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Efficacy and safety of ustekinumab in Russian patients with moderately to severely active ulcerative colitis: a subanalysis of global phase 3 induction and maintenance studies (UNIFI) up to 3 years

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ABSTRACT *AIM: to evaluate efficacy and safety of ustekinumab in Russian patients with ulcerative colitis in UNIFI study.*
PATIENTS AND METHODS: the UNIFI program (CNTO1275UC03001) consisted of two randomized placebo-controlled trials: an 8-week induction study and a 44-week maintenance study and long-term period. This analysis included patients from 14 Russian centers.
RESULTS: the induction study of the UNIFI program enrolled 74 patients from Russia, 89.2% patients (n = 66) were bionaive. The paper presents the results of bionaive patients. Sixty-six are included in the induction phase: 18 received ustekinumab 130 mg IV, 25 received ustekinumab 6 mg/kg IV, and 23 received a placebo. At week 8 in the groups of patients treated with ustekinumab at doses of 6 mg/kg and 130 mg, clinical remission was achieved in 24.0% and 16.7%, respectively, in the placebo group, the rate was 17.4%. The proportion of patients with clinical responses at week 8 was 68.0%, 50.0% and 39.1% in the ustekinumab 6 mg/kg, 130 mg and placebo groups, respectively. Mucosal healing at week 8 was achieved in 48.0% in the ustekinumab 6 mg/kg group, in 33.3% of patients in the ustekinumab 130 mg group, and in 21.7% of patients in the placebo group. Histoendoscopic mucosal healing at week 8 developed in 27.8% of patients in the ustekinumab 130 mg group, in 24.0% of patients in the ustekinumab 6 mg/kg group, and in 21.7% of patients in the placebo group. Forty bionaive patients were re-randomized for further participation in the maintenance phase: 13 patients received ustekinumab 90 mg subcutaneously every 12 weeks, 12 received ustekinumab every 8 weeks, and 15 received a placebo. At week 44, clinical remission was achieved in 46.2% of ustekinumab every 12 weeks, 75.0% of ustekinumab every 8 weeks (p = 0.054 compared with placebo), and 33.3% of placebo. Mucosal healing achieved in 46.2% of patients in the ustekinumab once every 12 weeks group, in 75.0% of patients in the ustekinumab once every 8 weeks group (p = 0.054 compared with. placebo), and in 33.3% of patients in the placebo group. Histoendoscopic mucosal healing achieved in 46.2% of patients in the ustekinumab once every 12 weeks group, while in the ustekinumab once every 8 weeks group, the percentage of such patients was 75.0% (p = 0.021 compared with placebo) and in the placebo group — 26.7%. Symptomatic remission at week 152 developed in 83.3% in the ustekinumab every 12 weeks group, 81.8% in the ustekinumab every 8 weeks group. In the induction phase decrease of CRP and FCP median levels detected in patients treated with ustekinumab, in the maintenance phase, median levels of laboratory inflammatory markers after induction were sustained by ustekinumab treatment. The rate of steroid-free symptomatic remission at week 152 was consistent with the rate of symptomatic remission. The safety profile of ustekinumab was generally consistent with placebo during all follow up period.
CONCLUSION: subanalysis confirmed short- and long-term efficacy and safety in Russian patients with moderate to severe active ulcerative colitis. The results of subanalysis are consistent with previously obtained data in the population of patients participating in the global UNIFI program.

KEYWORDS: *ulcerative colitis, ustekinumab, biologic therapy, genetically engineered biological agents, steroid-free remission*

CONFLICT OF INTEREST: *the authors declare no conflict of interest*

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INTRODUCTION

Ulcerative colitis (UC) is a chronic disease affecting the colon that is characterized by immune inflammation of the intestinal mucosa and usually requires life-long therapy due to its chronic, continuous, or relapsing nature [1–3].

To date, data on the incidence of ulcerative colitis in the Russian Federation are limited. Single epidemiologic studies indicate that the incidence of ulcerative colitis in Russia is 19.3–29.8 cases per 100,000 persons [4]. In real clinical practice, Russian patients with IBD, particularly ulcerative colitis, tend to have a late diagnosis (with the average time to diagnosis of 1.5 years) and initiate treatment, including biologic agents, late in the course of the disease. Moreover, Russian population demonstrates the prevalence of moderately severe and severe forms of ulcerative colitis as well as a high mortality rate [5].

More severe course of ulcerative colitis in Russian patients is evidenced by the data of the international multicenter retrospective and prospective non-interventional observational study INTENT (NCT03532932), which had been conducted in Russia, Belarus and Kazakhstan. According to the study 27,1% of patients with ulcerative colitis had a chronic, continuous disease (without periods of remission lasting for more than 6 months),frequency of complicated forms was 12.9%.[6,7].

Treatment of ulcerative colitis is aimed primarily at achieving and sustaining remission after glucocorticoid withdrawal, preventing UC complications, avoiding surgical intervention. Russian and international guidelines recommend that patients with active, moderate-to-severe ulcerative colitis and inadequate response or intolerability to conventional treatments are prescribed biologic agents [1,2].

When initiating biologic treatments for ulcerative colitis, possible treatment-related risks should be considered, such as the lack of primary response or loss of effectiveness associated with a possibility of disease progression and complications, as well as adverse events that comprise infections, including opportunistic infections, and malignancies, which may result in the withdrawal of a biologic agent [1,8,9]. All these factors underline the importance of a thoughtful choice of the first-line biologic agent.

Interleukins 12 and 23 (IL-12, 23) are two cytokines that play a significant role in inflammatory bowel disease; both promote T-cell differentiation and proliferation via Th-1, 2 and 17 pathways leading to the development of ulcerative colitis and Crohn's disease [10,11].

Ustekinumab is a monoclonal IgG1 antibody with the target the p40 subunit common to the Il-12/Il-23 proteins [12] approved for use in psoriasis, psoriatic arthritis, and Crohn's disease. In 2019, results from the UNIFI study (Study to Evaluate the Safety and Efficacy of Ustekinumab Induction and Maintenance Therapy in Participants With Moderately to Severely Active Ulcerative Colitis CNTO1275UCO3001) were published that demonstrated induction and maintenance therapy with ustekinumab to be safe and effective in patients with active, moderate-to-severe ulcerative colitis, which resulted in its approval for use in patients with ulcerative colitis [13].

AIM

Considering the clinical and epidemiological characteristics of Russian patients with ulcerative colitis and limited data on ustekinumab usage in early lines in ulcerative colitis the aim of this analysis was to assess the effectiveness and safety of ustekinumab in the Russian patients who participated in the UNIFI induction and maintenance studies and were predominantly naïve to treatment with biologics.

PATIENTS AND METHODS

Study population

The Phase 3 UNIFI program (CNTO1275UCO3001) consisted of two randomized, double-blind, placebo-controlled studies under the same protocol: an eight-week induction study and a forty-four-week maintenance study. It was conducted from August 2015 until August 2018 using the same protocol in 244 study sites worldwide. The program enrolled adult patients (aged ⩾ 18) with moderately severe or severe ulcerative colitis (defined as the total Mayo score of 6–12, including an endosciopic subscore ⩾ 2 as determined using central analysis of video endoscopy) that had been diagnosed at least 3 months before screening.

Totally 74 patients from 14 study sites in Russia participated in the UNIFI program, 66 (89.2%) of them were bionaive. The analyses in this paper focus on these bionaive patients.

At study entry, the patients showed inadequate response or intolerability to conventional nonbiologic treatment (i.e., corticosteroids and/or 6-mercaptopurine/azathioprine) or corticosteroid dependence. Key exclusion criteria were imminent risk of colectomy, recent gastrointestinal or intrabdominal surgery or a history of extensive bowel resectionmalignancies, and active infections (including tuberculosis). Aminosalicylates and immunomodulators at stable doses were allowed from induction baseline through week 44 of the maintenance phase. Oral corticosteroids at stable doses could be used during induction.For subjects who were receiving oral corticosteroids on entry into the maintenance study, the investigator was to taper the daily dose of corticosteroids beginning at Week 0 of the maintenance study(For definitions and for more details on the patients, randomization, assessments, and end points, see the Supplementary Appendix, available at NEJM.org.) [13].

Study design

A detailed description of the study design is provided in the articles by Sands B. et al. and Abreu M. et al. [13,14]. At week 0 of the induction study, the patients were randomized in a 1:1:1 ratio to receive a single intravenous (IV) infusion of ustekinumab 130 mg, a weight-range based dose that approxinmated 6 mg/kg of body weight, or placebo. Patients were stratified by previous biologic treatment results (treatment failure — yes or no) and their region of residence (Eastern Europe, Asia, or other countries) in randomization.

Patients who were in clinical response (defined asa decrease from induction baseline in the Mayo score by ⩾ 30% and ⩾ 3 points, with either a decrease from induction baseline in the rectal bleeding subscore ⩾ 1 or a rectal bleeding subscore of 0 or 1) at Week 8 were eligible to enter the maintenance study. Patients who were not in clinical response at Week 8 received either subcutaneous (SC) or IV ustekinumab in a blinded manner as follows: 1) those who initially received ustekinumab IV induction received a ustekinumab SC dose of 90 mg; and 2) those who initially received IV placebo induction received a ustekinumab IV dose of ~6 mg/kg. Patients who were in clinical response at Week 16 were also eligible to enter the maintenance study. Patients who failed to respond to ustekinumab treatment at week 16 were discontinued from further participation.

Patients who achieved clinical response to asingle IV induction dose of ustekinumab were randomized in a 1:1:1 ratio in the maintenance study, stratified by the induction treatment received (ustekinumab 130 mg, ustekinumab 6 mg/kg or placebo with consequent ustekinumab 6 mg/kg), clinical remission status (yes or no, defined as the Mayo score ⩽ 2 without any individual subscore of > 1) at baseline of the maintenance study, and use of oral corticosteroids (yes or no) at baseline of the maintenance study, to receive treatment with SC ustekinumab 90 mg every 12 weeks (q12w), 90 mg every 8 weeks (q8w), or placebo.

Patients who demonstrated a clinical response to placebo IV during the induction study received SC placebo, while those who had shown a delayed response to ustekinumab (at week 16) received SC ustekinumab at the dose of 90 mg q8w during the maintenance study. Patients in these two groups were not randomized. Subjects who completed the safety and efficacy

evaluations at Week 44 and who, in the opinion of the investigator, might benefit from continued treatment had the opportunity to participate in the long-term extension (LTE). The LTE began after the assessments listed for the maintenance Week 44 visit (M-44) were completed and will continue through Week 220.

Study unblinding occurred after the Week 44 analyses were completed. After unblinding, ustekinumab-treated patients continued in the LTE, whereas patients remaining on placebo were discontinued. Patients whose UC disease activity worsened [in the clinical opinion of the investigator] were eligible for a single dose adjustment (starting at Week 56) as follows: placebo SC to ustekinumab 90 mg SC q8w [prior to unblinding]; ustekinumab 90 mg SC q12w to ustekinumab 90 mg SC q8w; ustekinumab 90 mg SC q8w continued on ustekinumab 90 mg SC q8w [sham dose adjustment, prior to unblinding]. Efficacy assessments were conducted every 12 weeks until unblinding and then q8w or q12w at dosing visits.

The duration of the study was approximately one year of induction and maintenance therapy with further follow-up for 3 years in LTE. Study protocols at each study site were approved by the Independent Ethical Committee or the Review Board. Prior to study enrollment, all patients provided written informed consent.

Study endpoints

The primary endpoint in the induction study was clinical remission at week 8. Secondary endpoints at week 8 included mucosal healing (defined as the endoscopy Mayo subscore of 0 or 1), clinical response. Other endpoints included histologic healing (defined as < 5% neutrophils in the epithelium, absence of crypts and no evidence of erosions, ulcerations, or granulation tissue), histo-endoscopic mucosal healing (defined as the endoscopic and histologic healing combined) and faecal calprotectin and CRP levels during induction. [15].

The primary endpoint in the maintenance study was clinical remission at week 44. Secondary endpoints included sustained clinical response at week 44, mucosalhealing at week 44, clinical remission without corticosteroid use at week 44 (defined as clinical remission at week 44 without concomitant corticosteroid use at week 44). Other study endpoints included histo-endoscopic mucosal healing at week 44 and faecal calprotectin and CRP levels through 44 weeks.

Symptomatic remission (Mayo stool frequency subscore of 0 or 1 and a rectal bleeding subscore of 0) and steroid-free symptomatic remission (in symptomatic remission and not receiving corticosteroid) were evaluated in LTE.

Safety assessments included adverse events (AEs), serious AEs, infections and serious infections as assessed by the investigator, as well as infusion/injection-site reactions.

Immunogenicity

Antibodies to UST were evaluated by means of a drug-tolerant electrochemiluminescence assay over time during the study at scheduled visits.

Statistical methods

All analyses for Russian patients were performed as post hoc. Descriptive statistics were reported for baseline characteristics. Dichotomous endpoints were compared between each ustekinumab group and the placebo group using the Fisher exact test. For continuous efficacy endpoints, last observation carried forward was used for missing data, and induction baseline observation was carried forward from the time of first treatment failure (ie, a prohibited change of UC medication, a rescue medication for clinical flare, an ostomy or colectomy, discontinuation of study agent due to lack of efficacy or an AE of worsening of UC disease) onward. For dichotomous endpoints, nonresponder imputation were applied for patients who met treatment failure criteria or had missing data. Dose adjustment in LTE was not considered as a treatment failure. Safety was analyzed according to the period of reporting, ie, induction, maintenance Week 0 though Week 44, maintenance Week 0 through Week 156.

RESULTS

Patients

The induction study of the UNIFI program enrolled 74 patients from Russia: 22 patients received

Table 1. *Baseline characteristics of the Russian population of bionaive patients who were randomized during the induction study*

	Placebo IV	Ustekinumab IV 130 mg	Ustekinumab IV 6 mg/kg*	Combined	Total
Number of bionaive patients enrolled in the study (n)	23	18	25	43	66
UC duration (years)					
Mean (SD)	4,62 (5,26)	4,92 (3,45)	4,71 (4,50)	4,80 (4,045)	4,74 (4,47)
UC anatomy					
Left-sided	20 (87.0%)	11 (61.1%)	19 (76.0%)	30 (69.8%)	50 (75.8%)
Total	3 (13.0%)	7 (38.9%)	6 (24.0%)	13 (30.2%)	16 (24.2%)
UC severity					
Moderate disease (6 ⩽ Mayo score ⩽ 10)	22 (95.7%)	16 (88.9%)	21 (84.0%)	37 (86.0%)	59 (89.4%)
Severe disease (Mayo score > 10)	1 (4.3%)	2 (11.1%)	4 (16.0%)	6 (14.0%)	7 (10.6%)
Mayo Scale (0–12)					
Mean (SD)	8,3 (1,39)	8,7 (1,74)	9,0 (1,43)	8,9 (1,56)	8,7 (1,52)
C-reactive protein (mg/L)					
Mean (SD)	3,56 (5,04)	4,65 (4,66)	6,34 (10,15)	5,64 (8,29)	4,89 (7,31)
Fecal calprotectin (mg/kg)					
Mean (SD)	2428,95 (4863,88)	2637,53 (3726,70)	2176,08 (3191,23)	2367,41 (3385,86)	2388,26 (3908,30)

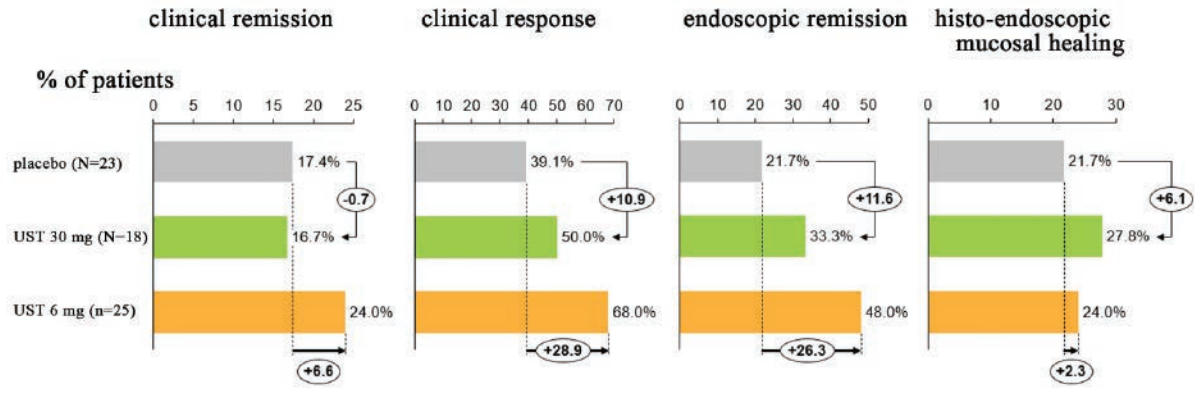

Figure 1. *Effectiveness measures at week 8 of the induction study in bionaive patients*

ustekinumab 130 mg intravenously, 26 patients received ustekinumab 6 mg/kg intravenously, and 26 patients received placebo at Week 0.

Among the study participants, 89.2% patients (n = 66) were bionaive, meaning that they had no history of previous biologic treatment: of these, 18 patients were allocated to the ustekinumab 130 mg group, 25 to the ustekinumab 6 mg/kg group, and 23 patients to the placebo group.

Disease characteristics of bionaive patients who were randomized during the induction study are provided in Table 1. At induction baseline, the mean age of patients was 38.9 years, 59.1% male, disease duration — 4.74 years. Most patients presented with left-sided ulcerative colitis — 75.8% (n = 50), moderately active disease (Mayo index 6–10 points) — 89.4% (n = 59) patients, the mean Mayo score was 8.7, CRP — 4.89 mg/L, faecal calprotectin — 2388.26 mg/kg. Demographics and disease characteristics were generally similar across treatment group in the induction study.

Induction study results

In ustekinumab 6 mg/kg and 130 mg groups clinical remission was observed in 24.0% and 16.7% of patients, respectively, while in the placebo group this outcome was reached by 17.4% of patients (Figure 1).

The proportion of patients with clinical response was 68.0%, 50.0%, and 39.1% for the ustekinumab 6 mg/kg, ustekinumab 130 mg and the placebo groups, respectively.

Mucosal healing was achieved by 48.0% of patients in the ustekinumab 6 mg/kg group, 33.3% of patients in the ustekinumab 130 mg, and 21.7% of patients in the placebo group.

Histo-endoscopic mucosal healing was observed in 27.8% of patients in the ustekinumab 130 mg group, 24.0% of patients in the ustekinumab 6 mg/kg group, and 21.7% of patients in the placebo group. Among Russian bionaive patients, the proportion of subjects in the ustekinumab 6 mg/kg group who achieved clinical remission, clinical response and mucosal healing at week 8 was numerically greater compared to both the placebo group and the ustekinumab 130 mg group.

MAINTENANCE STUDY RESULTS

Out of a total of 66 Russian bionaive patients who participated in the induction study, 40 patients were re-randomized in the maintenance study: 13 patients received 90 mg ustekinumab via subcutaneous injections every 12 weeks, 12 patients received ustekinumab every 8 weeks, and 15 patients were given placebo.

At week 44 of the maintenance study, clinical remission was achieved by 46.2% of patients who received ustekinumab every 12 weeks, 75.0% of patients who received ustekinumab every 8 weeks (p = 0.054 compared to placebo), and 33.3% of patients who received placebo (Figure 2). All patients who achieved clinical remission did not require treatment with corticosteroids.

Clinical response was observed in 84.6% and 83.3% of patients treated with ustekinumab every 12 and 8 weeks, respectively, and in 66.7% of patients in the placebo group.

Mucosal healing was observed in 46.2% in the ustekinumab q12w group, 75.0% in the ustekinumab q8w group (p = 0.054 compared to

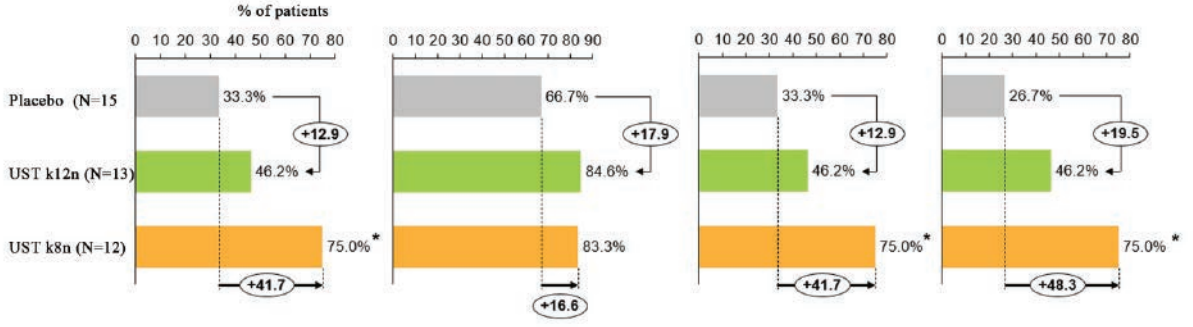

Figure 2. *Effectiveness measures at week 44 of the maintenance study in bionaive patients*

placebo), and in 33.3% of patients in the placebo group.

Histo-endoscopic mucosal healing was seen in 46% of patients in the ustekinumab q12w group, while in the ustekinumab q8w group the percentage of these patients was 75.0% (p = 0.021 compared to placebo), and in the placebo group — 26.7%.

The proportion of randomized patients in the ustekinumab q8w group who achieved clinical remission, clinical response, mucosal healing and histo-endoscopic mucosal healing at week 44 was numerically greater compared to both the placebo group and ustekinumab q12w [13].

Laboratory inflammatory markers over time

In the induction study decrease of median levels of CRP was demonstrated in patients treated with ustekinumab IV Median baseline CRP levels at the beginning of the maintenance study were 1.75 mg/L (IQ range 0.86; 2.62) for patients who received ustekinumab every 12 weeks, 0.68 mg/L (IQ range 0.34; 2.27) for patients who received it every 8 weeks, and 1.61(IQ range 0.86; 2.75) mg/L in the placebo group. In the maintenance phase median level of CRP after induction was sustained by ustekinumab SC treatments (Figure 3).

In the induction study decrease of median levels of faecal calprotectin was demonstrated in

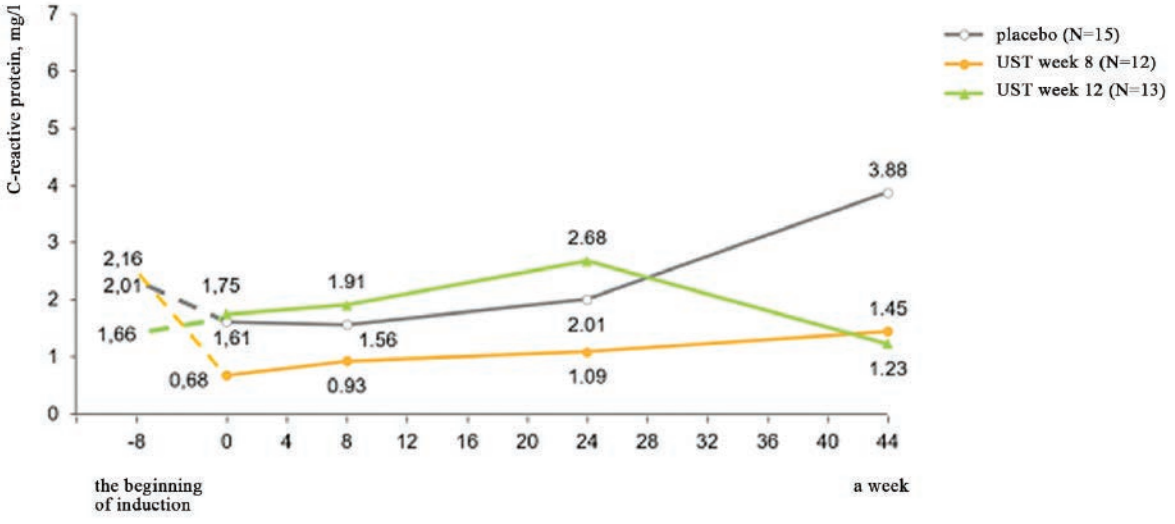

Figure 3. *Changes of median CRP levels over time during the maintenance study in bionaive patients through week 44*

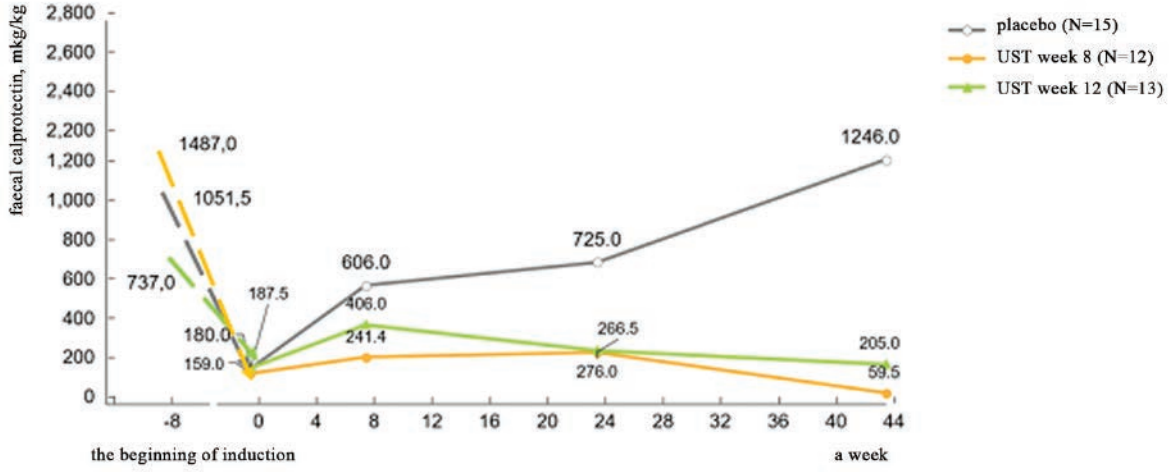

Figure 4. *Changes of median faecal calprotectin levels over time during the maintenance study in bionaive patients by treatment week 44*

patients treated with ustekinumab IV Median baseline faecal calprotectin levels at the beginning of the maintenance phase were 737.0 mg/kg (IQ range 142.5; 1464.5) in patients who received ustekinumab every 12 weeks, 1487.0 (IQ range 496.0; 4736.0) in those receiving it every 8 weeks, and 1051.5 (IQ range 600.0; 1553.0) in the placebo group. At week 8 of the maintenance phase, no meaningful differences in change from baseline values were noted between ustekinumab group and placebo, however, by weeks 24 and 44, faecal calprotectin levels were sustained in all ustekinumab groups as compared to placebo, where level increased($p < 0.004$ at week 24 and $p < 0.001$ at week 44) (Figure 4). Patients in the ustekinumab groups demonstrated persistent decreases in fecal calprotectin levels, while in the placebo groups these values appeared to increase over time from week 24 through 44.

Safety

Through the end of induction study the percentage of patients who reported at least one adverse event in the 130 mg ustekinumab group, 6 mg/kg ustekinumab group, and the placebo group was 22.2%, 40.0%, and 26.1%, respectively. No serious adverse events were reported in the ustekinumab groups; in the placebo group, 1 patient reported a serious adverse event. The proportion of patients with infections in the 130 mg and 6 mg/kg ustekinumab and the placebo groups was 5.6% (1 patients), 8.0% (2 patients) and 4.3% (1 patients) respectively.

The rate of adverse events from maintenance Week 0 through week 44 was comparable in the ustekinumab groups and the placebo group: 200.0, 164.9and 173.1 events per 100 patient-years in the ustekinumab q12w, ustekinumab q8w, and the placebo groups, respectively. The rate of serious adverse events reported in patients who received ustekinumab every 12 weeks was 0.0 events per 100 patient-years, 5.3 for patients who received ustekinumab every 8 weeks, and 19.2 in the placebo group.

The rates of infections as identified by the investigator through week 44 were: 0.0, 58.5, and 19.2 events per 100 patient-years in the ustekinumab q12w group, the ustekinumab q8w group, and the placebo group, respectively. In the ustekinumab q8w group, serious infections were reported at a rate of 5.3 (0.1, 29.6) events per 100 patient-years; no serious infections were reported in the ustekinumab q12w or placebo groups.

The rate of treatment discontinuation due to adverse events was 0.0 per 100 patient-years in the ustekinumab q12w group, 5.3 in the ustekinumab q8w group, and 19.2 in the placebo group.

No serious infections (including tuberculosis), malignancies or deaths were reported during the induction and maintenance studies.

Results from Long-term extension phase through 156 weeks

34 randomized bionaive patients from Russia were enrolled and treated in the long-term extension, 11 of whom received placebo, 12 received ustekinumab every 12 weeks, and 11 received ustekinumab every 8 weeks.

Symptomatic remission at week 152 was reported in 83.3% of patients in the ustekinumab q12w group, 81.8% in the ustekinumab q8w group. The proportion of patients in symptomatic remission and not receiving corticosteroids at week 152 was consistent with that of symptomatic remission.

Among all bionaive patients who were treated in LTE, from Week 0 of maintenance through Week 156, the rate of any adverse event was 142.00 in the ustekinumab q12w group, 125.35 in the ustekinumab q8w group, and 133.33 events per 100 patient-years in the placebo group. Infections were reported at a rate of 23.67 and 46.11 events per 100 patient-years for the q12w and q8w groups, respectively, and 40.74 events per 100 patient-years in the placebo group. Safety profile of ustekinumab was consistent with what was observed from Week 0 through Week 44, with the data reported for the Russian subpopulation through one year of exposure, including the induction and maintenance studies.

Immunogenicity

This study additionally evaluated the incidence of subjects who were positive for antibodies to ustekinumab. Among ustekinumab treated patients the majority were negative for antibodies

to ustekinumab. Among the 50 patients who entered the maintenance study. 8.0% (4 patients) were positive antibodies to ustekinumab through Week 44. Among 36 bionaive patients who were treated with ustekinumab during the LTE, from their first ustekinumab dose through Week 156, anti-ustekinumab antibodies were detected in 4 patients.

DISCUSSION

The additional analyses of the Russian patient population from the UNIFI study demonstrated that the patients with active, moderate-to-severe ulcerative colitis who were bionaive benefited from treatment with ustekinumab. Benefit was observed both during the induction and the maintenance studies as well as through the LTE. Patients who responded to induction therapy with intravenous ustekinumab, underwent a second randomization, q8w regimen of subcutaneous ustekinumab, achieved a clinical remission after 44 weeks of the maintenance period more often than those re-randomized to receive placebo treatment and q12w ustekinumab group.

It should be noted that all Russian patients who achieved clinical remission at week 44 of the maintenance period were not receiving glucocorticoids at Week 44, indicating that ustekinumab could be used to reduce patient's dependence on steroid agents. The majority of Russian bionaive patients treated with ustekinumab in the maintenance study achieved mucosal and histoendoscopic mucosal healing at Week 44.

In the induction phase decrease of CRP and faecal calprotectin median levels was demonstrated in patients treated with ustekinumab IV, in the maintenance phasemedian levels of laboratory inflammatory markers after induction were sustained by ustekinumab SC treatments.

Ustekinumab demonstrated a favourable safety profile in Russian patients. Rate of any adverse event among patients who received at least one dose of ustekinumab in the induction study or during 156 weeks of follow-up of the maintenance study was generally similar to that in the placebo group. Malignancy, active tuberculosis and death were not observed among these patients.

CONCLUSION

Taking into account limited global clinical practice data on the use of ustekinumab in early-line therapy for ulcerative colitis, this analysis was essential for choosing a biologic agent. The results of this analysis have allowed to confirm both the short- and the long-term effectiveness and safety of ustekinumab treatment in a Russian population of bionaive patients with active moderate-to-severe ulcerative colitis.

Overall, the results from the analysis of Russian patient population are consistent with earlier evidence from the overall patient population participating in the UNIFI program and allow us to consider ustekinumab asoptimal therapeutic option for early intervention in bionaive patients with ulcerative colitis.

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