ASX Release

Phase II GaRP-IBS (Irritable Bowel Syndrome) trial

Internal analyses of data subsets following headline results suggest positive trends and benefit

Highlights

- **Following the completion of Stage 2 of Anatara's GaRP-IBS (Irritable Bowel Syndrome) Phase II trial, the headline results for the primary endpoints of safety and efficacy (a statistically significant reduction in IBS-SSS versus placebo) was announced on 17 April 2025. The results confirm that no safety concerns were observed, and although a sustained reduction (improvement) in IBS-SSS was clearly observed in the treatment arm, it did not reach statistical significance. Following an internal audit of the study, a number of *post hoc* analyses were conducted.**
- **These internal analyses examined many aspects of the ITT (Intent-To-Treat) group and confirmed pleasing trends in symptomatic relief of levels experienced in both pain and abdominal distension. With the IBS-SSS broken down into the 5 individual scoring sections, there is an apparent trend of pain and distension relief with the more subjective descriptive categories not showing a clear pattern of improvement.**
- **The overall IBS-SSS ("SSS" Symptom Scoring System) showed a consistent and sustained improvement, with a reduction of more than 40% observed in the treatment arm, but did not reach statistical significance when compared to placebo. This trend meant the secondary endpoint of at least a 20% reduction in IBS-SSS versus baseline was achieved.**
- **The secondary endpoint of improvement in anxiety scores reached statistical significance (P-value 0.034, Week 8), which influenced the significance of the overall HADS score (P-value 0.025 at Week 8), with depression scores remaining stable.**
- **IBS subset analysis of IBS-D (Diarrhoea only) versus IBS-Mixed did not reveal any apparent difference in treatment response.**
- **Gender did not appear to alter response. Trial site performance and efficacy in treatment groups appear consistent over Stages 1 & 2.**
- **The GaRP project value within the robust pre-clinical IBD (Inflammatory Bowel Disease) studies and the positive outcomes from the GaRP-IBS trial are being formalised for potential commercial discussions.**
- **The GLP-1 agonism focused "Anti-Obesity Project" proof-of-concept pre-clinical mice studies are tracking to schedule, with the project scope to be further determined by observations and milestones within 6 months.**

ADELAIDE, 16 May 2025: Anatara Lifesciences (ASX: ANR or "the Company"), a developer of evidence-based, innovative products to address significant unmet need in human health, with a particular focus on conditions that involve the complexity of the gastrointestinal tract (GIT), provides details on the Company's review of GaRP-IBS trial headline analysis following an extensive internal analysis of the data. The review has been an important priority with the anti-obesity project and appraisal of other opportunities continuing.

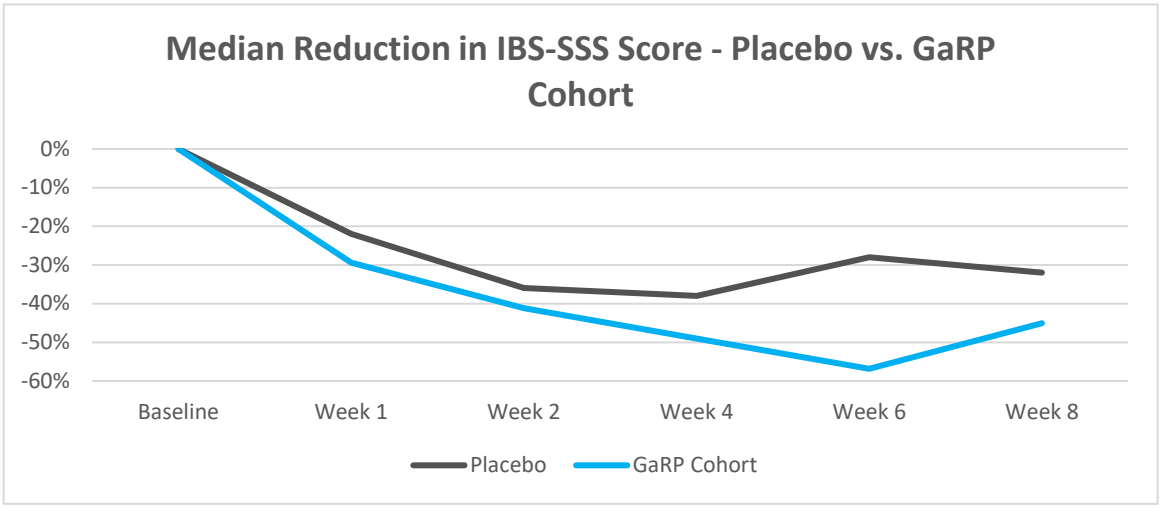
Headline analysis was of the primary endpoints of safety, including treatment related adverse events, and the IBS-SSS ("SSS" being Severity Scoring System) reduction compared to placebo. Secondary endpoints analysed included Adequate Relief (AR-IBS), Anxiety within the well-known HADS (Hospital Anxiety & Depression Scale) and at least 20% improvement in IBS-SSS compared to baseline.

Anatara met with the DSMB (Data Safety Monitoring Board) for the GaRP-IBS trial on the 15th April 2025. The DSMB confirmed the Company's interpretation that the results revealed no concerning safety signals and that the product was well tolerated. The Company noted the value of obtaining safety data, especially from a cohort of 78 participants assigned to the GaRP product treatment arms in a randomised, placebo-controlled, double-blind trial.

Anatara's Executive Chair Dr David Brookes commented: "*Following the formal independent statistical analysis, the Company has undertaken an extensive review of the trial data and procedures to ensure nothing has been overlooked in assessing the potential of the GaRP product. We have been very encouraged by the results of our internal review of the data when looking at subgroups and through the various scoring systems. It is pleasing to share these results, which will form the basis for any potential commercial interactions, as the treatment arm clearly outperforms the placebo when assessing symptom relief of pain and distension. Those who were involved are very much appreciated as this was a challenging trial and our review suggests that a simpler scoring system may have enhanced the experience and the results.*"

Headline Data Overview

The first graph has been previously released and demonstrates the anticipated strong placebo effect in the first 2 weeks. The mean reduction in the IBS-SSS appeared to be approaching significance before the Week 8 with the GaRP cohort having a greater improvement in symptoms. Week 8 is the last week of participants taking either the randomised placebo or product and the scoring from the cohort arms converge at the end of this week. An improvement in IBS-SSS of more than 100 points is sustained. The overall IBS-SSS was the main data used in the formal , independent statistical analysis of the efficacy primary endpoint. The following graph represents the modified ITT.



What is the IBS-SSS questionnaire? This scores the IBS symptoms by looking at 5 categories each with a maximum score of 100 to rate the IBS severity out of 500. The IBS severity is scored between 0-500 and then graded as "mild" 75-175; "moderate" 175-300; "severe" greater than 300. Scores <75 are considered IBS in remission or consistent with non-sufferers.

The scoring categories used were:

Question 1(a) – Establishes pain background. *"Do you currently (in the past 10 days) have or suffer from abdominal(stomach) pain?"* If the answer is "No" the participant scores zero and skips to Question 3(a).

Question 1(b) -Establishes severity of pain. *"How severe was your abdominal (stomach) pain in the past 10 days? "* (Please indicate a number from 0 to 100, with 0 meaning "no pain" and 100 meaning "very severe pain")

Question 2- Establishes the frequency of pain experienced. *"Please enter the number of days you had the abdominal pain in the past 10 days."* (For example, if you enter 4 it means that you had pain 4 out of 10 days. If you have pain every day, enter 10.) 1 pain day is scored as 10 points and so on, with all 10 days being the maximum of 100 points etc

Question 3(a) -Establishes the frequency of abdominal distension (bloating). "*Do you currently (in the past 10 days) suffer from abdominal distention (bloating, swollen or tight stomach)?" NB Female participants are asked to " Please ignore distention related to your period when answering this question".* If the answer is "No" the participant scores zero and skips to Question 4.

Question 3(b)-Establishes the severity of the distension/bloating. *"How severe was your abdominal distention/tightness in the past 10 days?" (Please indicate a number from 0 to 100, with 0 meaning "no distention" and 100 meaning "very severe distention")*

Question 4- Establishes a level of satisfaction with bowel function. *"How dissatisfied are you with your bowel functioning in the past 10 days?" (Please indicate a number from 0 to 100, with 0 meaning "Not dissatisfied" and 100 meaning "very dissatisfied")*

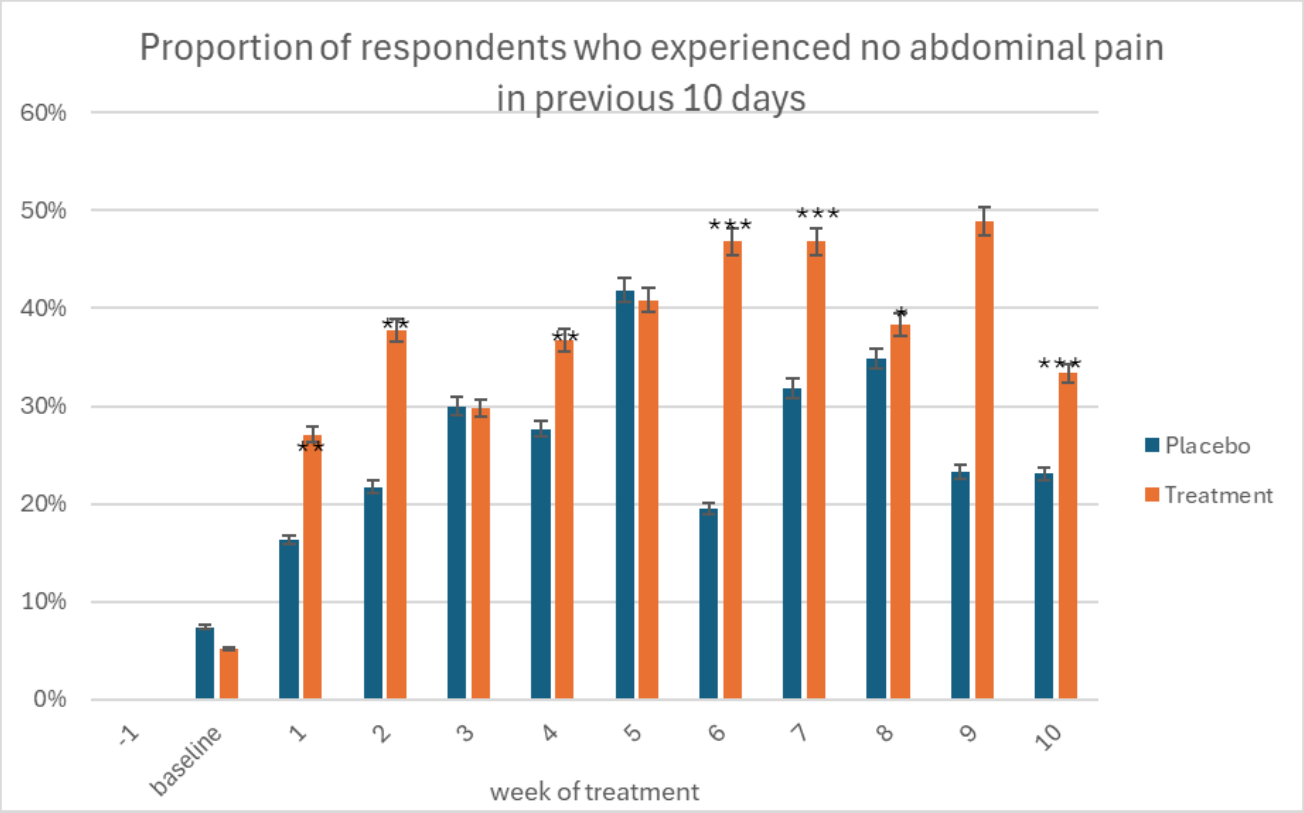
Question 5-Establishes the interference of symptoms and bowel habit on lifestyle. *"How much did abdominal pain or discomfort or altered bowel functioning affect or interfere*

with your life in general in the past 10 days?" (Please indicate a number from 0 to 100, with 0 meaning "Not at all" and 100 meaning "completely")

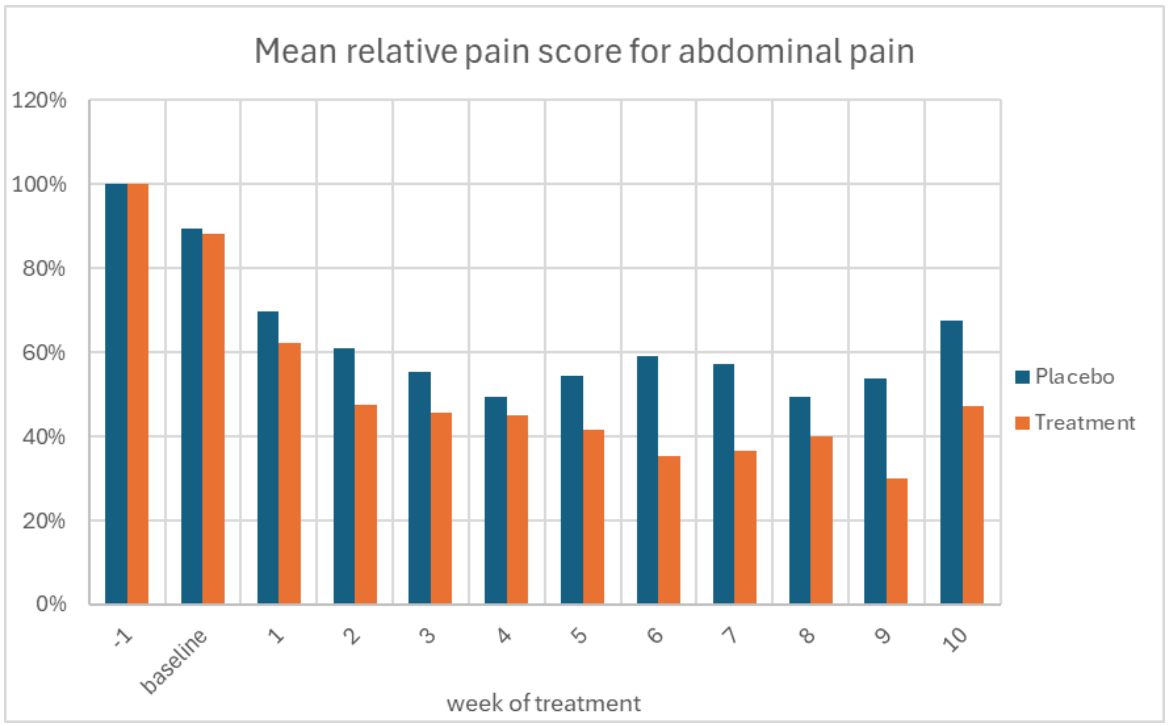
These **5 sections of the IBS-SSS scoring questionnaire**, each with a maximum score of 100, were assessed individually to determine efficacy signals and whether the overall scoring system may have blunted potential treatment signals.

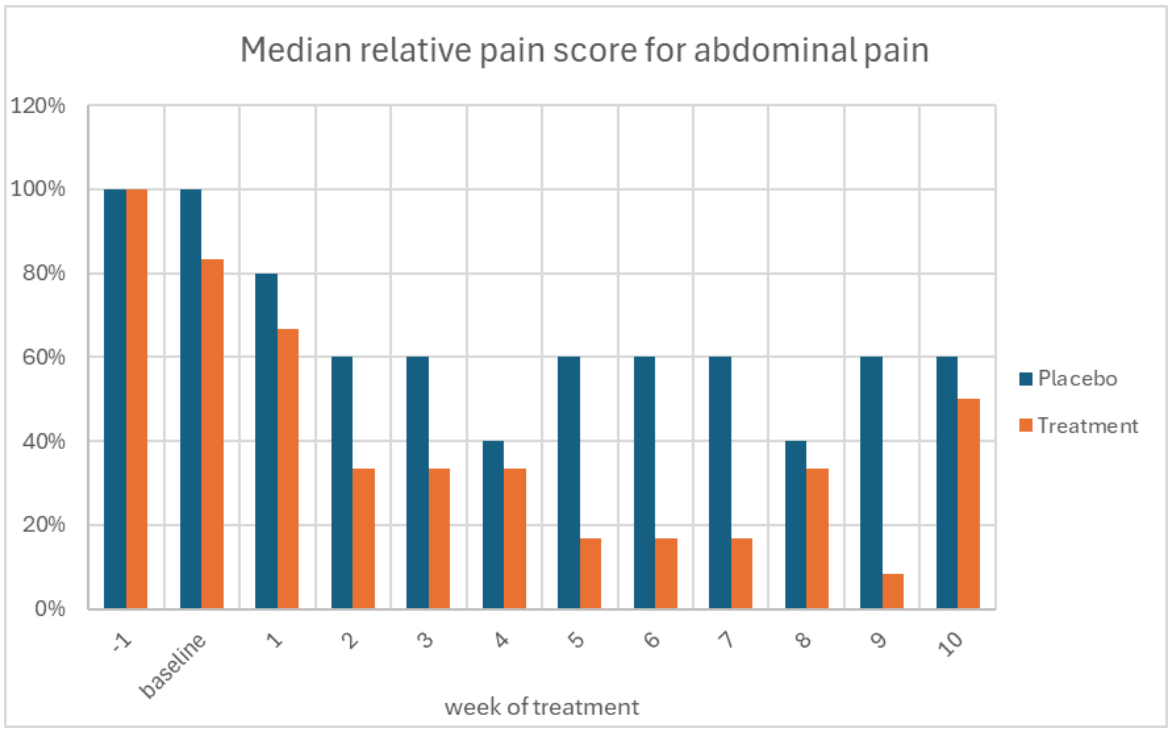
The internal analysis of each of these 5 questions in the IBS-SSS survey, to identify potential confounding influences, unfolded as follows:

Question 1a – Do you currently or have you in the past 10 days suffered from abdominal pain?
This is a binary (yes/no question). The results suggest treatment with GaRP results in statistically significant increase in "no pain" reported than placebo as recorded for weeks 1, 2, 4,6, 7, 8, 9 and 10

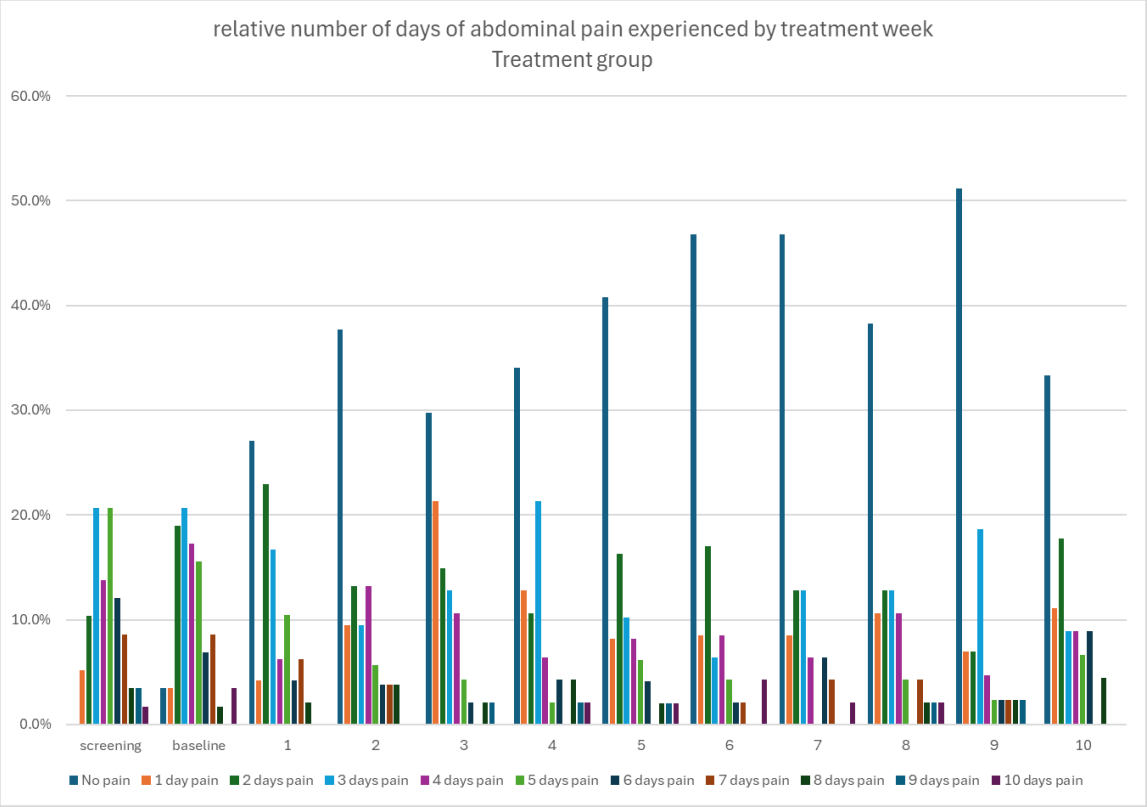


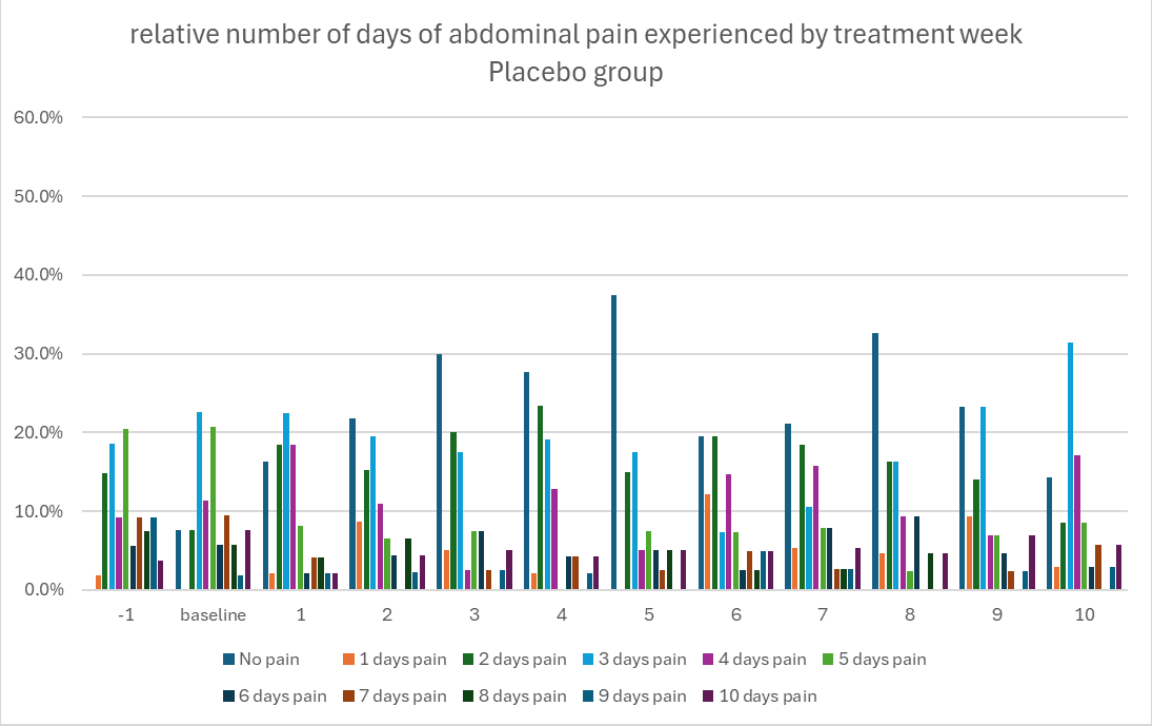
Question 1b – Participants who reported pain were asked to indicate the severity. If no pain was recorded in Q1(a) then a severity score of zero was assigned.



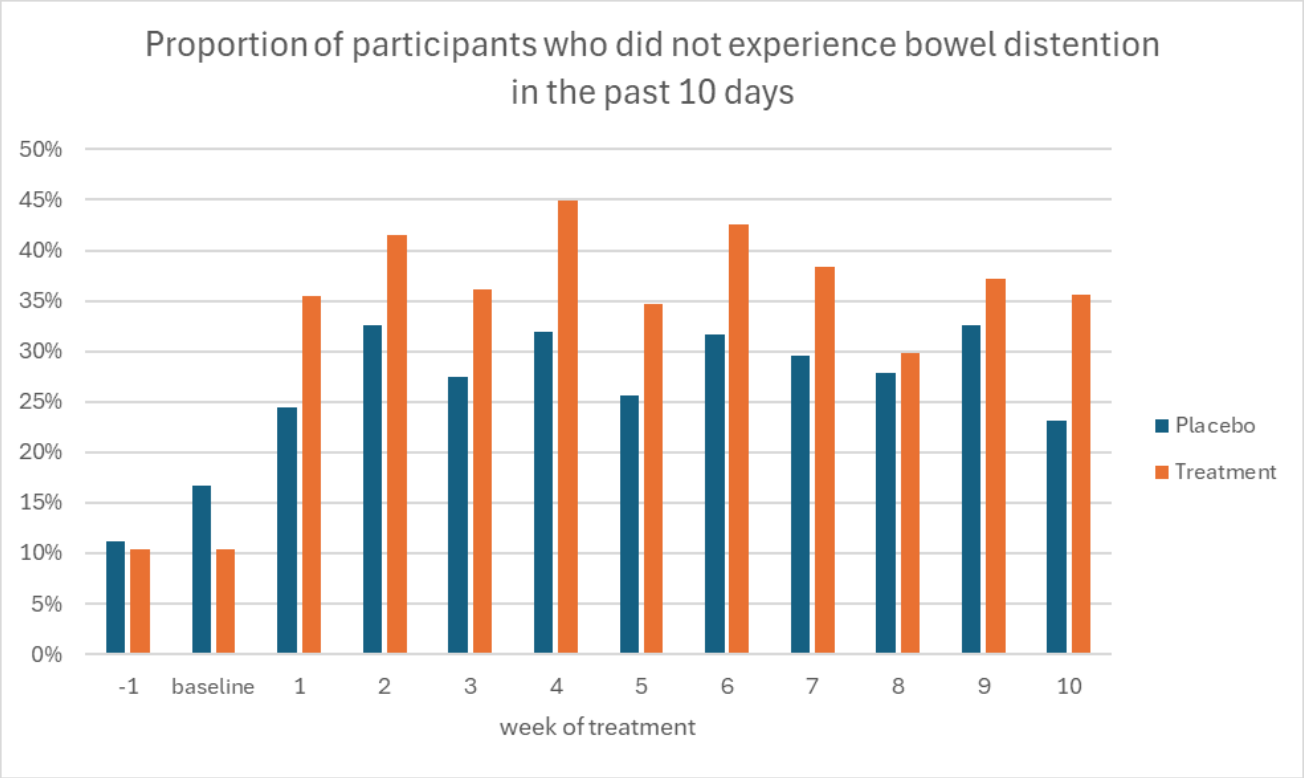


Question 2 continued – Average Number of days of pain is not the whole story! Next, we analyzed the frequency of pain days. Treatment resulted in a meaningful reduction in days with pain (i.e., the "No pain" days experienced over the last 10 days increased which indicates reduced pain experience.)



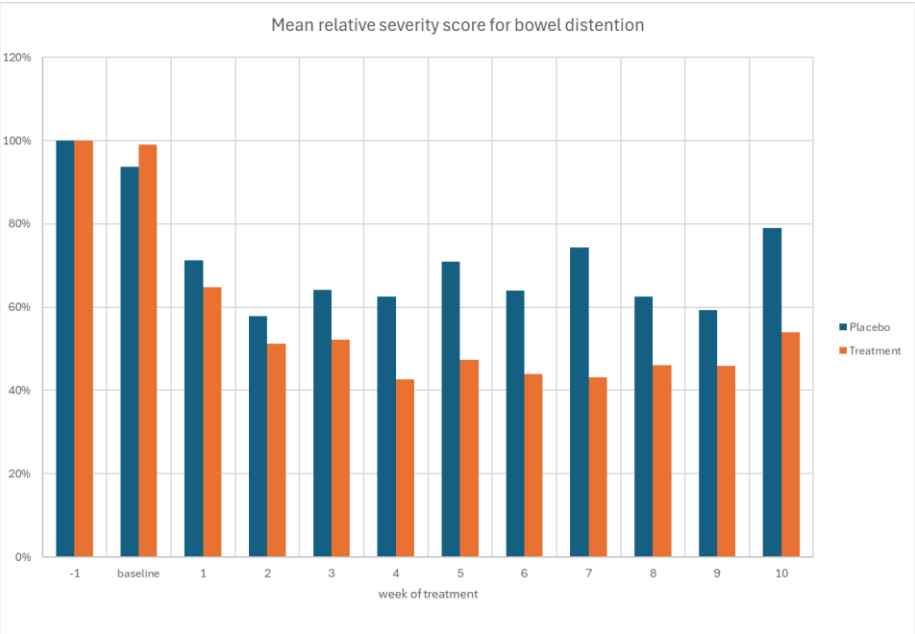


Question 3a – Do you currently or have you in the past 10 days suffered bowel distention?

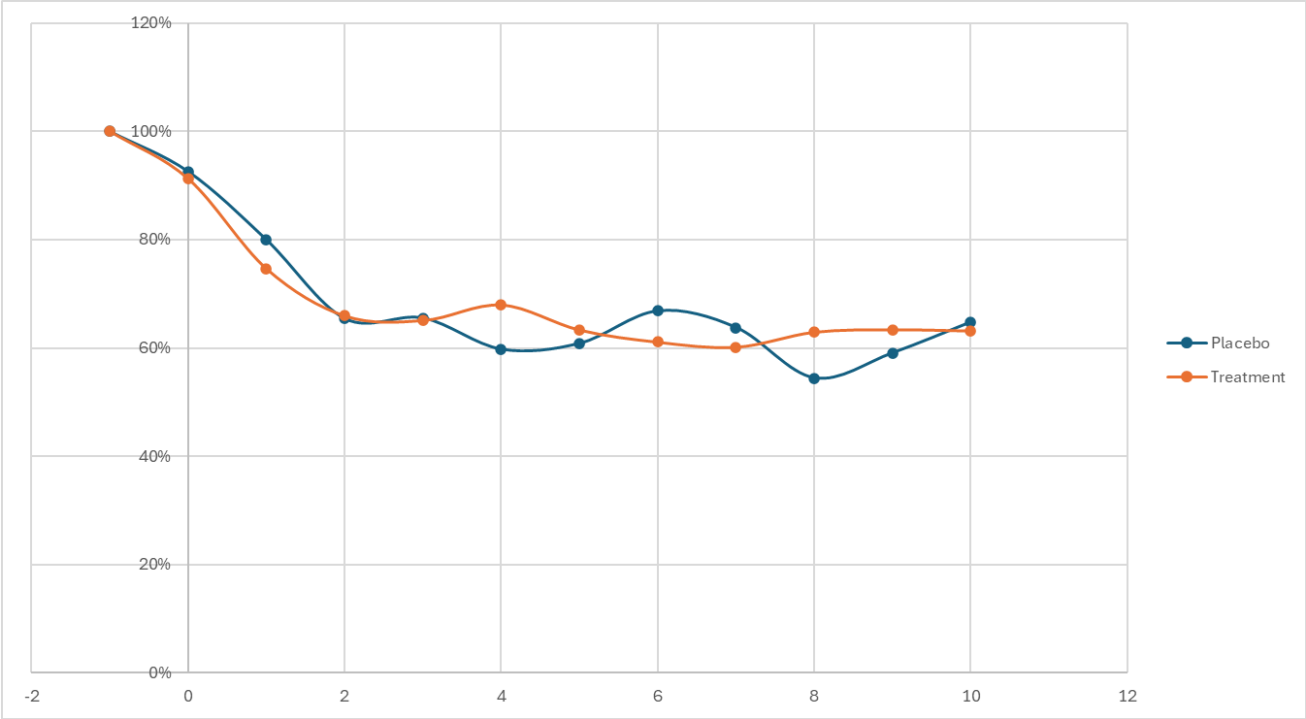


Over the study period (weeks 1 to 10 inclusive) 38% of participants in the Treatment group versus only 29% of participants in the placebo group reported NO bowel distention.
95% confidence intervals 27% - 31% Placebo and 35.4% - 41.6% Treatment.

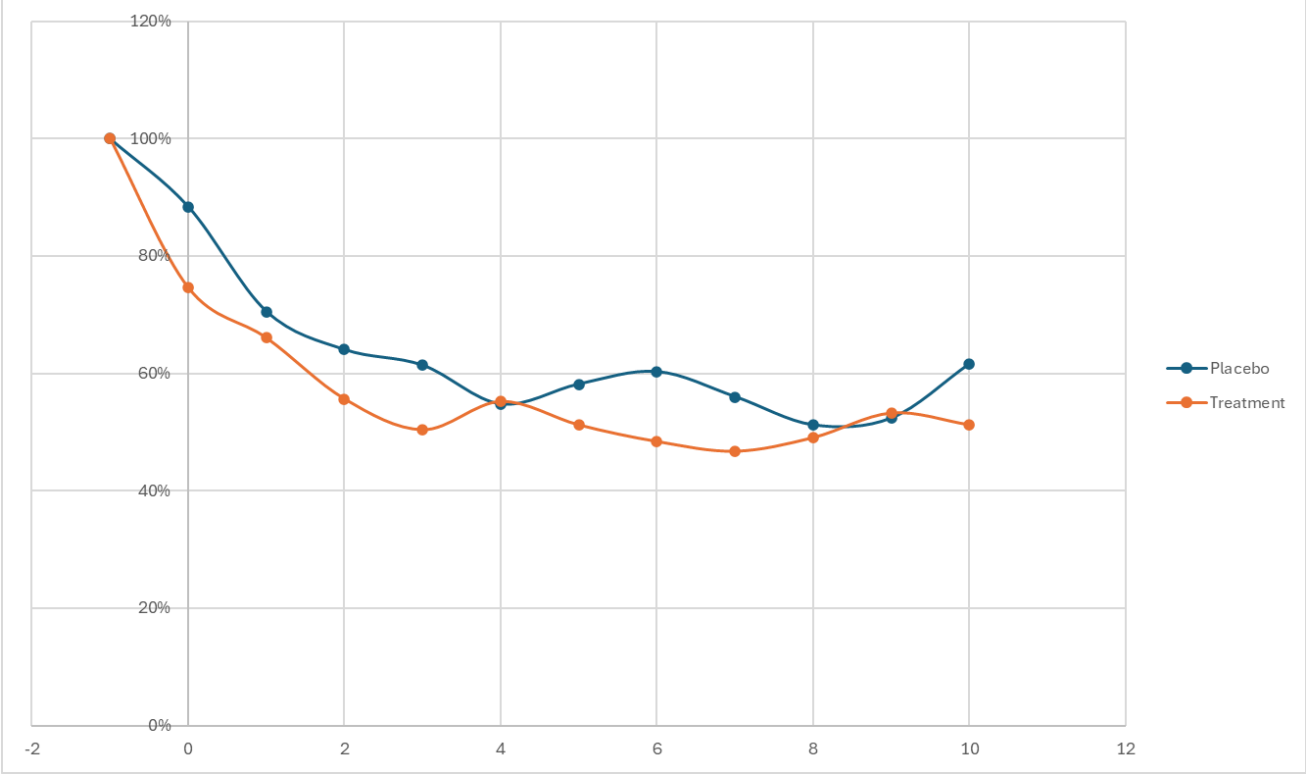
Question 3b – The relative severity of bowel distension was recorded. Participants who answered "No" to Q3(a) were given a zero score for severity.



Question 4 – How dissatisfied are you with your bowel functioning in the past 10 days?



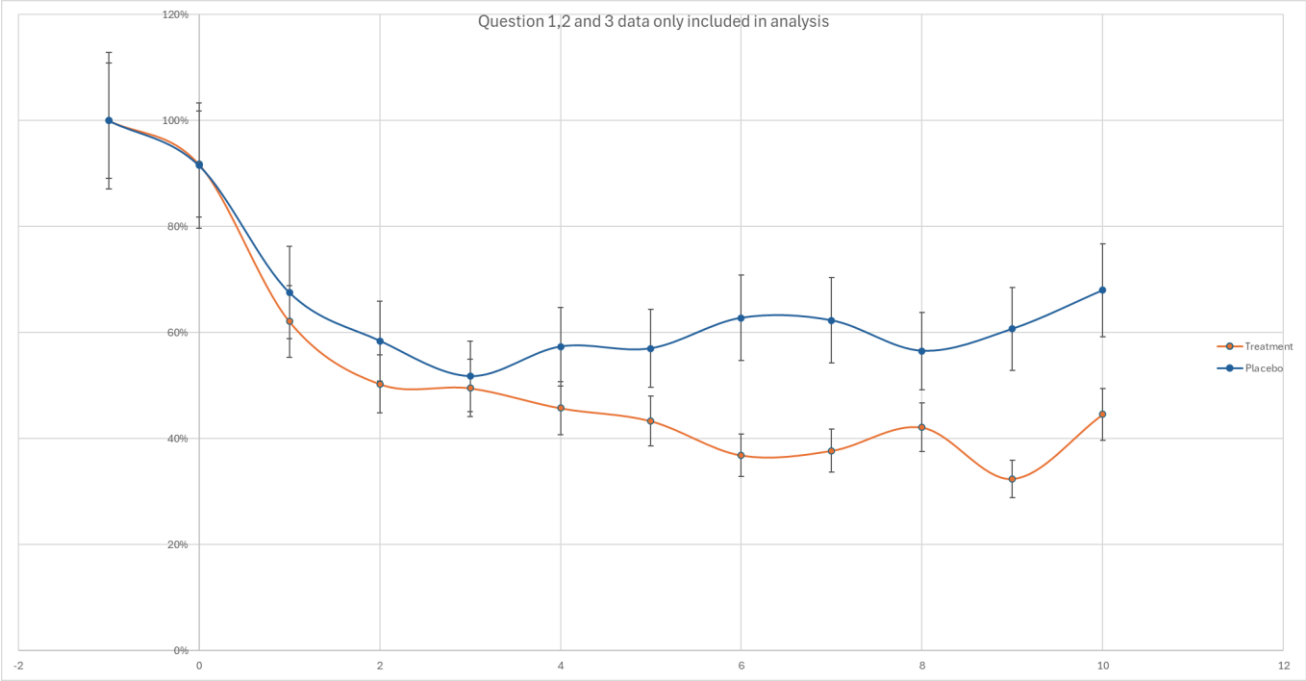
Question 5 – How much did abdominal pain or discomfort or altered bowel functioning affect or interfere with your life in general in the past 10 days?



Despite significant improvements in pain and bowel distention, participants expressed no difference in satisfaction of bowel function or the impact on their life. Questions 4 and 5 appear to confound the result presumably because the underlying disease is still present with a level of symptomatology.

Responders to Q1(a) *did you experience pain in the past 10 days* with a "No" are progressed to Q3(a)– skipping the severity and frequency questions. This reduces the number of participants in the formal headline analysis who then answer Q1(b) and Q2, while biasing the scores in Q1(b) and Q2 towards participants who experienced pain. In this analysis, participants who answered "No" to Q1(a) were assigned the lowest pain score in Q1(b) and the lowest frequency in Q2 (no incidents), thereby removing this bias. Similarly, for Q3(a) *did you experience bowel distention in the past 10 days*, participants were assigned the lowest score for Q3(b) (i.e. no distention).

Analysis of IBS-SSS Q 1, 2 and 3 only, removing confounding Q4 and Q5 data



95% confidence intervals shown as error bars

This graph of IBS-SSS on removing Q4 & Q5 suggests a significant improvement of more than **50%** in the treatment group for pain and distension. The more subjective nature of Q4 & Q5 are shown to track similarly for both the treatment and placebo cohorts and contribute to 40% of the traditional IBS-SSS. These questions clearly blunt the overall result of improvement that is seen in the combined Q1, Q2 & Q3 analysis graph. This highlights the difficulties of a trial for a condition without biomarkers and these more subjective scoring points impair the overall efficacy result for the GaRP-IBS trial. Achieving statistical significance using traditional IBS-SSS as the primary efficacy endpoint may have only been possible with greater numbers.

SECONDARY ENDPOINTS – Hospital Anxiety & Depression Score (HADS)

Hospital Anxiety and Depression Scale (HADS) is a 14-item self-reported measure that was specifically developed to assess anxiety and depression in people with medical illnesses. It has two subscales, which evaluate anxiety and depression.

Scoring: (for Depression and anxiety):

0-7 = Normal
8-10 = Borderline abnormal (borderline case)
11-21 = Abnormal (case)

Secondary Endpoint – Hospital Anxiety & Depression Score (HADS) Tables

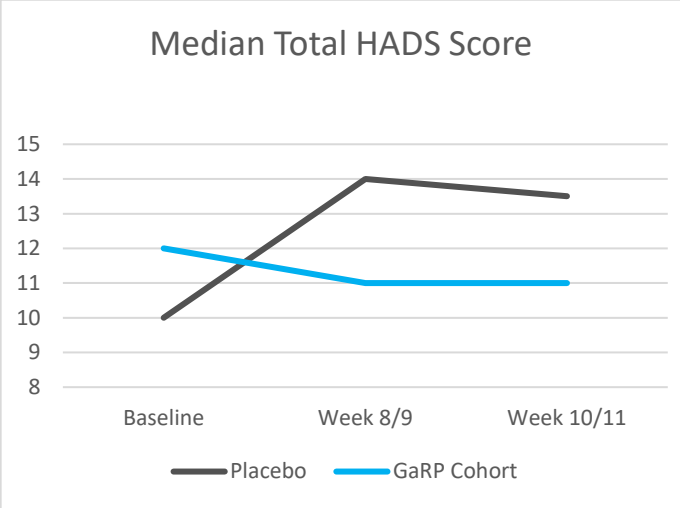
The next graphs show the statistically significant improvement in background anxiety scores, which is incorporated in the combined HADS score. Depression scores remain in the normal range and hence the conclusion is that there is no adverse emotional effect with the benefit of improving mild background anxiety for those participants on GaRP. This is encouraging data and consistent with the mechanism of action of the GaRP product being designed to assist repair and maintenance of the gastrointestinal tract as a barrier, as well as the homeostasis and dynamics of microbiome.

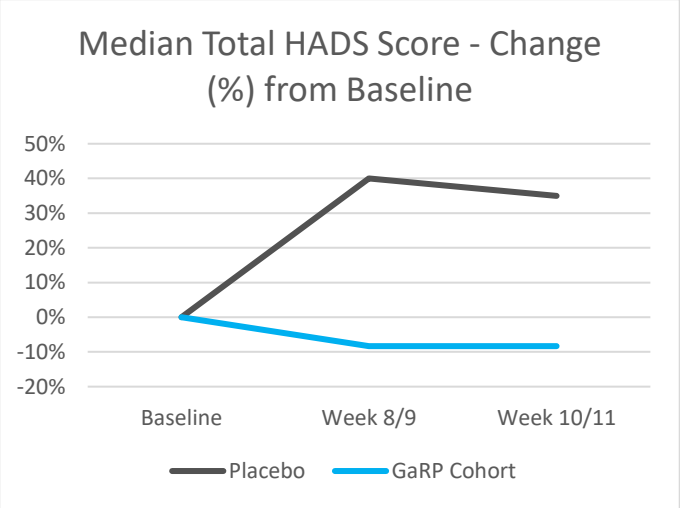
Median Total HADS Score – Baseline to week 10/11		
	Placebo	GaRP Cohort
	n=56	n=57
Baseline	10	12
Week 8/9	14	11
Week 10/11	13.5	11
Change from Baseline	**3.5**	**-1**
Change from Placebo		**(P=0.014)**

Median Total Anxiety Score – Baseline to week 10/11		
	Placebo	GaRP Cohort
	n=56	n=57
Baseline	7	9
Week 8/9	8	7
Week 10/11	8.5	7
Change from Baseline	**1.5**	**-2**
Change from Placebo		**(P=0.024)**

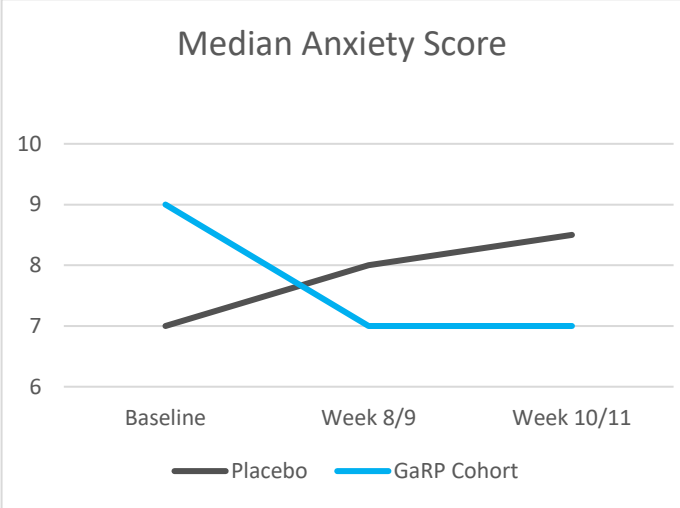
Total Hospital Anxiety & Depression Score (HADS)

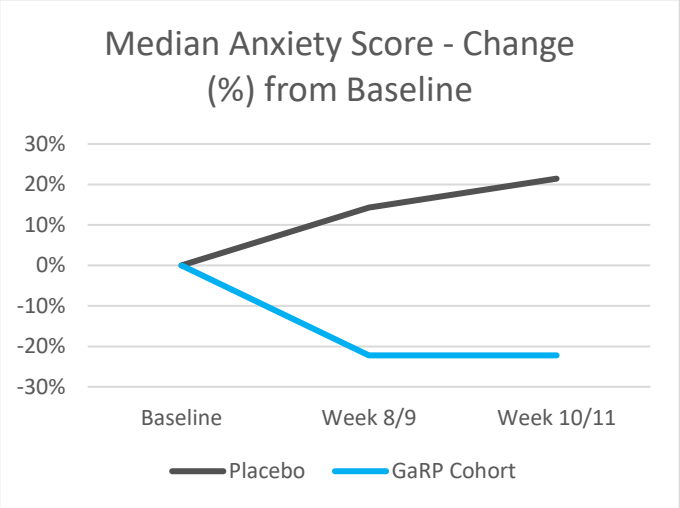
Baseline to week 10/11





Anxiety Scores Baseline to week 10/11





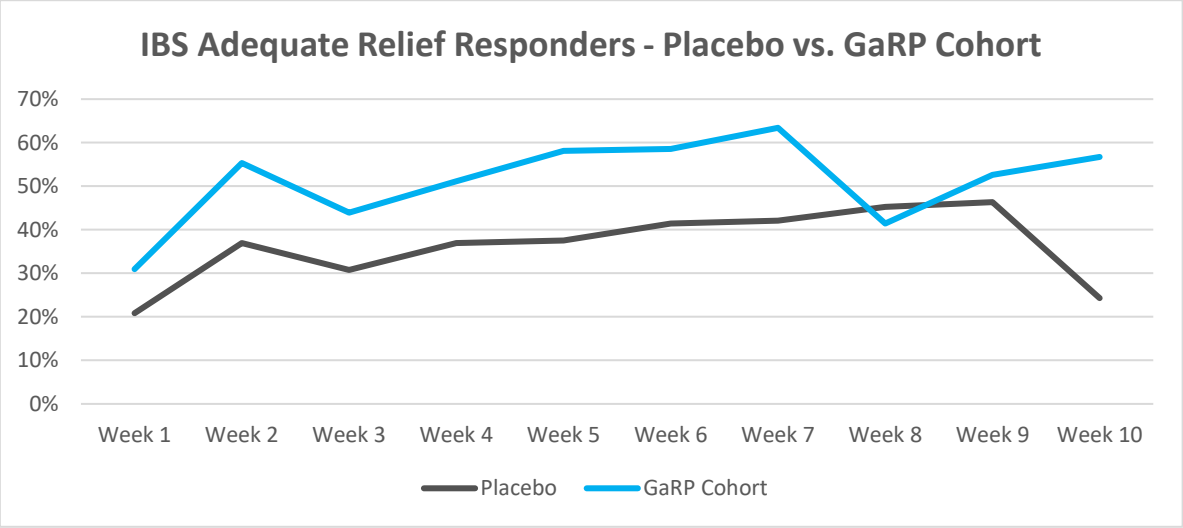
SECONDARY ENDPOINTS- Adequate Relief (AR)

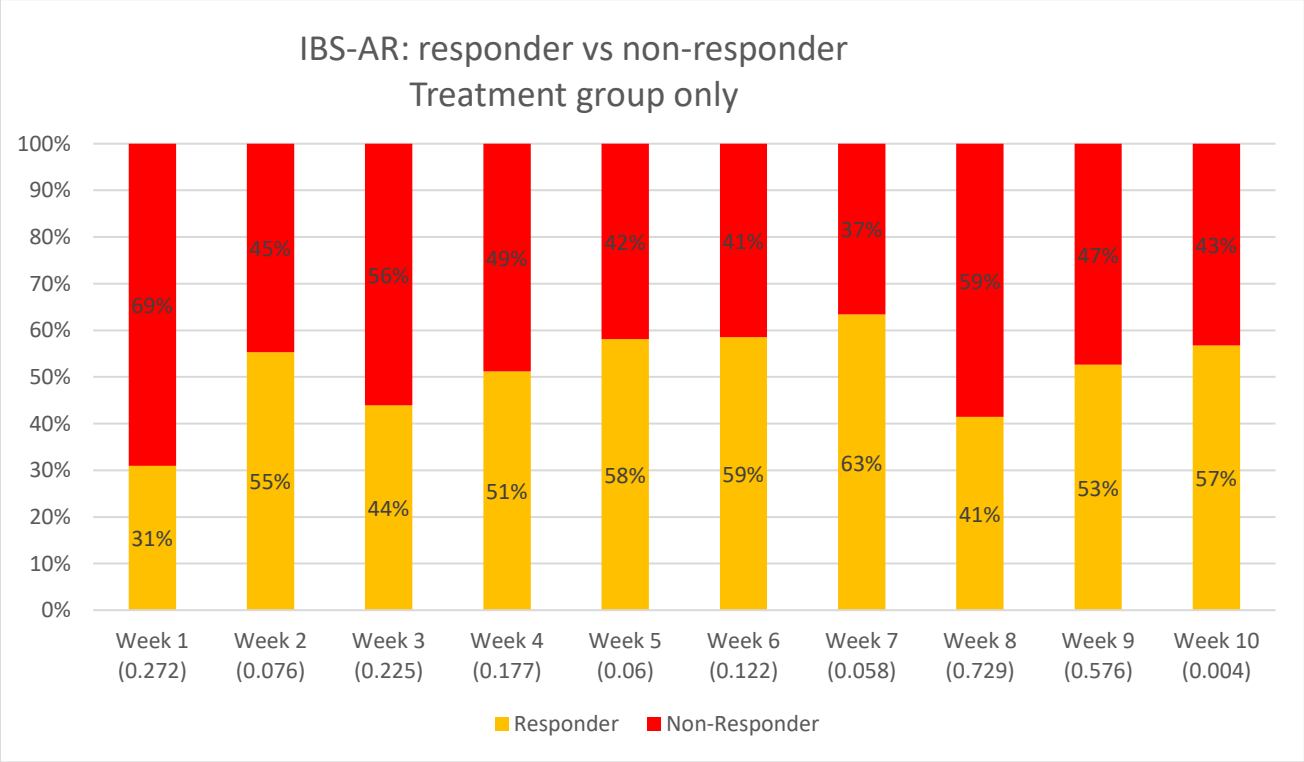
Adequate Relief for IBS Overview

The Adequate Relief for IBS (AR-IBS) graph highlights many of the observations and interpretation dilemmas. Again, there is separation with the GaRP cohort performance superior until the end of Week 8, in which the participants know it is the last week of observational recording while randomised to either the placebo or the GaRP treatment. There are no biomarkers for objective assessment of IBS disease activity and the scoring systems are subjective and drawn out. (i.e. AR-IBS simply answer, do you feel better or improved on what you are taking?)

The "Adequate Relief Responders "graph demonstrates the convergence seen in IBS-SSS at Week 8 and then an apparent sustained benefit that is statistically highly significant.

By Week 10, which is 2 weeks on from having ceased taking the product or placebo, the active treatment GaRP cohort arm maintains a perception of having had an "adequate response" and it is statistically highly significant versus placebo. This can be extrapolated to support the GaRP mechanism of action of restoring and maintaining the gastrointestinal tract lining as a barrier and the homeostasis of the microbiome dynamics, thereby maintaining a response post-treatment.





Q. Over the past week (7 days) have you had adequate relief of your IBS symptoms? YES/NO

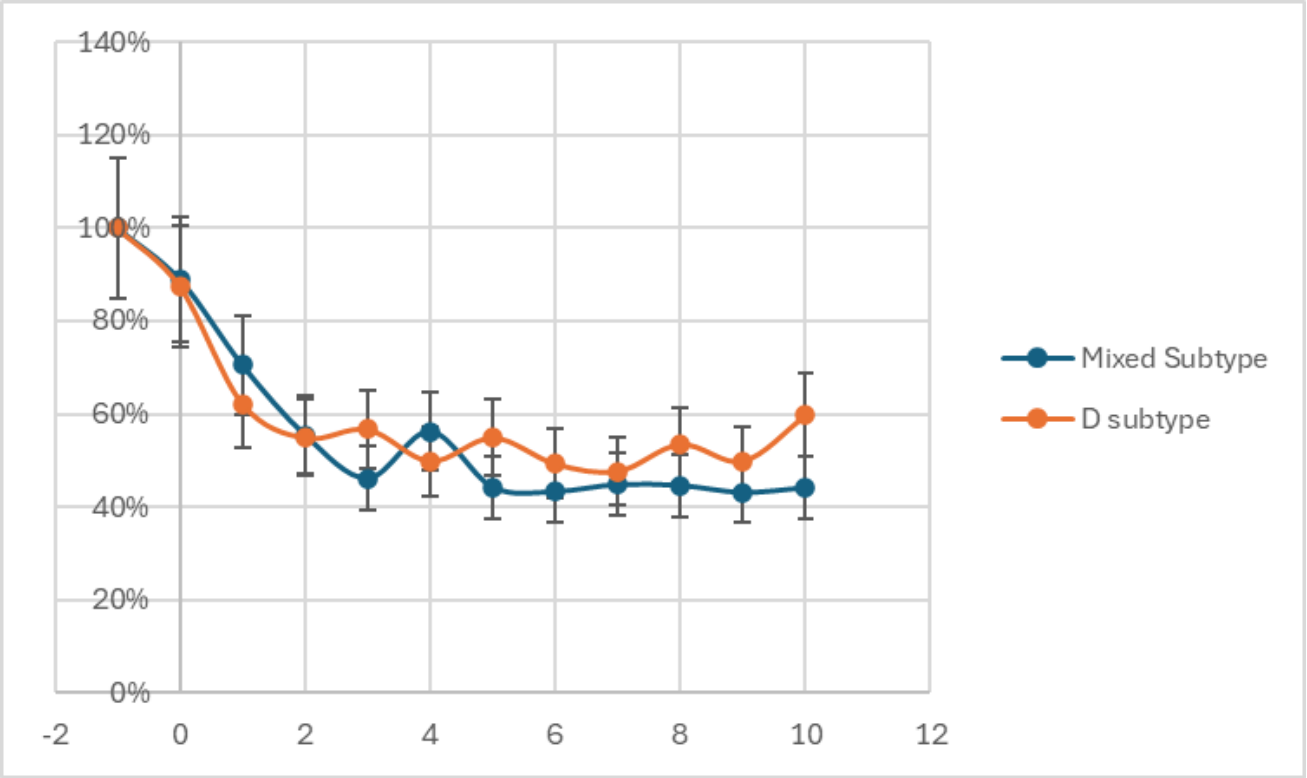
- → Treatment Arm: at weeks 2, 4, 5, 6, 7, 9, 10, **more than 50%** of participants responded that they **did have adequate relief** from IBS symptoms (*refer graph above)
- → Placebo Arm: at each timepoint, more than 50% of participants responded that they **did not have adequate relief** from IBS symptoms (*no graph)

ROME IV subtypes of IBS & could the modification to recruitment trial during Stage 1 have compromised the efficacy endpoint? To expedite recruitment, the inclusion criteria in the trial protocol was changed during Stage 1 from only the IBS-D subtype to include IBS-M.

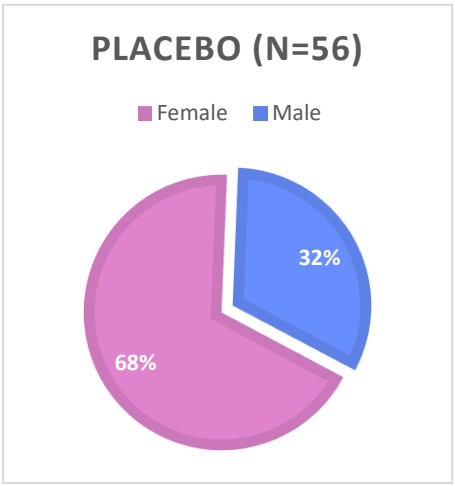
Total participants

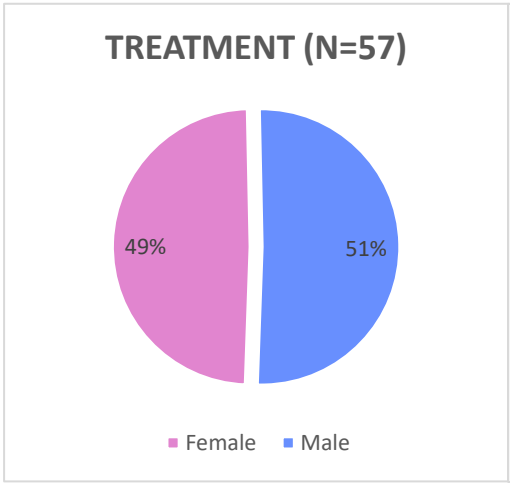
	Stage 1	Stage 2	Combined
% IBS-D	68.4	55.1	59.8
% IBS-M	31.6	44.9	40.2

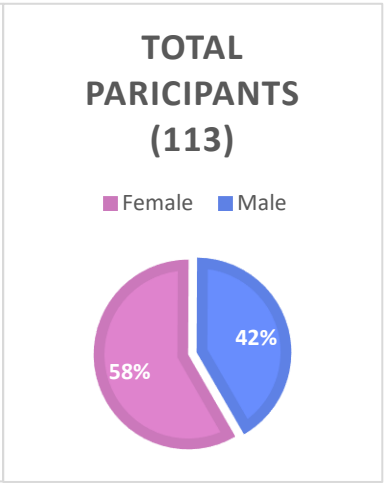
Reduction in IBS-SSS in the trial treatment group separated into IBS-M (Mixed pattern) versus IBS-D (Diarrhoea only)- showing no apparent significant difference in responsiveness to the GaRP product.

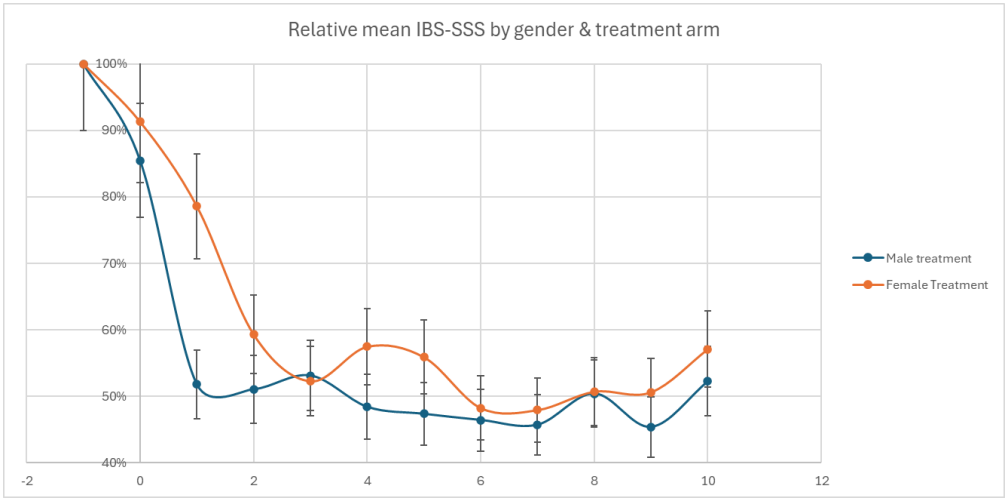


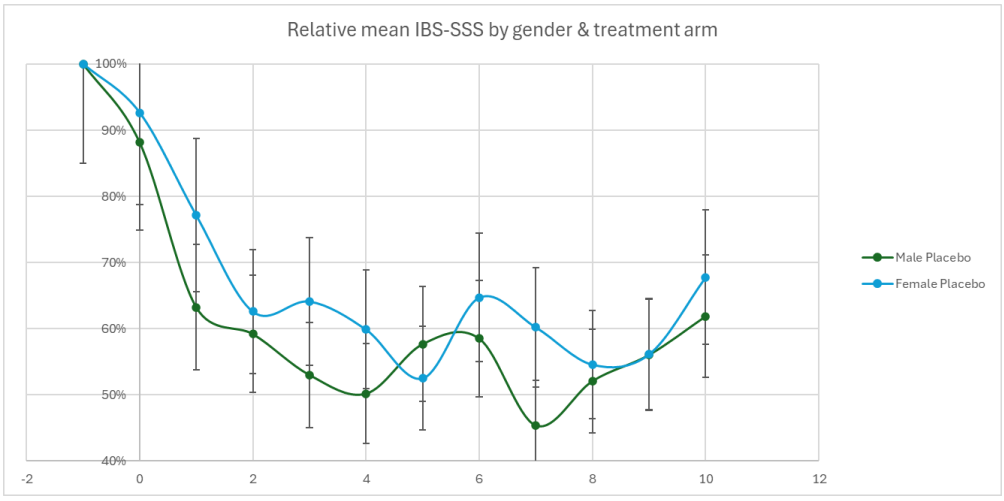
DEMOGRAPHICS -did gender influence result? The product appears to have a similar effect in females & males. (Noting the graphs are overall IBS-SSS)





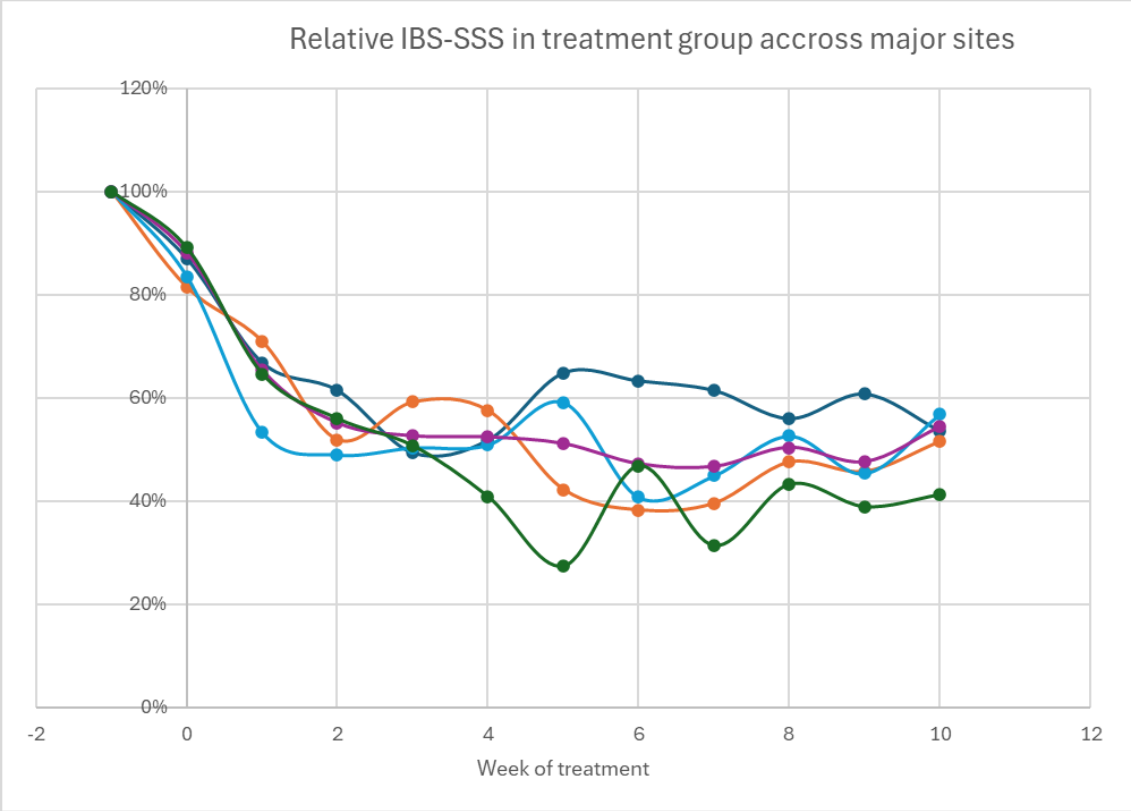






Could trial time delays or trial sites have impacted on the endpoint of efficacy?

This slide shows the major sites for the trial across Stages 1 & 2. Importantly, there is a trial site provider represented that only participated in Stage 1 and another group that only participated in Stage 2. There does not appear to be a significant difference. This also reinforces observations around product stability, activity and shelf-life.

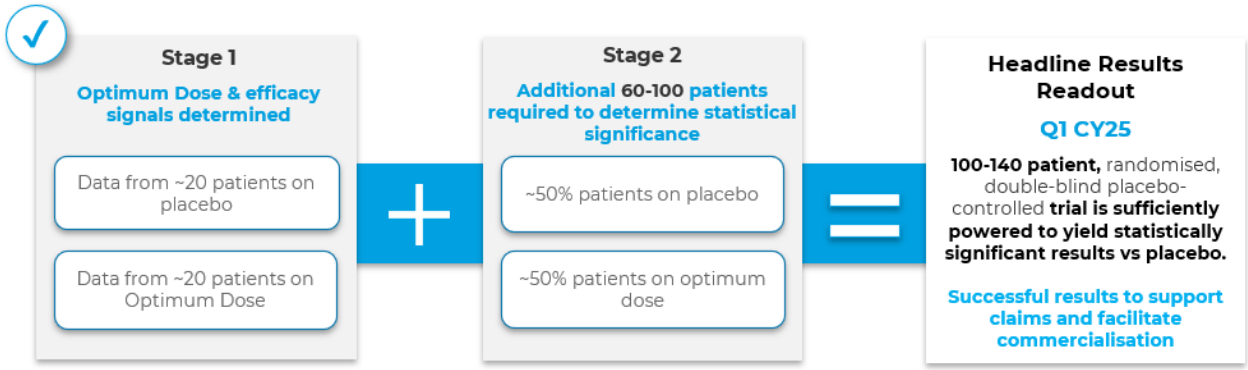


Stage 2 of the GaRP-IBS trial was the planned extension of the Phase II trial that followed the successful completion of Stage 1 which reported on 20 patients with a greater than a 50% reduction in IBS symptoms and with safety profile confirmed. Stage 2 was hoped to confirm the highly encouraging and clinically meaningful interim results from Stage 1 of the GaRP-IBS clinical trial which created partnering interest.

On the 14th January in the Quarterly Activities Report, the Company announced the Stage 2 enrolment number in the GaRP-IBS trial being confirmed as 71 Intent-To-Treat (ITT) participants. The trial participant numbers were in line with Company expectations, even after determining a fully assessable modified-ITT data set of 62 participants for IBS-SSS after taking into consideration those with an unacceptably low IBS-SSS at baseline. Hence, the Company analysed both the full ITT group and a modified-ITT that only included participants in the trial with a baseline IBS-SSS score equal to or greater than 150 at the commencement of trial involvement. The trial protocol had the IBS-SSS parameters of 175-350 in screening for eligibility to participate in the trial process. Anatara previously announced the intention to review data from the trial across a number of participant subsets, including criteria such as IBS-D (Diarrhoeal only) versus IBS-M (mixed diarrhoea and constipation) to further the understanding of the results and potential for the product.

The data from both Stages of the trial formed the basis of the completed data for the final analysis. The sub-groups of participants from Stage 1 are included with eligible participants from Stage 2 for the final analysis, which resulted in a total of approximately 100 participants in the modified-ITT analysis. The trial was intended to be sufficiently powered to deliver statistically significant results versus placebo. (Please see further detail on the Trial Design and GaRP below)

GaRP-IBS Clinical Trial Design



About GaRP

Anatara's GaRP product is a multi-component, multi-coated complementary medicine designed to address underlying factors associated with chronic gastrointestinal conditions such as IBS and IBD. GaRP is the working name for the product from the Company's Gastrointestinal ReProgramming project that was designed to assist restoration and maintenance of the gastrointestinal tract (GIT) lining as a barrier and assist the homeostasis of the microbiome. The product is made of GRAS (Generally Regarded As Safe) components.

Progress of Anti-Obesity Project

The planned *in-vivo* pre-clinical experiments, that have ethics approval, are underway with the University of Newcastle, as previously advised. The initial studies are anticipated to take approximately 6 months through to completion, depending on the observations of markers and weight control in the initial animal (mice) studies. The study length with the need for further mice cohorts will be determined on scientific outcomes and milestones, and these may extend the overall study a further few months.

The anti-obesity project has been designed to develop an oral medication to assist weight reduction and sustaining weight control in conjunction with other contemporary treatments and approaches. Specifically, the product is being developed with the target of assisting the maintenance of weight loss and limiting rebound weight gain following cessation of contemporary weigh loss medications.

While the Company needs to protect the project at this early stage, the mechanism of action involves the stimulation of endogenous GLP-1. The Company will assess several compounds of interest (that have been sourced/manufactured) in the pre-clinical studies to determine the best candidate/s going forward. The candidate compounds selected have been shown to target the same biochemical mechanism that is the focus of the Proof-of-Concept (POC). The dosage regimes have been predicted from published pre-clinical and clinical studies. The Company has allocated more than $350,000 to the POC studies for the anti-obesity project and will determine further steps as the results of these initial studies are assessed.

While committed to the Anti-Obesity Project Proof of Concept studies, the Company continues to assess other opportunities and directions. The summarisation of the GaRP project pre-clinical and clinical work has been a priority to enhance the understanding of the commercial possibilities for the GaRP product in gastrointestinal health. The patent position for the GaRP project is current and remains protected. The Company is still of the view that the product has the potential for broad indications, including in the management of a healthy gut-brain axis, and may attract commercial interest.

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About Anatara Lifesciences Ltd

Anatara Lifesciences Ltd (ASX:ANR) is developing and commercialising innovative, evidence-based health products where there is significant unmet need. Anatara is focused on building a pipeline of human health products with a particular focus on conditions that involve the complexity of the gastrointestinal tract. Underlying this product development program is our commitment to delivering real outcomes for patients and strong value for our shareholders.

Disclaimer

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