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Multi Donor Intense Faecal Microbiota Transplantation is an Effective Treatment for Resistant Ulcerative Colitis: A Randomised Placebo-Controlled Trial

Mon, May 23 | *Abstract # 600 | Sudarshan Paramsothy[1], Michael A. Kamm[2,3], Alissa Walsh[4], Johan van den Bogaerde[5], Douglas Samuel[6], Rupert W. Leong[6], Susan J. Connor[7], Wa Sang Watson Ng[7], Ramesh Paramsothy[7], Nadeem Kaakoush[8], Hazel M. Mitchell[8], Wei Xuan[9], Enmoore Lin[10], Thomas Borody[10]*

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Background: The gut microbiota is the antigenic drive in ulcerative colitis (UC), but the efficacy of microbial manipulation using faecal microbiota transplantation (FMT) is unclear. Preliminary low dose studies in active UC have suggested benefit. The value of such therapy in patients with conventional-drug resistant colitis, the dosing of treatment, and the importance of specific donors are unknown.

Methods: In this double-blind, 3-centre study, patients with active UC (Mayo score 4-10) resistant to standard treatments were randomised to receive a single FMT or placebo colonoscopic infusion on day 1 followed by FMT or placebo enemas 5 days per week for 8 weeks. Each active enema was derived from 3 to 7 unrelated donors. Patients on corticosteroids underwent mandatory weaning and cessation. The primary endpoint was steroid-free clinical remission together with endoscopic remission or response (total Mayo score ≤2 points with subscores ≤ 1 for each of rectal bleeding, stool frequency and endoscopic appearance, and ≥1 point reduction from baseline in endoscopy subscore) at week 8. Secondary endpoints included steroid free clinical remission (combined total score of ≤ 1 for both rectal bleeding and stool frequency Mayo subscores), clinical response, endoscopic remission (UCEIS score ≤ 1), endoscopic response, quality of life and safety. All analyses were intention to treat. At blinded therapy conclusion placebo-treated patients were offered 8 weeks of open label active treatment.

Results: Of 81 patients the primary endpoint of steroid-free clinical remission and endoscopic remission or response was achieved in 11 of 41 (27%) patients receiving FMT versus 3 of 40 (8%) patients receiving placebo ($p = 0.02$). Steroid free clinical remission and clinical response rates were 44% vs. 20% ($p = 0.02$) and 54% vs. 23% ($p < 0.01$) respectively. Steroid free endoscopic remission and endoscopic response rates were 17% vs. 8% ($p = 0.19$) and 37% vs. 10% ($p < 0.01$) respectively. There was no difference in adverse events between the study arms. 37 patients initially randomized to placebo progressed to open label FMT, of whom 10 (27%) met the primary endpoint, 17 (46%) experienced clinical remission and 9 (24%) experienced endoscopic remission, consistent with the blinded FMT outcomes. 3 serious adverse events occurred during blinded therapy comprising worsening of colitis [2 active FMT treatment (including 1 patient who required colectomy for severe UC) and 1 placebo].

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Conclusions: This largest controlled trial of FMT has demonstrated that intense multi-donor colonoscopic and enema FMT is effective in inducing strictly-defined clinical and endoscopic remission in patients with resistant active ulcerative colitis.