

STUDY PROTOCOL

EFFICACY AND SAFETY OF NEW ORAL BUDESONIDE-MMX™ (CB-01-02) 6 MG AND 9 MG EXTENDED RELEASE TABLET FORMULATIONS IN PATIENTS WITH MILD OR MODERATE, ACTIVE ULCERATIVE COLITIS. A MULTICENTER, RANDOMIZED, DOUBLE-BLIND, DOUBLE DUMMY COMPARATIVE STUDY VERSUS PLACEBO, WITH AN ADDITIONAL REFERENCE ARM EVALUATING ASACOL® 2400 MG

1. PATIENT ENROLMENT

1.1 INCLUSION CRITERIA

Patients fulfilling the following criteria at the screening visit are eligible for participation in the study:

- Male and female patients, 18-75 years old, suffering from ulcerative colitis for at least 6 months.
- Diagnosis of ulcerative colitis in active phase, of mild or moderate entity with Ulcerative Colitis Disease Activity Index (UCDAI) ≥ 4 and ≤ 10 according to Sutherland.
- All females of child-bearing potential must have a negative serum pregnancy test immediately prior to enrollment. In addition, all females of child-bearing potential must agree to be completely abstinent or be using an accepted form of contraception throughout the entire study period. Accepted forms of contraception are defined as those with a failure rate $<1\%$ when properly applied and include: combination oral pill, some intra-uterine devices, and a sterilised partner in a stable relationship. Female subjects must also not be actively breast-feeding through the entire study period.
- Ability to comprehend the full nature and purpose of the study, including possible risks and side effects.
- Ability to co-operate with the investigator and to comply with the requirements of the entire study.
- Must be able to understand and voluntarily sign written informed consent prior to inclusion in the study.

1.2 EXCLUSION CRITERIA

Patients who meet any of the following criteria at screening visit are to be excluded from study participation:

- Patients with limited distal proctitis (from anal verge up to 15 cm above the pectineal line).
- Patients with severe ulcerative colitis (UCDAI >10).
- Patients with infectious colitis.
- Evidence or history of toxic megacolon.
- Severe anemia, leucopenia or granulocytopenia.
- Use of oral or rectal steroids in the last 4 weeks.
- Use of immuno-suppressive agents in the last 8 weeks before the study.

- Use of anti-tumor necrosis factor alpha (anti-TNF α) agents in the last 3 months.
- Concomitant use of any rectal preparation.
- Concomitant use of antibiotics.
- Concurrent use of CYP3A4 inducers or CYP3A4 inhibitors. See Section 4.2, Table 5 for complete list.
- Patients with intolerance to salicylates.
- Patients with verified, presumed or expected pregnancy or ongoing lactation.
- Patients with liver cirrhosis, or evident hepatic or renal disease or insufficiency, and/or severe impairment of the bio-humoral parameters (i.e. 2 x upper limit of normal for ALT, AST, GGT or creatinine).
- Patient with severe diseases in other organs and systems.
- Patients with local or systemic complications or other pathological states requiring a therapy with corticosteroids and/or immuno-suppressive agents.
- Patients diagnosed with type 1 diabetes.
- Patients diagnosed with, or with a family history of glaucoma.
- All patients with known hepatitis B, hepatitis C or with human immunodeficiency virus (HIV), according to the local privacy policy.
- Participation in experimental therapeutic studies in the last 3 months. (Note: patients who participated in observational only studies are not excluded).
- Any other medical condition that in the principal investigator's opinion would make the administration of the study drug or study procedures hazardous to the subject or obscure the interpretation of adverse events.