

# Pharmacological Treatment of Acute Ischaemic Stroke: Certainties and Doubts

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Ischaemic stroke represents the second cause of death worldwide and the third in Western Countries, furthermore, it is the leading cause of adult disability [1]. The incidence of first episode of ischaemic stroke in Italy is 180/230 new cases /100.000 /year. 20% of these cases were dead after the first month, while 35-40% showed relevant disability and morbidity. Nearly 80% of all ischaemic strokes are found in first episodes, while nearly 20% are represented by ischaemic stroke's recurrences. However, the risk of ischaemic stroke in the general population shows a relevant increase after the age of 55 years, while the risk of recurrences of an ischaemic stroke raises 10% after 7 days and 18% after 3 months of an acute ischaemic stroke/ minor stroke [2]. Furthermore, after a first episode of ischaemic stroke, the risk to develop another atherothrombotic disease, as stroke's recurrence or acute coronary syndrome, raises 20% for stroke's recurrence and 17% for acute coronary syndrome, respectively [3].

We should observe a doubling mortality for ischaemic stroke within 2020 because of the persistent trend to smoking and also the increasing of ageing with the following increase of the number of frail elderly patients.

The treatment of the acute phase of ischaemic stroke is based on the guidelines of SPREAD that show different levels of clinical evidence [4].

Treatment based on Thrombolysis is suggested by the recommendation 10.2 of the SPREAD's guidelines. Thrombolysis is based on the administration i.v. of r-TPA 0.9 mg/kg, max dose 90 mg; 10% as i.v. bolus, and 90% in the following 60 minutes, and is suggested within three hours after the clinical onset of symptoms (level 1A). However, clinical characteristics of patients that may benefit from Thrombolysis are clearly showed in the study SITS-MOST [5]. So, Thrombolysis is suggested only for active neurological centers not only with stroke unit, but also that may optimise the interval between the incoming of patient and the neurologic clinical evaluation and the beginning of the treatment and surveillance for the follow up.

Recently data published in the Literature by the SITS group [6] and after data reported in the study ECASS III [7]

show that thrombolytic treatment based on the administration of alteplase may have a good efficacy within 3-4 hours from the clinical onset. More data will be available from another study (i.e. IST 3), which is a double blind randomised trial, based on a large population, that will compare the risk/benefit ratio of a thrombolytic treatment with alteplase vs placebo within 6 hours from the clinical onset. Moreover, this study will evaluate also the efficacy of the described treatment and risk/benefit ratio in very elderly patients (i.e. > 80 years old) and the clinical enrolment will end this year.

Based on these reasons and limitations, Thrombolysis is not performed for all patients with ischaemic stroke incoming in any emergency room and/or neurological divisions. So, for patients affected by ischaemic stroke for a cerebral atherothrombosis, that are not candidate to Thrombolysis for any reason, antithrombotic treatment is based on antiplatelet drugs.

On this topic Guidelines published by the SPREAD underline several suggestions:

- Aspirin (160-300 daily) is useful for the treatment of all patients not ongoing to Thrombolysis or oral anticoagulation (level A). For patients underwent to Thrombolysis, antiplatelets treatment based on aspirin may be started after 24 hours.
- Patients that develop an ischaemic stroke, with a significant atherosclerosis of any extra cranial vessels (e.g. common carotid, internal carotid and so on) during primary or secondary thromboprophylaxis with aspirin, aspirin may be substituted with ticlopidine, 500 mg daily, or clopidogrel 75 mg daily, or dipyridamole 200 mg daily associated with aspirin 25 mg daily (level D). Patients' ongoing antiplatelet treatment with ticlopidine should perform a follow up of haemocrome several times in the first month of treatment.

So, doubts about the better antithrombotic treatment with antiplatelets drugs start because of these different choices. Moreover, doubts are based not only on the choice of antiplatelets drugs, but also on the secondary prophylaxis, because there are no guidelines nor evidences nor relevant studies that underline significant differences for antiplatelets drugs in the clinical outcome of the treatment of the acute phase of ischaemic stroke.

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