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Response to Letter Regarding Article, “Targeting recombinant tissue-type plasminogen activator in acute ischemic stroke based on risk of intracranial hemorrhage or poor functional outcome: An analysis of the third international stroke trial”

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Dear Editors

We agree with Dr Dai et al.¹ that the existing clinical prognostic models for the prediction of SICH or poor outcome after thrombolysis perform only modestly, and are unable to identify a group of patients at a very high risk of SICH.

In the IST-3 trial, we found that groups of patients who were predicted to be at a ‘high risk of SICH with rtPA treatment’ by clinical prognostic models tended to have a better functional outcome when they were treated with r-tPA than when they were treated with control.² We agree this is surprising, but is not due to defects in the statistical methods in our study; instead it is because the existing models do not reliably identify a group of patients with a very high risk of SICH.

If existing clinical prognostic models cannot reliably identify patients with a very high risk of SICH, what is the way forward? First, there may be predictors of SICH (for example novel imaging or blood markers) that might better identify those at highest risk. Second, the risk of SICH might be reduced with different thrombolysis regimes, for example lower doses, with treatment to lower blood pressure or with different agents, as are currently being tested in the ENCHANTED (NCT01422616), TASTE (ACTRN12613000243718) and ATTEST (NCT01472926) trials.

Yours sincerely

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DISCLOSURES The authors declare that they have no conflicts of interest.

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