Responsiveness of the Work Productivity and Activity Impairment questionnaire for irritable bowel syndrome with constipation (WPAI:IBS-C) to clinically meaningful change

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ABSTRACT

Objective: The work productivity and activity impairment measures of the Work Productivity and Activity Impairment questionnaire for irritable bowel syndrome (WPAI:IBS) have been shown to discriminate among patients with different disease severity. The purpose of this investigation was to test the responsiveness of these measures to clinically meaningful changes in symptom severity among IBS patients with constipation (IBS-C)

Methods: Female patients (18–65 years old) who met Rome II criteria for IBS, excluding those with frequent diarrhea, were assessed during a randomized, double-blind, placebo-controlled, multicenter study of tegaserod 6 mg b.i.d. or placebo for 4 weeks. Absenteeism, presenteeism, overall work productivity loss, and activity impairment due to IBS symptoms during the previous 7 days were measured with the WPAI:IBS-C, which excludes diarrhea as an IBS symptom. Patients were classified as responders at Week 4 if they reported satisfactory relief of abdominal discomfort/pain, or relief of overall IBS symptoms in at least 3 of the 4 treatment weeks. The association between WPAI:IBS-C scores and responder status was tested using a Cochran-Mantel-Haenszel test stratified by treatment group

Results: A total of 2,660 women were randomized and of these 1,675 (tegaserod [n=1,363], placebo [n=312]) were employed and completed WPAI:IBS-C questionnaires. At Week 4, compared to non-responders, responders with relief in abdominal discomfort/pain reported significant reductions in absenteeism (p=0.02), presenteeism (p<0.0001), overall work productivity loss (p<0.0001), and activity impairment (p<0.0001). When overall IBS symptom relief was considered, compared with non-responders, responders reported significant reductions in all measures (p<0.0001), except absenteeism where the reduction was not significant

Conclusion: The WPAI:IBS-C work productivity and activity impairment measures are responsive to clinically meaningful change in IBS symptom severity and are useful tools for measuring outcomes in IBS-C

BACKGROUND

- Irritable bowel syndrome (IBS) is a chronic and episodic gastrointestinal motility and sensory disorder characterized by abdominal pain or discomfort, bloating and altered bowel habit (constipation, diarrhea, or alternating periods of both)
- IBS has a significant negative impact on patients' quality of life by restricting their daily routines, social lives, personal relationships and emotional well-being[1]
- IBS symptoms can also have a detrimental effect on sufferers' work productivity. The indirect costs associated with absenteeism (missed days of work) and presenteeism (reduced on-the-job effectiveness) attributable to IBS are estimated to be as high as $20 billion[2]
- To assess the effectiveness of IBS treatment interventions on reducing work productivity and daily activity impairments, valid and responsive measures are needed

BACKGROUND (cont'd)

- The Work Productivity and Activity Impairment questionnaire for IBS (WPAI:IBS) measures absenteeism, presenteeism, overall work productivity loss (absenteeism plus presenteeism), and daily activity impairment due to IBS symptoms during the previous 7 days[3]
- The WPAI:IBS has been validated against three measures of IBS disease severity: retrospective diaries, a debriefing questionnaire, and other self-report measures of work and activity impairment,[3] but its sensitivity to detect clinically meaningful changes in IBS disease severity is not known

OBJECTIVE

- The aim of this study was to evaluate the responsiveness of the WPAI:IBS, modified to exclude diarrhea as an IBS symptom (WPAI:IBS–C), to clinically meaningful changes in IBS-C symptoms

METHODS

- Women (18–65 years of age) meeting Rome II criteria for IBS-C were randomized in a double-blind, placebo-controlled, multicenter study of tegaserod 6 mg b.i.d. or placebo (ZENSAA: Zelnorm® in Europe, North and South America and Africa).[4] The study comprised a 2-week treatment-free baseline period and two 4-week, double-blind treatment periods (P1, P2), separated by a treatment-free interval
- Patients completed the WPAI:IBS-C at baseline and at Weeks 2 and 4 of P1
- Patients were classified as responders at Week 4 of P1 if they reported relief of overall IBS symptoms or satisfactory relief of abdominal discomfort/pain in at least 3 of the 4 treatment weeks
- Extended Cochran-Mantel-Haenszel tests, stratified by treatment group, were used to assess whether the WPAI:IBS-C could discriminate between patients whose IBS symptoms clinically improved (responders) and patients whose IBS symptoms did not improve (non-responders), regardless of treatment group
- Analyses were based on the intent-to-treat (ITT) population who completed the WPAI:IBS-C

RESULTS

Patient characteristics

- A total of 2,660 women were randomized in P1; 2,135 received tegaserod and 525 received placebo. Of these patients, 1,363 in the tegaserod group and 312 in the placebo group were employed and completed the WPAI:IBS-C
- Baseline demographics of these subjects are shown in Table 1. Patients in the tegaserod and placebo groups were comparable for age and race; mean age was 40.8 years and the majority of patients were Caucasian (approximately 86%) in both groups (Table 1)

RESULTS (cont'd)

Table 1. Baseline demographics of patients completing WPAI:IBS-C.

Characteristic	Tegaserod (n=1,363)	Placebo (n=312)
Age (years), mean (SD)	40.8 (10.7)	40.7 (10.6)
Race, n (%)		
Caucasian	1,162 (85.3)	269 (86.2)
Black	45 (3.3)	10 (3.2%)
Asian	12 (0.9)	3 (1.0%)
Other	144 (10.6)	30 (9.6%)

Responsiveness of WPAI:IBS-C to clinically meaningful change in IBS symptoms

- The sample sizes available for analyses of the various WPAI:IBS-C measures of responsiveness to overall IBS symptom relief, and relief of abdominal discomfort/pain, are shown in Table 2 and Table 3

Table 2. Patients analyzed for WPAI:IBS-C responsiveness to overall IBS symptom relief.

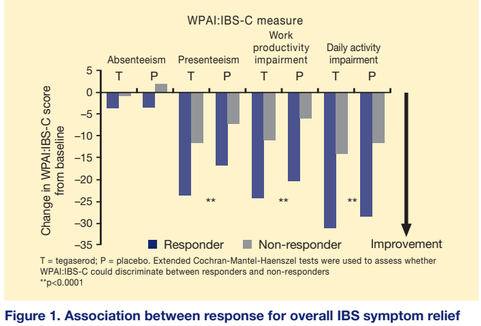
	Tegaserod n (%)	Placebo n (%)
Absenteeism		
Responder	404 (34.5)	58 (23.7)
Non-responder	767	186
Presenteeism		
Responder	442 (34.8)	66 (23.6)
Non-responder	828	213
Work productivity loss		
Responder	403 (34.5)	58 (23.7)
Non-responder	762	186
Daily activity impairment		
Responder	687 (35.1)	121 (25.9)
Non-responder	1,269	345

Table 3. Patients analyzed for WPAI:IBS-C responsiveness to relief of abdominal discomfort/pain.

	Tegaserod n (%)	Placebo n (%)
Absenteeism		
Responder	376 (32.1)	52 (21.3)
Non-responder	795	192
Presenteeism		
Responder	411 (32.4)	56 (20.1)
Non-responder	859	223
Work productivity loss		
Responder	375 (32.2)	52 (21.3)
Non-responder	790	192
Daily activity impairment		
Responder	637 (31.6)	109 (23.3)
Non-responder	1,319	357

RESULTS (cont'd)

- The responder rates for overall IBS symptom relief were 33.7% and 24.2% in the tegaserod and placebo groups, respectively (Table 2)
- The responder rates for relief of abdominal discomfort/pain were 31.3% and 22.1% in the tegaserod and placebo groups, respectively (Table 3)
- Responders for overall IBS symptom relief reported significantly greater reductions in WPAI:IBS-C measures of presenteeism, work productivity loss and daily activity impairment compared with non-responders. Although a reduction in absenteeism score was observed in responders compared with non-responders, the difference was not statistically significant (Figure 1)



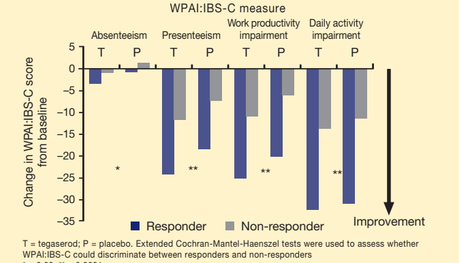
T = tegaserod; P = placebo. Extended Cochran-Mantel-Haenszel tests were used to assess whether WPAI:IBS-C could discriminate between responders and non-responders
**p<0.0001

Figure 1. Association between response for overall IBS symptom relief and WPAI:IBS-C scores.

- Responders for relief of abdominal discomfort/pain reported significantly greater reductions in each of the WPAI:IBS-C measures compared with non-responders (Figure 2)
- For both overall IBS symptom relief and relief of abdominal discomfort/pain:
  - scores for WPAI:IBS-C measures for responders and non-responders improved (score decreased) during the study, with the exception of absenteeism, which worsened (score increased) for placebo non-responders (Figures 1 and 2)
  - the reductions in WPAI:IBS-C scores for all measures except absenteeism in the overall IBS symptom relief analysis appeared greater in the tegaserod responders compared with placebo responders, although this difference was not examined statistically

RESULTS (cont'd)

- Responsiveness testing using WPAI:IBS-C measures of overall IBS symptom relief and relief of abdominal discomfort/pain yielded comparable results



T = tegaserod; P = placebo. Extended Cochran-Mantel-Haenszel tests were used to assess whether WPAI:IBS-C could discriminate between responders and non-responders
*p=0.02; **p<0.0001

Figure 2. Association between response for relief of abdominal discomfort/pain and WPAI:IBS-C scores.

CONCLUSIONS

- WPAI:IBS-C work productivity and daily activity impairment measures are responsive to clinically meaningful changes in both overall IBS symptoms and abdominal discomfort/pain
- The WPAI:IBS-C, therefore, is a valid and responsive measure to assess the effectiveness of IBS treatments on overall work productivity and daily activities

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