Letter to the Editor

Pain therapy with high risk: One-sided presentation of the results from the latest phase III study on tanezumab in osteoarthritis pain

To the Editor,

The authors of the recently published phase III study on tanezumab evaluate progressive osteoarthritis (OA) as a mild to moderate adverse event and claim that no new safety signals regarding the use of the antibody could be identified in their own work. In fact, in this study tanezumab was found to produce significant improvements in OA pain of the hip and the knee, in global assessments and in function compared with oxycodone and placebo [2]. The recommendations by the independent adjudication committee (IAC) regarding the usage of the antibody were not incorporated in the publication.

Tanezumab seemed in some clinical studies to be highly effective in treating OA pain of the hip and the knee. However, in June 2010 the U.S. Food and Drug Administration placed all clinical trials on hold after 87 cases of osteonecrosis were reported in the context of the use of tanezumab medication in OA. Although the IAC investigated and found that only 2 of these cases represented a drug-related side effect, it was evident that in 68 cases progressive OA was associated with higher doses of tanezumab (10 mg) or its combination with nonsteroidal anti-inflammatory drugs [1].

Before complete recruitment of all 800 estimated patients, the study by Spierings et al. also was put on clinical hold in June 2010 [2]. After reviewing 2 cases of reported osteonecrosis in this study, which required total joint replacement, the IAC came to the conclusion that 1 patient underwent surgery due to rapidly progressive OA and 1 due to normally progressing OA. These results were evaluated in the final report of the IAC as it is described in the next to last paragraph of the publication by Spierings et al. [2]. Thus, it is evident that the findings by Spierings et al. contributed to reveal new safety signals regarding the use of tanezumab in OA. In contrast, however, Spierings et al. stated in the abstract as well as in the last paragraph of their report that no new safety signals could be identified [2].

At present, the genesis of developing rapid progressive OA associated with tanezumab is uncertain. Nevertheless, after thorough assessment of all cases, the IAC recommended certain measures to optimize the benefits and minimize the risks of tanezumab therapy. Two key IAC recommendations were to exclude tanezumab 10 mg from further investigation in OA and to exclude concomitant use of nonsteroidal anti-inflammatory drugs. Being aware of these facts, I would expect the authors of the study recently published in PAIN to discuss the limitations of their study more thoroughly in the last paragraph of the discussion. In particular, they needed to more precisely address the evaluation and the recommendations of the IAC. The findings of the IAC should encourage the authors to take a more critical point of view regarding their own results and the results of the literature and to draw a conclusion from it.

The authors need to make it clear to the readers that there can be severe consequences related to the application of tanezumab. Rapid progressive OA should not be dismissed as a mild or moderate adverse event. It appears as if the authors are trying to conceal the fact that the use of tanezumab is not yet entirely safe. Further studies are needed to identify which patients are at risk for serious drug-related adverse events such as rapid progressive OA, and which patients should not be exposed to this drug. Among the crucial topics for further investigation are the optimal dose of tanezumab and the optimal time period in the progression of disease for using this drug.

In summary, I feel it is important and necessary for authors to openly discuss our own results and to judge them with a critical point of view in the context of the current literature and findings. In some cases, pain relief overall needs to be considered in the light of potential joint damage. This would indicate a therapy with high risk.

References


Benjamin Panzram
University Clinic of Heidelberg, Department of Orthopaedics, Trauma Surgery and Paraplegiology, Schlierbacher Landstr. 200a, 69118 Heidelberg, Germany
* Tel.: +49 (0)622156 35399; fax: +49 (0)622156 26347.
E-mail address: Benjamin.Panzram@med.uni-heidelberg.de

Marcus Schiltenwolf
University Clinic of Heidelberg, Department of Orthopaedics, Trauma Surgery and Paraplegiology, Heidelberg, Germany

http://dx.doi.org/10.1016/j.pain.2014.08.006
0304-3959/© 2014 International Association for the Study of Pain. Published by Elsevier B.V. All rights reserved.

A phase III placebo- and oxycodone-controlled study of tanezumab in adults with osteoarthritis pain of the hip or knee: Response

To the Editor:

We thank Drs. Panzram and Schiltenwolf for their thoughtful response to our article [2] and appreciate their contributions. Panzram and Schiltenwolf appear to have taken the statement “no new safety signals were identified” out of context. In