

EDITORIAL

Japanese Society of Hypertension official comment on valsartan papers

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Recently we have seen important action taken with regard to the papers that reported results from the two large clinical trials of the hypertension drug valsartan (Diovan): the 'Kyoto Heart Study'¹ and the 'Jikei Heart Study'.² Investigations by the universities that hosted these trials (Kyoto Prefectural University of Medicine and Jikei University School of Medicine, respectively) have found evidence of data manipulation and conflicts of interest in the articles^{1,2} reporting the above trials.

As a society representing researchers and clinicians specializing in hypertension and cardiovascular diseases, we take these issues very seriously and are most concerned about the impact these series of reports will have on hypertensive patients and the general public. Modification of data used in papers reporting clinical trials, no matter whether it is minor or otherwise, is unethical and unacceptable behavior, which negatively impacts on perceptions of reliability and trust of the drug being tested, and the people involved. The impact also reaches to the broader pharmaceutical industry and clinical trials system in Japan. We strongly urge that the universities concerned and Novartis Japan continue their full investigations into these studies and clinical trials. The Japanese Ministry of Health, Labour and Welfare (MHLW) has also established a special study committee to examine this matter. Taking advice from the committee, we will work to prepare measures to proactively avoid problems like these in future.

Related to this issue, the Japanese Society of Hypertension has taken following actions.

In response to the interim report on the JIKEI HEART Study³ recommending the retraction of the study (Mochizuki *S et al.*)², the Japanese Society of Hypertension (JSH) announced revisions to the Japanese Society of Hypertension Guidelines for the Management of Hypertension (JSH2009)⁴ on 6 August 2013. These revisions are as follows:

- Reference No. 217 in the Japanese version of the JSH2009 Guidelines be deleted.
- Reference No. 194 in the English version of the JSH2009 Guidelines be deleted.
- The following sentence in Chapter 5 of JSH 2009⁴ be deleted: 'With these mechanisms combined, ARBs may not only reduce blood pressure but also directly inhibit organ damage and consequently prevent the occurrence of diseases.'

As described in the Instructions to Authors of *Hypertension Research* (http://mc.manuscriptcentral.com/societyimages/htr/HR_GTA.pdf), the journal requires that reports of clinical trials should meet the requirements of International Committee of Medical Journal Editors (ICMJE),⁵ and indicate whether the procedures were in accordance with the ethical standards of the responsible committee on human experimentation (institutional or regional), or with the Helsinki Declaration.⁶ All papers in *Hypertension Research* must also declare any Conflict of Interest following the guideline and detailed regulations set by the JSH in 2012.⁷ At JSH, we have also recently established an independent study group to look into the issues concerning clinical trials. Taking suggestions from the group, we will work to build on our current standards and policies to further ensure that our members design and conduct clinical trials appropriately. We will also strive to work alongside other learned societies in Japan and government groups to develop a common code of conduct for clinical trials along internationally accepted guidelines.^{6,8}

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- 1 Sawada T, Yamada H, Dahlöf B, Matsubara H, for the KYOTO HEART Study Group. Effects of valsartan on morbidity and mortality in uncontrolled hypertensive patients with high cardiovascular risks: KYOTO HEART Study. *Eur Heart J* 2009; **30**: 2461–2469.
- 2 Mochizuki S, Dahlöf B, Shimizu M, Ikewaki K, Yoshikawa M, Taniguchi I, Ohta M, Yamada T, Ogawa K, Kanae K, Kawai M, Seki S, Okazaki F, Taniguchi M, Yoshida S, Tajima N, for the Jikei Heart Study group. Valsartan in a Japanese population with hypertension and other cardiovascular disease (Jikei Heart Study): a randomised, open-label, blinded endpoint morbidity-mortality study. *Lancet* 2007; **369**: 1431–1439.
- 3 Kazuhiro Hayashi for the 'JIKEI Heart Study' Investigation committee, Jikei University School of Medicine, Interim report on the clinical trial JIKEI Heart Study (in Japanese), 2013. www.jikei.ac.jp/news/pdf/20130730.pdf.
- 4 Japanese Society of Hypertension guidelines committee. JSH 2009 Guidelines for the Management of Hypertension. *Hypertens Res* 2009; **32**: 4–107.
- 5 International Committee of Medical Journal Editors (ICMJE). Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals (updated 2013) www.icmje.org/icmje-recommendations.pdf.
- 6 World Medical Association Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects (latest version adopted in 2008), <http://www.wma.net/en/30publications/10policies/b3/17c.pdf>.
- 7 Japanese Society of Hypertension. JSH conflict of interest management policy. (in Japanese) 2002. www.jpnsh.org/data/coi_all.pdf.
- 8 Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO). International Ethical Guidelines for Biomedical Research Involving Human Subjects, Geneva, 2002.