages[J]. Nature, 2025, 642(8067): 458-466.

[2] Dolinger M, Torres J, Vermeire S. Crohn's disease[J]. Lancet, 2024, 403(10432):1177-1191.

[3] 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]. J Clin Med, 2024, 13(23):7192.

[4] Feagan BG, Sandborn WJ, Gasink C, et al. Ustekinumab as induction and maintenance therapy for Crohn's disease[J]. N Engl J Med, 2016, 375(20):1946-1960.

[5] 中华医学会消化病学分会炎症性肠病学组，中国炎症性肠病诊疗质量控制评估中心. 中国克罗恩病诊治指南(2023年·广州)[J]. 胃肠病学, 2024, 29(4): 200-235.

[6] Hanauer SB, Sandborn WJ, Feagan BG, et al. IM-UNITI: three-year efficacy, safety, and immunogenicity of ustekinumab treatment of Crohn's disease[J]. J Crohns Colitis, 2020, 14(1): 23-32.

[7] Johnson AM, Barsky M, Ahmed W, et al. The real-world effectiveness and safety of ustekinumab in the treatment of Crohn's disease: results from the SUCCESS consortium[J]. Am J Gastroenterol, 2023, 118(2):317-328.

[8] Scharl M, Christensen B, Bressler B, et al. Real-world clinical effectiveness and safety of vedolizumab and ustekinumab in biologic-naive patients with Crohn's disease by disease location: results from the EVOLVE expansion study[J/OL]. J Clin Gastroenterol, 2025. (2025-06-20)[2025-12-10].https://pubmed.ncbi.nlm.nih.gov/40554515/.

[9] 李影，杨姚，张国桃. 维得利珠单抗治疗溃疡性结肠炎的疗效及安全性评价[J]. 中国临床研究，2025，38(11)：1726-1730.

[10] Lichtenstein GR, Loftus EV, Afzali A, et al. ACG clinical guideline: management of Crohn's disease in adults[J]. Am J Gastroenterol, 2025, 120(6):1225-1264.

[11] Gordon H, Minozzi S, Kopylov U, et al. ECCO guidelines on therapeutics in Crohn's disease: medical treatment[J]. J Crohns Colitis, 2024, 18(10):1531-1555.

[12] Huang ZC, Diao N, Guo Q, et al. Comparative effectiveness of infliximab vs ustekinumab for endoscopic and transmural remission in biologic Naïve Crohn's disease[J]. Clin Gastroenterol Hepatol, 2026, 24(1):172-180.

[13] Yiu TH, Ko Y, Pudipeddi A, et al. Meta-analysis: persistence of advanced therapies in the treatment of inflammatory bowel disease[J]. Aliment Pharmacol Ther, 2024, 59(11):1312-1334.

[14] Shi JH, Pan YP, Gao Y, et al. Balanced inpatient and outpatient reimbursement versus hospitalization-favored insurance reduces Crohn disease costs and improves biologic drug persistence: a mediation analysis[J]. Medicine, 2025, 104(37):e44475.

[15] 谢栋，王煜，林浩佳，等. 乌司奴单抗与乌帕替尼治疗炎症性肠病的药物不良事件分析：基于FAERS数据库的药物警戒信号挖掘[J]. 协和医学杂志, 2025, 16(6):1376-1383.

[16] Liu RB, Li ZL, Ye LN, et al. Risk of tuberculosis and hepatitis B reactivation in patients with Crohn's disease on ustekinumab: a nationwide real-world study[J]. Inflamm Bowel Dis, 2024, 30(1): 45-52.

[17] Sandborn WJ, D'Haens GR, Reinisch W, et al. Guselkumab for the treatment of Crohn's disease: induction results from the phase 2 GALAXI-1 study[J]. Gastroenterology, 2022, 162(6): 1650-1664.e8.

[18] D'Haens G, Panaccione R, Baert F, et al. Risankizumab as induction therapy for Crohn's disease: results from the phase 3 ADVANCE and MOTIVATE induction trials[J]. Lancet, 2022, 399(10340): 2015-2030.

[19] Ferrante M, D'Haens G, Jairath V, et al. Efficacy and safety of mirikizumab in patients with moderately-to-severely active Crohn's disease: a phase 3, multicentre, randomised, double-blind, placebo-controlled and active-controlled, treat-through study[J]. Lancet, 2024, 404(10470):2423-2436.

[20] 孙宇静，孙薛亮，张兆征，等. 白细胞介素-23p19抑制剂精准治疗克罗恩病的前景：机制与临床证据[J]. 中华炎性肠病杂志(中英文), 2025, 9(5):390-396.

收稿日期：2025-12-16　**修回日期**：2026-01-28　**编辑**：石嘉莹