A Randomized, Double-Blinded, Placebo-Controlled Trial of TU-100 in Patients Undergoing Laparoscopic Colectomy

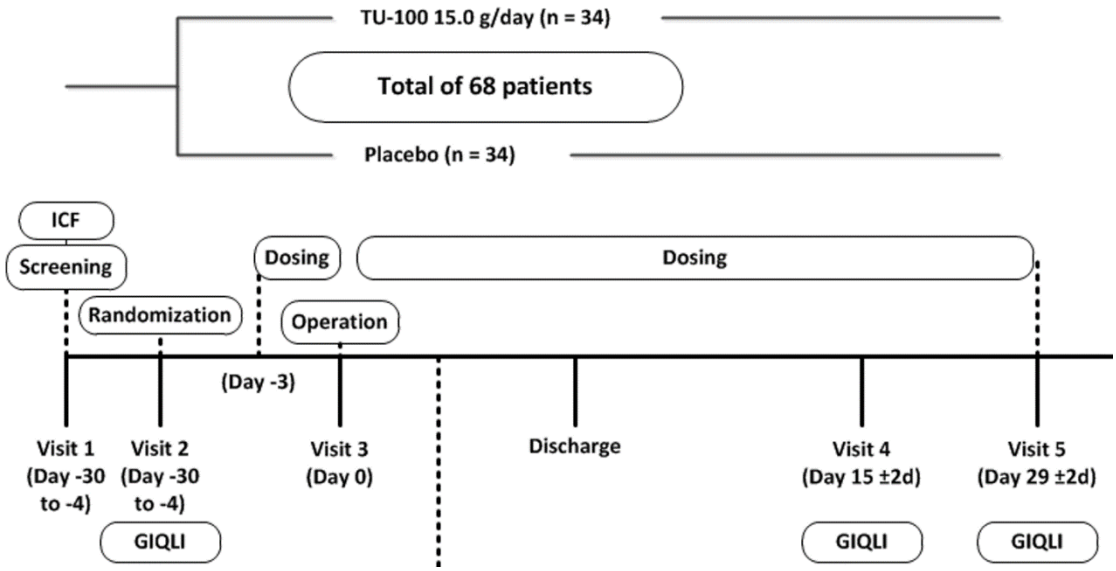
Study Protocol and Statistical Analysis Plan

Objectives

The primary objective of this study was to assess the effect of TU-100 on postoperative quality of life in patients undergoing laparoscopic colectomy.

Methodology

This multicenter, randomized, double-blinded, placebo-controlled study evaluated the effect of TU 100 on postoperative quality of life in patients undergoing straight, hand-assisted, or robot-assisted laparoscopic colectomy. A total daily dose of 15 g TU 100 or matching placebo (1:1) was administered for 3 days before surgery and for 28 days after surgery.



Number of Patients (planned and analyzed)

Approximately 68 patients were planned to be included in the study.

Diagnosis and Main Criteria for Eligibility

Inclusion Criteria:

- Were at least 18 years of age
- Had a current diagnosis of colon cancer, diverticulitis, or benign colonic neoplasm
- Required straight, hand-assisted, or robot-assisted laparoscopic colectomy
- Required hospitalization for surgery and recovery

Exclusion Criteria:

- Had been diagnosed with rectal cancer, advanced or metastatic colon cancer, Crohn's

disease, ulcerative colitis, or volvulus.
- Required resection of rectal lesion
- Had received or is scheduled to receive preoperative or postoperative chemotherapy during the duration of the study
- Required emergency surgery or surgery in the presence of ongoing infection, bowel obstruction or perforated bowel
- Had any other serious condition that might adversely affect suitability for participation in this study, such as liver disorder, kidney disorders, heart failure, blood disorders, or metabolic disorders
- Had a history of any invasive abdominal or thoracic surgery in the past 12 weeks.
- Planned to receive any abdominal irradiation
- The patient required the formation of a stoma (ileostomy or colostomy)

Dose and Duration of Treatment

Patients receiving the 15 g/d dose ingested two 2.5 g sachets of TU 100 t.i.d. for 3 days preoperatively and 28 days postoperatively; patients receiving placebo followed the same dosing schedule as the patients receiving TU-100.

Criteria for Evaluation

Primary efficacy endpoint:

- Change in GIQLI questionnaire global score from baseline to Visit 4

Secondary efficacy endpoints, including but not limited to, as follows:

- Change in GIQLI global score from baseline to Visit 5
- Incidence of postoperative complication (i.e., surgical site infection, prolonged and recurrent postoperative ileus, and anastomotic leak)

Statistical Analysis Plan

The overall effect of TU-100 on the primary endpoint was assessed by using an analysis of covariance (ANCOVA) model with change from baseline value as the dependent variable and treatment group, baseline GIQLI global score, scheduled surgical location in the colon, and solid food before/after the first flatus as explanatory variables. The secondary endpoints were assessed by using an ANCOVA model or a Cox proportional hazards model.

The intent-to-treat (ITT) population was used for all efficacy analyses. The safety population was used for all safety analyses.

The frequencies of AEs were summarized by treatment group and by severity within treatment group. AEs were coded using the Medical Dictionary for Regulatory Activities (version 16.0). All AEs were reported.