Effect and safety of tenecteplase in stroke patients with atrial fibrillation. Post-hoc analysis of the Norwegian Tenecteplase Stroke Trial NOR-TEST

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Background

Although there has been a revolutionary progress of endovascular treatment, intravenous thrombolysis remains the pillar of reperfusion therapy. Patients with atrial fibrillation (AF) are at increased risk of stroke and these strokes tend to be the most serious ones. It is therefore essential to find the most effective thrombolytic treatment in order to resolve also cardiac emboli more sufficiently. Alteplase (tPA) has well recognized limitations, and there is an imperative to continue efforts to find more efficient and safer lytic treatment in acute ischemic stroke.

NOR-TEST was the first randomized controlled phase 3 trial to investigate the safety and efficacy of tenecteplase versus a tPA in acute ischemic stroke.

Aim

The purpose of this post hoc analysis of the NOR-TEST study was to assess the effect and safety of tenecteplase versus tPA in patients with acute ischemic stroke and AF, and to assess the outcome in stroke patients with AF compared to patients with sinus rhythm.

Material and methods

The patients were randomized to receive either tenecteplase 0.4mg/kg or alteplase 0.9 mg/kg. Atrial fibrillation was defined as documented paroxysmal or chronic prior to the ischemic stroke or documented atrial fibrillation during the hospital stay. Patients with atrial fibrillation were compared to patients without atrial fibrillation.

Results

Totally 183 patients (16.6 %) in the NOR-TEST population (n=1100) were diagnosed with AF. In 120 patients (10.9 %), AF was known prior to the ischemic stroke (87 with paroxysmal AF and 33 chronic AF) and 63 patients were diagnosed with AF during the acute phase. There was a significantly lower proportion of stroke mimics among patients with AF compared to patients with SR. In AF patients, hypertension was more frequent in the tenecteplase group and diabetes mellitus more frequent in the tPA group. There were no statistical significant differences in any other baseline characteristics between patients treated with tenecteplase and tPA. Male sex, lower age and NIHSS score were associated with better outcome (per protocol).

Table 2. Baseline characteristics in patients with AF treated with tenecteplase (TNK) versus alteplase.

Variables	All patients			Per protocol		
	TNK	tPA	P	TNK	tPA	P
NIHSS on admission	7.6 (7.7)	7.2 (5.9)	.64	7.9 (7.9)	7.4 (5.9)	.64
NIHSS at 24 hours	6.0 (8.6)	4.4 (6.7)	.18	6.4 (8.7)	4.7(6.8)	.16
NIHSS at 7 days	3.3 (5.7)	3.2 (5.5)	.87	3.6 (5.9)	3.4 (5.6)	.84
mRS ≤2 at day 7	39 (48)	57 (56)	.30	39 (48)	57 (56)	.30
Mortality at day 7	5 (6)	1 (1)	.05	5 (7)	1 (1)	.05
mRS ≤2 at 3 months	50 (62)	72 (71)	.21	46 (61)	68 (71)	.16
Mortality at 3 months	10 (12)	7 (7)	.20	10 (13)	7 (7)	.20
Any intracerebral hemorrhage	12 (15)	16 (16)	.87	12 (16)	16 (17)	.88
Symptomatic intracerebral hemorrhage	3 (4)	5 (5)	.69	3 (4)	5 (5)	.70

Table 3. Logistic regression mRS ≤ 2 at 3 months per protocol.

Variables	Odds ratio	95% CI	P
Male	2.8	1.3-6.1	.008
Age	0.92	0.87-0.97	.002
NIHSS score on admittance	0.84	0.78-0.90	<.001
Alteplase versus tenecteplase	1.8	0.8-3.8	.15

Conclusions

This is the first randomized controlled study to report the effect and safety of tenecteplase in acute ischemic stroke in relation to AF. There were no major differences in outcome between the tenecteplase and alteplase group in the subgroup of patients with AF although female sex was associated with more serious strokes and less effect of tenecteplase.

Table 1. Baseline characteristics and outcome in patients with AF versus sinus rhythm (SR).

Variables	All patients			Per protocol		
	AF N=183	SR N=917	P	AF N=172	SR N=738	P
Age	77.0 (8.8)	69.8 (14.3)	<.001	77.2 (8.6)	71.7 (12.5)	<.001
Female	75 (17)	365 (83)	.77	72 (21)	275 (79)	.26
NIHSS score on baseline	7.4 (6.7)	5.3 (4.9)	<.001	7.6 (6.8)	5.6 (5.2)	<.001
Prior cerebral infarction	38 (21)	134 (15)	.04	37 (22)	114 (15)	.054
Active smoking	24 (13)	209 (23)	.008	23 (13)	168 (23)	.006
NIHSS score at 24 hours	5.1 (7.6)	3.4 (5.6)	.001	5.4 (7.7)	3.8 (6.0)	.004
mRS at day 7	2.1 (1.8)	1.5 (1.6)	<.001	2.2 (1.8)	1.7 (1.7)	.004
mRS at 3 months	2.0 (1.9)	1.4 (1.6)	<.001	2.0 (1.9)	1.6 (1.7)	.003
Any intracerebral hemorrhage	28 (15)	69 (8)	.001	28 (16)	66 (9)	.004