



Università degli Studi di Messina

DIPARTIMENTO DI MEDICINA CLINICA E SPERIMENTALE

DIRETTORE: PROF. GIOVANNI RAIMONDO

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AVVISO PUBBLICO

di ricerca di Enti/Aziende finanziatori non condizionati del progetto:

Mesalazine in maintaining remission in Ulcerative Colitis: adherence and daily dosing.

1- CARATTERISTICHE DEL PROGETTO

- a) Struttura coinvolta: UOSD Malattie Intestinali Croniche dell Dipartimento di Medicina Clinica e Sperimentale dell'Università di Messina
- b) Valore del progetto: Euro 5.000 (cinquemila), per i costi del personale, l'elaborazione statistica e la preparazione manoscritto per la realizzazione del progetto
- c) Durata progetto: 6 mesi
- d) Responsabile del progetto e della relazione intermedia e finale: Prof. Walter Fries (fwalter@unime.it)

2- SCADENZA DELL'AVVISO E LETTERE DI INTENTI

- 2.1. Le lettere di intenti relative all'avviso de quo, redatte in conformità al modello fac-simile riportato in calce al presente avviso, dovranno pervenire entro e non oltre il **31 dicembre 2019**
- 2.2. Saranno considerate valide le lettere di intenti inoltrate, entro la data di scadenza dell'avviso, tramite una delle seguenti modalità:
 - a mezzo di servizio postale, facendo fede, a tal fine, il timbro della data dell'Ufficio Postale accettante
 - a mezzo di e-mail al seguente indirizzo di posta elettronica: dipartimento.dimed@pec.unime.it
 - direttamente a cura dell'interessato o di persona delegata munita di copia fotostatica non autenticata di un documento di identità non scaduto, con sottoscrizione apposta allo sportello in presenza del dipendente addetto a ricevere la pratica

BACKGROUND

Ulcerative Colitis (UC) is a chronic inflammatory disease characterized by a continuous mucosal inflammation of the colon. It involves the rectum and, to a variable extent, the colon in a continuous fashion with a chronic-relapsing course. Although inflammation involves only the surface of the colon, in severe forms it can also involve the deeper layers of the bowel wall. The extent of the inflammation varies from proctitis with more or less disease activity, to distal form and can progress or even start as a severe pancolitis. Severe extensive UC may not respond to conventional medical treatment requiring rescue

therapy or colectomy. [1] Oral treatment with 5-aminosalicylic acids (5-ASA; mesalazine) is first line treatment in inducing and maintaining remission in mild to moderate UC. In relapsing disease a good treatment option is to increase daily dose of 5-ASA or adding topical formulation of 5-ASA or corticosteroids. In the induction of remission of distal forms, topical administration of 5-ASA is superior to corticosteroid therapy and combination therapy with oral and topical 5-ASA is more effective than disjointed therapy [2-3]. A daily dose more than 2 gr is effective in inducing and maintaining remission. In extensive disease as pancolitis, a daily dose of 2,4 gr is superior to 1,2 gr in preventing disease relapse (142 days vs 47 days). In the distal forms of UC combined therapy is more effective than oral only in preventing relapse. However most of patients prefer maintenance treatment with only oral treatment. [5-7] Mesalazine also has an important role in reducing incidence of colorectal cancer (CRC). [8]

Several studies showed the *non-adherence* to treatment prescription, not only for UC, leads to an increasing mortality and health costs. In UC patients adherence to 5-ASA improves outcome and prevents disease relapse.

Clinical trials for IBD-related treatment, reported rate of adherence ranging from 70 to 95% but in real life this percentage does not exceed 40% - 60% [12-15].

A recent Czech republic's study showed that the compliance with mesalazine in patients with UC was related only to educational level and not to sex, age, duration of treatment, marital status, type of job, number of doses per day, pharmaceutical form (i.e., small tablets/large tablets/sachets/rectal form/combinations) or concomitant therapy with corticosteroids, immunosuppression or biological therapy. [16]

AIMS.

The aims of this study is:

- to evaluate patients adherence to mesalazine in UC maintenance therapy and identify risk factors for non-adherence to confirm in the Italian setting the Keil R. [16] data. The following risk factors will be evaluated: sex, age, duration of treatment, marital status, type of job, education level, concomitant therapy (number of other drugs ingested weekly), Charlson comorbidity index, year of diagnosis, localization and extension.
- to evaluate the average daily dose used in clinical practice of mesalazine to maintain remission and the mean time to recurrence

Remission is defined as a partial Mayo score (pMS) ≤ 2 for U without steroid use. Recurrence is defined as relapse of symptoms and/or biochemical and/or endoscopic evidence of active disease.

Primary outcome

- To assess the adherence and risk factors for non-adherence

Secondary outcome

- To assess the average daily dose used in clinical practice to maintain remission.
- To assess the mean time to recurrence related to the daily dosage of mesalazine

METHODS.

Primary endpoint

- Patients adherence to mesalazine

Secondary endpoint

- Maintaining remission with mesalazine

Study: observational retrospective monocentric study

Inclusion criteria:

- Outpatients with mild to moderate UC in remission followed in our IBD-unit from diagnosis for at least 3 years.
- Age > 18 years

Exclusion criteria

- Patients with severe UC
- Patients on biologics
- Patients on immunomodulators
- Colectomized patients

Definition of adherence:

Adherence is defined as the agreement between the patient's behavior and the prescriber's recommendations (at least 90%). We will evaluate retrospectively if therapy declared by the patient is the same prescribed at the previous visit (Morisky medication adherence scale).

Data to collect:

The following data will be collected retrospectively from an available database:

- Dosage of mesalazine prescribed for maintenance of remission
- Time to the last remission
- If available, time between two flare and the maintenance therapy adopted
- Anamnestic data (year of diagnosis, localization and extension, treatment)

The following data will be collected from the clinician during the visit:

- Morisky adherence scale (the referred therapy will be collected and then confronted with the prescribed one from the database)
- Anamnestic data (age, gender, comorbidity, duration of treatment, marital status, type of job, education level, concomitant therapy (number of other drugs ingested weekly))
- Clinical activity of the disease according to partial Mayo score (**see Fig 1**)
- Charlson comorbidity index

Fig. 1. Mayo score for Ulcerative colitis.

Measure	Scoring system
Stool frequency (per day)	0 = normal number of stools for patient 1 = 1–2 more stools than normal 2 = 3–4 more stools than normal 3 = 5+ more stools than normal
Rectal bleeding	0 = no blood seen 1 = streaks of blood with stool less than 50% of time 2 = obvious blood with stool most of time 3 = passes blood without stool
Findings on endoscopy	0 = normal or inactive disease 1 = mild disease 2 = moderate disease 3 = severe disease
Physician's global assessment	0 = normal 1 = mild disease 2 = moderate disease 3 = severe disease

Population: 90 - 120 consecutive patients that will match the inclusion/exclusion criteria

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LETTERA DI INTENTI (FAC SIMILE)

_____, con sede legale in _____,
via _____ N. _____ C.F. _____ e
P.I. _____, nella persona del legale rappresentante
_____ facendo seguito all'avviso
pubblico _____

COMUNICA

la propria disponibilità a finanziare il progetto di cui all'avviso succitato e dichiara, fin da ora, di accettare le condizioni contrattuali formulate nell'avviso e gli impegni, previsti dalla normativa in materia, che saranno meglio dettagliati nel contratto che si andrà a sottoscrivere.

Da allegare una lettera con evidenza di:

- breve illustrazione dell'attività svolta dalla Società che intende candidarsi per la sponsorizzazione;
- indicazione del progetto cui va destinato l'importo offerto;
- entità della somma offerta;
- impegno all'erogazione della somma in unico versamento;
- indicazione dell'indirizzo di posta elettronica e del nominativo del proprio referente.

Firma Legale del Rappresentante
