

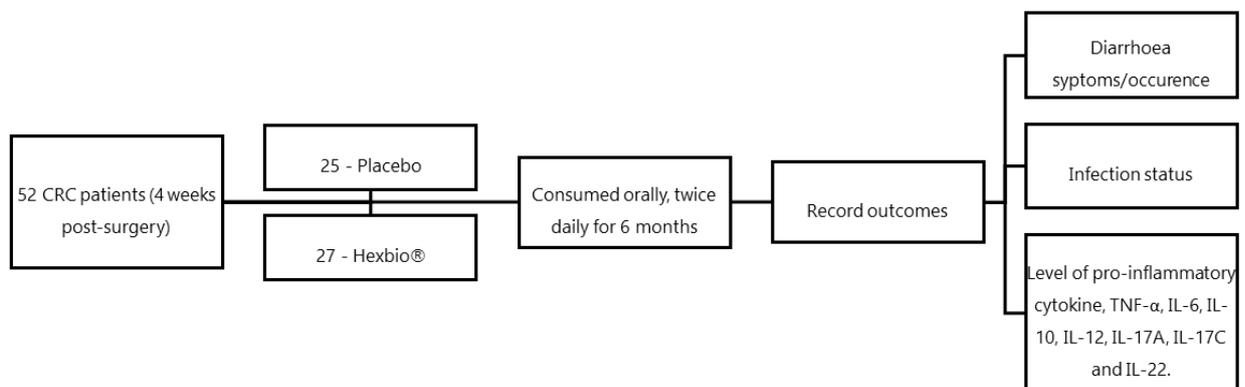
## **A Randomized Double-Blind Placebo Controlled Trial of Probiotics in Post-Surgical Colorectal Cancer**

**ARTICLE:** Zaharuddin, L., Mokhtar, N. M., Muhammad Nawawi, K. N., & Raja Ali, R. A. (2019). A randomized double-blind placebo-controlled trial of probiotics in post-surgical colorectal cancer. *BMC Gastroenterology*, 19(1). doi:10.1186/s12876-019-1047-4

Colorectal cancer (CRC) is the second most common cancer in males and the third most common in females in most developed countries after discounting non-melanotic skin cancer. It is estimated that colorectal cancer global incidence will reach 2.2 million new cases by the year 2030.

This study provides evidence that probiotic has the potential to change host inflammatory status thus produces an option for probiotic to be as supplementary for cancer target immunotherapy. Among clinical benefits of probiotics, pertaining to CRC surgery including reduction in the duration of hospital stay, less superficial incisional surgical site infection, also preventing chemotherapy and antibiotic induced diarrhoea.

A total of 52 patients with colorectal cancer were randomized at four weeks after surgery to receive either a placebo (n = 25) or Hexbio® (n = 27), orally twice daily for the period of six months.



### **What were the parameters evaluated in this study?**

The primary outcome evaluated was the circulating cytokine level. The secondary outcome measured were diarrhoea symptoms or reoccurrence, infection status and requirement of antibiotics.

### **What was the outcome of intervention with HEXBIO® for 6 months?**

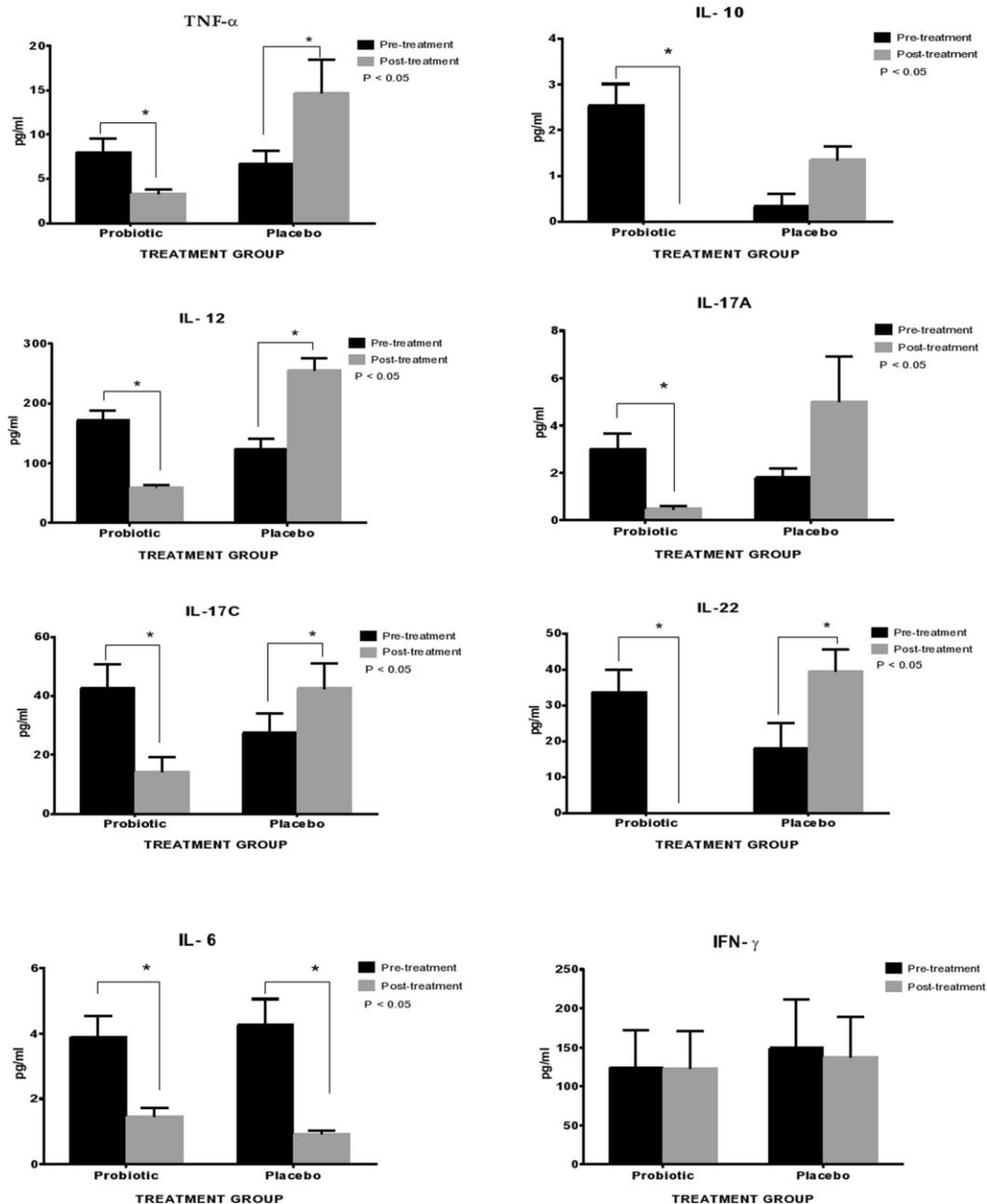
The results of the study showed that there was significant ( $P < 0.05$ ) decrease/reduction in the level of pro-inflammatory cytokine, TNF- $\alpha$ , IL-6, IL-10, IL-12, IL-17A, IL-17C and IL-22 observed in CRC patients who received HEXBIO® as compared to pre-treatment level. However, there was no significant difference in the IFN- $\gamma$  in both groups.

This study also showed that the consumption of HEXBIO® did not exacerbate diarrhoea in patients. However, there were no difference in the diarrhea severity among patients either taking HEXBIO® or placebo. No surgical infection occurred and no antibiotics were required.

Refer to Figure 1 for the level of circulating inflammatory cytokines baseline (pre-operative) and post intervention following six months of probiotics consumption.

## How significant are the benefits of reduced pro-inflammatory levels in CRC patients?

Raised levels of inflammatory markers may be found in many conditions, particularly infections, autoimmune conditions, and certain cancers. This study provides evidence on lactic acid “immunobiotics” effects in colorectal cancer patients where consumption of HEXBIO® twice daily for six months reduced the level of pro-inflammatory cytokines TNF- $\alpha$ , IL-17A, IL-17C, IL-22, IL-10 and IL-12 as well as prevented post-surgical complications in colorectal cancer patients. Probiotic has the ability to interfere with the signaling pathways, thus, effecting the level of cytokines production. These findings demonstrates that probiotic has a high potential to be a promising supplementary for colorectal cancer prevention and treatment.



**Fig 1.** The level of preoperative and post six months inflammatory markers between probiotics and placebo groups. The bar errors indicate the standard error of mean (SEM). Asterisk in the figure representing the strength of statistical difference within the groups at  $p < 0.05$