Granulocyte colony-stimulating factor

In the background section of their abstract, Woei-Cherng Shyu and associates[1] state that because granulocyte colony-stimulating factor (G-CSF) has anti-inflammatory and neuroprotective properties and the capacity to mobilize stem cells, it has the potential to be used in treatment of stroke. However, there are limited data about the effects of G-CSF on hemostasis.[2,3] It has been suggested that G-CSF may induce a hypercoagulable state, possibly by increasing levels of endothelial markers and thrombin generation or by stimulating tissue factor.[4,5] A few reported cases of acute arterial thrombosis in patients receiving G-CSF support the hypothesis of induction of a transient hypercoagulable state.[6,7] In addition, acute arterial thrombosis in healthy donors, possibly related to G-CSF, has been reported.[2] A transient hypercoagulable state related to G-CSF may be important for thrombophilic, atherosclerotic or immobilized patients.

Therefore, whenever G-CSF is administered, the patient should be followed carefully.

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Having reviewed the baseline functional stroke scale scores reported by Woei-Cherng Shyu and associates,[1] I cannot share the excitement displayed by Cesar Borlongan and David Hess in their accompanying commentary.[2] The methodologic limitations of such a small phase 1 study are addressed in the commentary, but I have an additional concern: the 3 patients in the control group were significantly more impaired at the outset than the 7 patients who were randomly assigned to receive the treatment. It is well recognized that presenting impairment, as measured with scales such as the European Stroke Scale (ESS), the ESS Motor Subscale and the Barthel Index, is a strong predictor of ultimate outcome for stroke patients,[3–5] regardless of treatment. It is therefore crucial to recognize that patients presenting with the greatest of impairments are likely to improve least; conversely, those with milder impairments are more likely to improve more rapidly and more completely.[6,7]

Thus, it is not surprising that the 7 patients who were treated (who on average had more than 10% better stroke scale scores at recruitment) ultimately fared better than the 3 patients in the control group.

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[Drs. Shyu, Lin and Li respond:]

Following the guidelines on using G-CSF for stem cell mobilization,[1] we carefully adjusted the dose of G-CSF (15 μg/kg) for up to 5 days to avoid the leukocyte numbers rising above 70×10^9/L (in fact, the leukocyte count for all patients was below 61.3×10^9/L). In addition, we also prescribed moderate hydration and antiplatelet medicine, as suggested by LeBlanc and colleagues,[2] to minimize hyperosmolarity and hypercoagulability. During the clinical course of G-CSF treatment, there were no abnormal findings for biochemistry, bleeding time, coagulation time or C-reactive protein. Therefore, we conclude that no patient receiving G-