

# Intravenous Alteplase for Acute Ischemic Stroke in Taiwan: Can We Expand the National Health Insurance's Reimbursement Criteria?

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Despite the evidence of improving recovery, the utilization of intravenous thrombolysis with alteplase was very low in Taiwanese patients with acute ischemic stroke<sup>(1)</sup>. One of the reasons is the strict reimbursement guideline made by the Bureau of National Health Insurance (NHI) in 2004<sup>(2)</sup>. In this issue of the *Acta Neurologica Taiwanica*, Yu-Hsiang Su and co-authors<sup>(3)</sup> retrospectively evaluated outcomes of their thrombolysed stroke patients who were “mismatched” between updated clinical practice guideline and NHI reimbursement criteria. They concluded that the outcomes of patients treated according to guidelines were comparable between the reimbursement and non-reimbursement groups. Despite the inherent selection bias and no comparison with the non-treated patients in this observational study, it might serve the an important local evidence for physicians in Taiwan when evaluating intravenous thrombolysis for acute ischemic stroke.

## SO, CAN WE EXPAND THE REIMBURSEMENT CRITERIA FOR INTRAVENOUS ALTEPLASE IN STROKE PATIENTS?

At the present time, the answer may still probably be NO!

The insurance payer, usually after an economic evaluation, may decide to pay a pharmaceutical product for its beneficiaries. As a rule of thumb, insurance reimbursement criteria should not be greater than the labelled prescribing information. Thus, the essence of this question should be back to the labelled indications and contraindications of alteplase for stroke, made by Taiwanese regulator in Nov 2002<sup>(4)</sup>. Although data from high-quality meta-analyses<sup>(5,6)</sup> of new trials in the past decade challenged some of the major contraindications, such as onset > 3 hours or age > 80 years, the Taiwan's Food and Drug Administration has turned down twice the application by the manufacturer to change the package insert regarding those two contraindications. The reasons were mostly “insufficient of benefits”. Without the change of labelled prescribing information, the NHI reimbursement criteria cannot be expanded.

## WHAT CAN WE DO NOW?

Pragmatically, physicians should consider the potential medicolegal consequences if the potentially lethal symptomatic intracranial hemorrhage occur after such “off-label” uses of alteplase in their stroke patients. The problems may get even worse if the fee of alteplase is paid with patients' out-of-pocket money. Nevertheless,

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the potential solution of this issue may be still medical technology and stroke science themselves.

For stroke patients not eligible for intravenous thrombolysis at present time, the use of endovascular therapy (EVT) or screening for the eligibility of ongoing clinical trials might be considered. In Jan 2016, three novel devices for EVT in stroke patients with large vessel occlusion got reimbursement by Taiwan's NHI<sup>(7)</sup>. The reimbursement criteria were much wider than intravenous alteplase, e.g., the time window may be as long as 8 hours for an anterior circulation stroke, and there's no upper limit of age. And for those with unclear onset time of stroke (e.g. the "wake-up stroke"), screening with modern imaging technique for penumbra and determining the eligibility of large multicenter randomized thrombolysis trials may be another option<sup>(8,9)</sup>. Administrrating intravenous thrombolysis under the setting of a well-conducted clinical trial in patients not eligible according to current labelled indication should be more appropriate than the previous "off-label" practice pattern. It is not only safer medicolegally and ethically for the patients and physicians, but also provides more solid evidences to change or generate new label indications of thrombolysis for stroke patients in the future.

In conclusion, the non-reimbursement group in Su, et al<sup>(3)</sup>. is a mixture of stroke patients with very heterogeneous characteristics. With the advances of imaging selection modalities and new hyperacute treatment options nowadays, they should no longer be considered as an identical group of patients. We strokologists, as an emerging subspecialists, should devote more in dedicated and individualized selection of stroke patients for appropriate early recanalization therapy to improve their outcomes.

#### Conflict of Interest Disclosure:

I received speaker fee from Boehringer Ingelheim for Actilyse® ([http://grsp2013.innovarad.tw/2016/07/rt-pa\\_forum\\_hsiehcy\\_share.html](http://grsp2013.innovarad.tw/2016/07/rt-pa_forum_hsiehcy_share.html)).

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