

Unknown

From: Aked Dominic DM  
Sent: Thursday, October 26, 2000 9:30 PM  
To: Rak Ihor IW  
Cc: O'Brien Shawn SP; Shadwell Pamela PG; Holdsworth Debbie D; Jones Martin AM - PHMS  
Subject: RE: Data for weight neutral slide

Hi Ihor

Many thanks for this important feedback.

I agree we need to be able to tell a convincing story to our internal and external customers. I'm sure we can do this.

- Re US PI: From what I can see any mention of weight gain in the US PI relates to short-term studies. We may be able to make a clear distinction between this clinical situation and long-term treatment (that is, acutely psychotic relapse versus long-term maintenance). Presumably the latter is what is important clinically given that patients receive long-term treatment.

A promotional claim **'Seroquel is weight neutral during long-term treatment'** should help to make this distinction.

- There may be a rationale to explain why acutely psychotic patients may gain weight in the short term, following effective therapy. The relief of negative symptoms, apathy etc, disorganised thinking, may result in return to normal activities like having regular meals.

There are useful indicators in the patient satisfaction study to support the view that effective long term therapy with Seroquel helps to normalise eating.

Benefits noticed in last 6 mo by patients on Seroquel

55% patients prepare and cook meals

64% go shopping for food/personal items

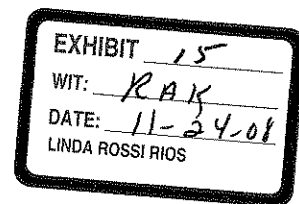
**73% eat more normally**

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One additional comment (where there's a ying there's a yang): if we look at incidence of patients gaining >7% baseline weight, we should also consider looking at patients losing >7% baseline weight, or what would be considered a clinically significant weight loss.

Kind regards

Dom

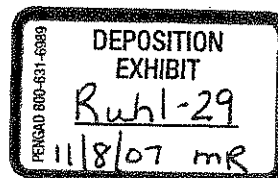


From: Rak Ihor IW  
Sent: 25 October 2000 02:16  
To: 'Rob Kite'; Holdsworth Debbie D; Jones Martin AM - PHMS  
Cc: Shadwell Pamela PG; Ashworth Phillip P; Aked Dominic DM; Gavin Jim JP; O'Brien Shawn SP  
Subject: RE: Data for weight neutral slide

All

I had the pleasure of presenting 5 weight slides (from the International Speaker's Training meeting) to the US SEROQUEL Product Team.

The titles of the 5 slides were: SEROQUEL-minimal effect on weight long term; SEROQUEL- neutral effect on weight at all doses; 3 slides-- Long-term SEROQUEL monotherapy has neutral effect on weight (1 with confidence intervals, another n=112 of 53 weeks exposure and longer shifts in BMI category, and another shifts in BMI category in obese/severely obese patients).



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They had some very good suggestions based on their having to deal with the US label which states that SEROQUEL causes dose related weight gain (NDA dataset).

1. Best to tell a story. Data from clinical trials showed this, but limitations are these. hence another dataset analysed
2. using different datasets raises suspicions if not adequately explained and justified.
3. when selecting a cohort of patients who were treated for 26 or 53 weeks minimum, suspicions are immediately raised about the patients "censored": what was their mean weight change. For both cohorts of patients (those displayed and those censored) how many experienced adverse events (weight gain >7% of body weight), how any discontinued from the OLE due to weight gain, etc
4. BMI shifts not quickly understood; patients can not shift from these severely obese BMI category (already mentioned)

Certainly, the more of these comments that we examine and address, the more confidence we will have in our weight neutral message.

Ihor

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**From:** Jones Martin AM - PHMS  
**Sent:** Friday, October 20, 2000 10:25 AM  
**To:** 'Rob Kite'; Holdsworth Debbie D  
**Cc:** Shadwell Parnefa PG; Ashworth Phillip P; Rak Ihor IW; Aked Dominic DM; Gavin Jim JP  
**Subject:** RE: Data for weight neutral slide  
**Importance:** High

Rob

Please find attached a word document containing the data that you need. There are 40 pages in totally. The first 20 refer to all doses, the last 20 to data from within the 150-750 mg dose range.

In yesterday's Communication Planning Team meeting, it was decided to focus on the all dose cohort, for which we have 178 schizophrenic patients, with weight data beyond day 182, with BMI data. This data is slightly different to that previously included in my slide.

The summary data for this cohort starts on page 6, with :

	N	Mean	LOL	UOL	(Median)	Min	Max	Std	Err	t
[Prob 0] TINV										
ALL	178	0.410	-0.719	1.742	-0.450	-27.00	37.000	0.891	0.674	0.612
0.729										
4.973										

From this you should be able to get all the required data. The following page contains mean dose data for the entire cohort.

The next dozen or so pages divide these 178 patients into demographic sub-groups i.e. baseline BMI, gender, age group, race, mean dose group (interesting ?). All the tables should contain data for 178 patients !

The analyses are then repeated for the 150-750 mg group.

Hope this helps.

I am away on holiday next week, but Pamela, or Phill Ashworth may be able to help you with any queries.

Regards

