SVEDO study

Switching from VEDOlizumab intravenous to subcutaneous formulation in patients with ulcerative colitis in clinical remission: an observational study

PROTOCOLLO PRINCIPALE

Versione del Protocollo: 1.0 (del 15/01/2021)

Promotore: IGIBD Italian Group for the study of Inflammatory Bowel Disease

Sperimentatore Principale: Dott. Davide Giuseppe Ribaldone

INTRODUCTION

Ulcerative colitis (UC) is a chronic, inflammatory disease of the bowel. Despite a fair number of new treatments, an optimization of theirs way of administration could improve the quality of life of patients (working days lost, travelling costs) and the impact on the health system (overload of day hospitals DH, commitment of nurses).

Vedolizumab is a fist in class biological drug able to induce and maintain remission in UC with a good safety profile. This drug is administered intravenously in DH, with an impact on life of patients and on hospital organization, especially when a large number of patients are treated in a centre.

Recently the randomized clinical trial VISIBLE 1 has been published. Patients affected by UC, after an induction of intravenous vedolizumab 300 mg at weeks 0 and 2, were randomized from week 6 (if they achieved clinical response) to intravenous vedolizumab 300 mg every 8 weeks, subcutaneous vedolizumab 108 mg every 2 weeks or placebo. Subcutaneous formulation achieved not statically different results regarding efficacy and side effects compared to intravenous formulation.

NEEDS THAT THE PROJECT INTENDS TO SATISFY

No study has been published about the efficacy and tolerability of subcutaneous formulation of vedolizumab in a cohort of patients in maintenance therapy with intravenous vedolizumab formulation.

MAIN OBJECTIVES OF THE PROJECT

The aim of this study is to evaluate the non-inferiority of subcutaneous formulation of vedolizumab after switching from intravenous formulation in patients affected by UC in clinical remission in a large, real-life cohort of Italian patients.

Primary endpoint is reached if less than 15% of patients experience diseases activity (pMAYO >=2) or need oral steroids or stop vedolizumab during the 6 months of follow-up after the switch.

Secondary endpoints include rate of study drug discontinuation, overall remission status, changes in C-reactive protein (CRP) as well as changes in faecal calprotectin levels.

ESTIMATED TIME FOR THE REALIZATION OF THE PROJECT

The recruitment of the patients will start from June 1st, 2021 and will finish of December 31st, 2021. The last day of follow-up for the last recruited patient will be on June 30th, 2022.

EXPECTED ACTIVITY

Once approved by the Ethic Committee of the coordinator centre and satellite centres, the data collection can start. A shared database will be created. After the deadline of 07/2022, available data will undergo to statistical analysis, as already described above.

SELECTION OF PATIENTS

The SVEDO study is an observational, multicentre, spontaneous and not financially supported study on patients affected by UC that switch from intravenous to subcutaneous formulation of vedolizumab.

Number of subjects enrolled

At McNemar test, setting a type I error = 0.05, a type II error of 0.2, considering clinically significant a 15% of patients undergoing disease relapse or needing for oral steroid or stopping vedolizumab during the 6 months of follow up, the power of the study is reached if at least 50 patients are recruited.

All patients will be prospectively followed on the outpatient clinics by inflammatory bowel disease expert clinicians with regular appointments. Clinical, biochemical, and endoscopic evaluation will be performed during follow-up at physician's discretion.

Inclusion criteria

- UC in clinical remission (pMAYO < 2) without oral systemic or low absorbable steroids since at least 8 months before the switch
- At least 6 months of follow-up after the switch
- Will of the patient to share their clinical data

Exclusion criteria

- Total colectomy
- No clinical data 6 months before the switch, at the switch, 6 months after the switch.

Measures of safety is planned to include clinical and laboratory adverse events. Safety assessment also included laboratory data, infusion reactions.

Data collection

The following data will be collected: date at switch (T0), age at T0, smoking habit at T0, sex, disease extension at worst diseases stage (E1, E2, E3), previous anti-TNF, months of intravenous vedolizumab at T0, disease duration at T0, CRP at T0, calprotectin at T0, pMAYO at T0, thiopurines at T0, frequency of administration at T0, side effects T-6 - T0, CRP at 6 months (T6) after the switch, calprotectin T6, pMAYO T6, oral steroids at T6, thiopurines at T6, side effects T6 - T0, vedolizumab retention, reason for vedolizumab discontinuation, UC-related hospitalization T6 - T0, UC-related intestinal surgery T6 - T0.

Ethical considerations

The study will be approved by the ethical committee of the proposing centre and then by the ethical committees of all the satellite centres.

Statistical Analysis

Descriptive statistics will be used to characterize the patient population. Results will be provided as numbers (percentages) for discrete variables and median (range) for continuous variables and as frequencies and percentages for categorical variables. Differences in not normally distributed paired parameters will be tested with the Wilcoxon signed rank test.

We regarded a non-inferiority margin of 15% as appropriate on the basis of the rate of relapse of vedolizumab in patients in remission (Danese S et al. Vedolizumab treatment persistence and safety in a 2-year data analysis of an extended access programme. Aliment Pharmacol Ther. 2020 Nov 18) and according to literature definition of non-inferiority (Jørgensen KK et al. Switching from originator infliximab to biosimilar CT-P13 compared with maintained treatment with originator infliximab (NOR-SWITCH): a 52-week, randomised, double-blind, non-inferiority trial. Lancet. 2017 Jun 10;389(10086):2304-2316.).

The pMAYO, CRP, ESR, calprotectin value at T0 will be compared with theirs values at T6 with Paired sample t-test or Wilcoxon test according to distribution of the values.

A p-value of < 0.05 will be considered to be statistically significant. All statistical analyses will be performed using MedCalc Statistical Software version 18.9.1 (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2018).

Patient's consent

Only patients who have given their free, informed and informed consent by signing on the appropriate form will be enrolled in the study. Before signing, patients will have received from the principal investigator and co-investigators all the information regarding:

- the purpose of the study
- the duration of their participation
- the clinical procedures to which they will be subjected
- the benefits, foreseeable risks, disadvantages that could derive from participation in the study
- the confidential nature of their personal data
- the voluntary nature of their participation
- the possibility of withdrawing consent at any time, without this implying any consequence on their normal therapeutic process

Safety assessment and side effects

No risks or side effects are anticipated.

Risk / benefit ratio

This study does not present significant risks and side effects for the patient's health. However, this study will provide, for the first time in literature, data about efficacy and safety of switching from intravenous to subcutaneous formulation of vedolizumab in patients treated for years with intravenous formulation of vedolizumab and in clinical remission. If the data from VISIBLE-1 trial will be confirmed in a real life cohort of patients affected by UC with a long history of vedolizumab treatment we expect that the vast majority of patients with IBD currently treated with intravenous formulation will be switched to subcutaneous formulation with great advantages for the quality of life of patients and for the commitment of hospitals without loss of effectiveness or increase of side effects for patients.

Criteria for leaving the study

Patients can withdraw their consent to the study at any time, without this in any way affecting the subsequent treatments that may be necessary for the pathology from which they are suffering.

Measures for the protection of the rights of the person

The nature, purpose, and meaning of the study will be explained to the patient in a comprehensive and understandable way. He must express a favorable opinion on participation by signing an acceptance model (attachment). He will be entitled to withdraw from participation in the study at any time.

Patient data will be collected and stored in an "anonymous" manner, meaning that each patient will be assigned an identification code known only to the researchers, doctors and nurses involved in the project. The code key will be stored in a protected environment following the laws on the protection of privacy and personal data protection (Pursuant to EU Regulation 2016/679 General Data Protection Regulation (GDPR) concerning the protection of individuals with regard to the processing of personal data , as well as the free circulation of such data (hereinafter GDPR EU 2016/679)).

ADDITIONAL COSTS

None

EFFICACIA DELL'ATTIVITÀ

The parameters that will allow to evaluate the effectiveness of the proposed activity are:

- reach an enrollment of at least 50 patients at the end of 6 years from the beginning of the work;

- publish the results in international scientific journals indexed on recognized databases (e.g. PubMed), disseminate the results of this study at national and international conferences (IG-IBD, ECCO, UEGW)

COMPOSIZIONE DEL GRUPPO DI RICERCA

Rispetto al passato, ora si intende istituire una biobanca-IBD ed effettuare parte delle indagini molecolari a Torino grazie al ruolo attivo che coinvolge il Laboratorio di Epatologia e Gastroenterologia Molecolare (Dipartimento di Scienze Mediche dell'Università di Torino).

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CO-SPERIMENTATORI MEDICI

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