Author's Reply

Reply to Letter Regarding Article, "Effect of Autologous Bone-marrow Cell Transplantation on Ischemic Ulcer in Patients With Buerger's Disease"

We greatly appreciate the interest and comments by Akar et al.¹ The issues they raise are important and we reply to them below. The diagnosis of Buerger's disease may be difficult and could be made only after exclusions of other diseases, such as atherosclerotic obliteration or collagen diseases. Regarding this point, our definition for Buerger's disease is not much different from that of Durdu et al.² Of course, we made every effort to exclude other vascular diseases, and the diagnostic criteria proposed by the Committee for Buerger's disease of the Japanese Ministry of Health and Welfare was very similar to that of Shionoya,³ which they adopted.

Although Akar et al mentioned several biochemical markers in their correspondence,¹ it is well known that there are no specific biomarkers for Buerger's disease. In all patients enrolled in our study,⁴ Buerger's disease was diagnosed at least 8 years prior to our cell therapy. Thus, the disease was long-lasting and they underwent diagnostic tests many times at several hospitals. To rule out cardiac diseases, malignant diseases, and retinopathy, we routinely performed Holter monitoring, echocardiography, coronary angiography, computed tomography of the total body, gastroscopy, colonoscopy, and fundoscopy, as described in a previous report.⁵ Apparent from their history of many admissions, all patients previously received optimal treatments, including intravenous administration of PGE-1 or

other oral prostaglandin analogues, but the effects were not appreciable.

Because of the limited number of patients for follow-up, we were unable to demonstrate angiographic findings. However, in this reply, we are happy to report one case showing increased number of visible collateral arteries (Fig 1). These findings are very similar to those of Durdu et al.²

Smoking is the biggest risk factor for Buerger's disease and cessation of smoking improves its clinical condition. Thus, improvement of the ischemic ulcer in our patient may well have been due to the cessation of smoking. In this regard we are very respectful to Akar et al,¹ who were able to prevent their patient from smoking for a long time. Our patients tried to stop smoking many times in the past but it was not successful and abstinence from smoking did not produce appreciable effects for them. Hence, improvement of the ischemic ulcer in our patient was most likely due to cell therapy rather than cessation of smoking.

Finally, we are very glad to know that Durdu et al² reported the therapeutic efficacy of cell therapy for Buerger's disease in the greater number of patients and with some clinical improvements other than of ischemic ulcer. Hopefully, we will be able to conduct an international collaborative study with Akar and colleagues because of the small number of cases of Buerger's disease.

References

1. Akar AR, Durdu S, Baran C. Letter by Akar et al Regarding Article, "Effect of Autologous Bone-Marrow Cell Transplantation on Ischemic Ulcer in Patients With Buerger's Disease". *Cir J* 2008; **72**: 684.
2. Durdu S, Akar AR, Arat M, Sancak T, Eren NT, Ozyurda U. Auto-

Fig 1. Representative angiographic photos of the treated left lower limb in one patient, showing a markedly increased number of collateral arteries in the lower thigh, pastern, and tiptoe after not only 4 weeks, but also 24 weeks of cell transplantation.

- logous bone-marrow mononuclear cell implantation for patients with Rutherford grade II-III thromboangiitis obliterans. *J Vasc Surg* 2006; **44**: 732–739.
3. Shionoya S. Diagnostic criteria of Buerger's disease. *Int J Cardiol* 1998; **66**: S243–S245.
 4. Saito Y, Sasaki K, Katsuda Y, Murohara T, Takeshita Y, Okazaki T, et al. Effect of autologous bone-marrow cell transplantation on ischemic ulcer in patients with Buerger's disease. *Circ J* 2007; **71**: 1187–1192.
 5. Tateishi-Yuyama E, Matsubara H, Murohara T, Ikeda U, Shintani S, Masaki H, et al. Therapeutic angiogenesis for patients with limb ischaemia by autologous transplantation of bone-marrow cells: A

pilot study and a randomised controlled trial. *Lancet* 2002; **360**: 427–435.

Ken-ichiro Sasaki, MD

Tsutomu Imaizumi, MD

*Department of Internal Medicine,
Division of Cardio-Vascular Medicine,
Kurume University School of Medicine,
Kurume, Japan*