Mesenchymal Stromal Cells of Bone Marrow Reduce the Risk of Postoperative Recurrence of Crohn’s Disease

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BACKGROUND: Crohn’s disease (CD) in the form of terminal ileitis occurs in approximately 1/3 of CD patients and is often complicated by the formation of ileum stricture. The operation recurrence of CD.

CONCLUSION(S): Anadale Crohn Center named after A. S. Loginov, Moscow, Russia; Medical Radiological Research Center, Moscow, Moscow, Russia; Moscow Scientific Center named after A. S. Leginov, Moscow City, Moscow, Russia; Medical Radiological Research Center, Obniex, Kaluga Region, Russia.

BACKGROUND: The Crohn’s disease (CD) in the form of terminal ileitis occurs in approximately 1/3 of CD patients and is often complicated by the formation of ileum stricture or ileocecal valve. The operation and safety between EBD with and without fluoroscopic guidance for CD strictures. Clinical success was defined as improved obstructive symptoms.

METHODS: A total of 43 patients with CD strictures were identified (11 at EBD with fluoroscopic guidance group and 32 at EBD without fluoroscopic guidance group). Technical success was achieved in 10 patients (90.9%) at EBD with fluoroscopic guidance and 32 patients (100%) at EBD without fluoroscopic guidance (P = 0.084). Clinical success was achieved in 4 patients (36.4%) at EBD with fluoroscopic guidance and 18 patients (56.3%) at EBD without fluoroscopic guidance (P = 0.253). Additional surgery was performed in 4 patients (36.4%) at EBD with fluoroscopic guidance and 8 patients (25.0%) at EBD without fluoroscopic guidance (P = 0.469). Secondary EBD was performed in 2 patients (18.2%) at EBD with fluoroscopic guidance and 6 patients (18.8%) at EBD without fluoroscopic guidance (P = 0.967). There were no serious complications in both groups.

CONCLUSION(S): There were no significant differences in efficacy and safety between EBD with and without fluoroscopic guidance for CD strictures. EBD guidance for CD strictures could be safe and effective in the setting without fluoroscopic guidance.

Phase 1a Safety and Pharmacokinetic Effects of GB004, a Novel Prolyl Hydroxylase Inhibitor and Potential Therapy for Inflammatory Bowel Disease

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BACKGROUND: GB004 is a small molecule prolyl hydroxylase inhibitor (PHDI) that stabilizes hypoxia inducible factors (HIF)-α, key transcription factors involved in the adaptive and protective cellular responses at the intersection of hypoxia and inflammation. GB004 is being developed as a therapy for inflammatory bowel disease (IBD). For diseases as IBD, an ideal profile for a PHDI is a molecule that has a gut targeted PK profile and preferentially activates tissue specific protective mechanisms to a greater extent than other pathways where HIF transcription factors have a role (e.g., erythropoietin (EPO) production). GB004 was selected to meet this profile, and consistent with it, orally administered GB004 in animal models of colitis demonstrated a significant reduction in disease activity, an improvement in histology, greater exposure in GI tissue relative to plasma, and no increase in inflammatory or epithelial changes.

METHODS: This was a randomized, double-blind, placebo-controlled, single-ascending dose, Phase 1a study conducted at a single site in Canada. Single oral solution doses were investigated in 5 sequential cohorts (20, 60, 120, and 240 mg in 50 ml solution, and 240 mg in 100 ml solution), consisting of 2 placebo and 6 GB004 male subjects per cohort. PK and safety were evaluated through follow-up day 8. EPO and VEGF levels were collected at baseline, 4, 8, and 12 hours post dose.

RESULTS: 40 subjects were randomized. The mean age and BMI were 36.2 yrs and 25.6 kg/m2, respectively. All subjects completed the study. GB004 was rapidly absorbed with a median Tmax of 0.5 hours for all doses. Cmax of GB004 increased in a dose proportional manner while AUC of GB004 was approximately 50% higher in GB004-treated subjects and higher than in placebo treated subjects: nausea (20.0% GB004 vs 0% placebo), vomiting (13.3% vs 0%), feeling cold (13.3% vs 10.0%), and somnolence (10.0% vs 0%). All AEs reported in GB004-treated subjects were mild, and the incidence of AEs for GB004 240 mg in 100 ml was lower than 240 mg or 120 mg in 50 ml. CONCLUSION(S): This study demonstrated that single doses of GB004 solution are generally well tolerated, with no effects observed on serum EPO or VEGF levels, consistent with the intended PK profile and animal model data. Clinical studies of GB004 are ongoing in patients with ulcerative colitis to explore PK and PD both systemically and within colonic tissue (NCT03860998). A future formalisation of this is being developed.

Endoscopic Balloon Dilatation of Crohn’s Disease Strictures With or Without Fluoroscopic Guidance

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BACKGROUND: Structures are common complications in Crohn’s disease (CD). CD-associated strictures are usually managed with medical, endoscopic, and surgical approaches, or combinations. Endoscopic therapy is easier to perform in experienced hands and helpful to avoid the need for surgery. In clinical practice, endoscopic balloon dilatation (EBD) under a fluoroscopic guidance is preferred. The fluoroscopic guidance allows for the delineation of the stricture and the orientation of the entire balloon catheter. The use of fluoroscopy exposes the patient, the endoscopist, and the endoscopic nurses to excessive radiation. EBD is performed without fluoroscopic guidance in some cases. However, the benefit of fluoroscopic guidance for dilating CD strictures has not been readily demonstrated. The hypothesis of the study is that there are no significant differences in efficacy and safety between EBD with and without fluoroscopic guidance for CD strictures. The aim of this study is to compare efficacy and safety between EBD with and without fluoroscopic guidance for CD strictures.

METHODS: We performed a retrospective review of EBD for strictures between 2016 and 2017. We investigated the technical success and clinical success as the efficacy in EBD with and without fluoroscopic guidance for CD strictures. Technical success was defined as the ability to pass the scope through the stricture after balloon dilatation. Clinical success was defined as improved obstructive symptoms.

RESULTS: A total of 43 patients with CD strictures were identified (11 at EBD with fluoroscopic guidance group and 32 at EBD without fluoroscopic guidance group). Technical success was achieved in 10 patients (90.9%) at EBD with fluoroscopic guidance and 32 patients (100%) at EBD without fluoroscopic guidance (P = 0.084). Clinical success was achieved in 4 patients (36.4%) at EBD with fluoroscopic guidance and 18 patients (56.3%) at EBD without fluoroscopic guidance (P = 0.253). Additional surgery was performed in 4 patients (36.4%) at EBD with fluoroscopic guidance and 8 patients (25.0%) at EBD without fluoroscopic guidance (P = 0.469). Secondary EBD was performed in 2 patients (18.2%) at EBD with fluoroscopic guidance and 6 patients (18.8%) at EBD without fluoroscopic guidance (P = 0.967). There were no serious complications in both groups.

CONCLUSION(S): There were no significant differences in efficacy and safety between EBD with and without fluoroscopic guidance for CD strictures. EBD guidance for CD strictures could be safe and effective in the setting without fluoroscopic guidance.