Letter: Therapeutic potential of ketotifen in irritable bowel syndrome (IBS) may involve changes in mast cells at sites beyond the rectum: Reply
Boeckxstaens, G.E.; Klooker, T.

Published in:
Gut

DOI:
10.1136/gut.2010.226217

Citation for published version (APA):
Therapeutic potential of ketotifen in irritable bowel syndrome (IBS) may involve changes in mast cells at sites beyond the rectum

The recent study published in *Gut* by Klooher and coworkers\(^1\) reported very early work\(^4\) we studied mast cells across depending on the IBS subtype, gender or Gut March 2011 Vol 60 No 3 423

sites beyond the rectum may involve changes in mast

in irritable bowel syndrome (IBS) tissue investigated by Klooher cell numbers or activation that simply were attributable to direct effects on either mast

paper, one cannot rule out the possibility based on the evidence presented in this study. The authors suggest, be through H1 receptor effects of ketotifen therapy occur independently of the region where the biopsies are taken, may not actually reflect physiologic release. We agree with Dr O’Sullivan that we need to continue our search for better and more optimal markers in order to better evaluate the mechanism of action of drugs in general on mucosal mast cells.

Guy E Boeckxstaens,1,2 Tamira Klooher2

1Department of Gastroenterology, University Hospital of Leuven/Catholic University of Leuven, Leuven, Belgium; 2Academic Medical Center, Amsterdam, The Netherlands

Correspondence to Guy E Boeckxstaens, Department of Gastroenterology, University Hospital of Leuven/ Catholic University of Leuven, Herestraat 49, 3000 Leuven, Belgium; guy.boeckxstaens@med.kuleuven.be

Competing interests None.

Provenance and peer review Not commissioned; not externally peer reviewed.

Published Online First 4 October 2010

Gut 2011;60:423. doi:10.1136/gut.2010.226217

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The Authors’ reply We would like to thank Dr O’Sullivan for her positive comment\(^2\) on our paper recently published in *Gut*.\(^2\) We agree that the exact mechanism of action of ketotifen, either through mast cell stabilisation or H\(_4\_) receptor blockade, needs further study. We tend to disagree, however, that we may have missed differences between patients with irritable bowel syndrome (IBS) and healthy subjects by studying the rectum. Concerning the number of mast cells, as illustrated in figure 2A of our paper,\(^2\) similar findings were obtained in the colon descen-
dents of patients with IBS and healthy subjects as in the rectum. In line with our data, Cenac et al.\(^3\) also reported similar results in rectal and ascending colon biopsies. Obviously, depending on the patient popula-
tion studied, mast cell numbers may vary along the gastrointestinal tract as described by Dr O’Sullivan\(^4\) but, in our study, rectal and colonic biopsies yielded similar results, making it less likely (but not excluding the possibility) that, in our patient population, rectal tissue is an inappropriate marker. In the same way, in preliminary experiments we compared the release of both histamine and tryptase in the supernatant of rectal and descending colon biopsies and found similar results. Also, proteolytic activity in the supernatant and tissue mRNA levels of trypsin and tryptase are comparable in the rectum and ascending colon, as recently reported by Cenac et al.\(^3\) Nevertheless, as pointed out in our discussion, our results do not rule out the possibility that ketotifen stabilises mast cells in the gastrointestinal tract, particularly as we feel that the mediator release detected in the supernatant, independent of the region where the biopsies are taken, may not actually reflect physiologic release. We agree with Dr O’Sullivan that we need to continue our search for better and more optimal markers in order to better evaluate the mechanism of action of drugs in general on mucosal mast cells.

Guy E Boeckxstaens,1,2 Tamira Klooher2

1Department of Gastroenterology, University Hospital of Leuven/Catholic University of Leuven, Leuven, Belgium; 2Academic Medical Center, Amsterdam, The Netherlands

Correspondence to Guy E Boeckxstaens, Department of Gastroenterology, University Hospital of Leuven/ Catholic University of Leuven, Herestraat 49, 3000 Leuven, Belgium; guy.boeckxstaens@med.kuleuven.be

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1. O’Sullivan M. Therapeutic potential of ketotifen in irritable bowel syndrome (IBS) may involve changes in mast cells at sites beyond the rectum. *Gut* 2011;60:423.


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The Authors' reply
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Gut 2011 60: 423 originally published online October 4, 2010
doi: 10.1136/gut.2010.226217

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