Cerebrovascular disease during nilotinib treatment

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AIM:
To evaluate the presence of cerebral and cervical artery stenosis and/or the occurrence of cerebrovascular events in patients in therapy with nilotinib

Materials and methods:
We examined Twelve patients affected by Chronic Myeloid Leukaemia (CML) in treatment with Nilotinib (first, second, or third line treatment). The mean age was 56 years (range 35 -72 years). The period of treatment was between six months and seven years (mean: three years). In every subjects, we looked for the anamnestic presence of cerebrovascular risk factor (hypertension, smoke, dyslipidaemia, diabetes) and the occurrence of myocardial infarction, ischemic stroke and peripheral artery occlusive disease. Every subject underwent 1) Ecocolordoppler of cervical arteries to evaluate the intima-media thickness (IMT), the presence of atherosclerotic plaques and/or lumen stenosis, 2) Transcranial Ecocolordoppler to evaluate intracranial stenosis which were suspected in presence of abnormality of flow (turbulence, dispersion or acceleration).

Results:
None of the subjects reported stroke, myocardial infarction and peripheral artery occlusive disease. One subject reported amaurosis fugax, due to transient retinal ischemia. Eight patients (67 %) showed abnormalities in the cervical and/or intracranial cerebral arteries. In six subjects, we found a low grade atherosclerosis of the cervical arteries (increased IMT or not hemodynamically significant plaques). Five out of six had at least two vascular risk factors. Two patients had an internal carotid artery stenosis > 50 %. In both patients we also found multiple intracranial artery stenosis. One of this subjects did not show neurological symptoms, while the other one had un amaurosis fugax, ipsilateral to the carotid stenosis. Both patients showed at least two vascular risk factors.

Discussion and conclusion
The tyrosine kinase inhibitor nilotinib is used for the treatment of CML. Nilotinib is considered well tolerated but several reports exist on the occurrence of accelerated atherosclerosis, peripheral arterial occlusive disease and myocardial infarction. No data are available on the influence of nilotinib on cervical and cerebral artery atherosclerosis and, to our knowledge, only two case of cerebrovascular disease concomitant to this therapy were reported in literature. In spite of small size, our study documents a high prevalence of cervical and cerebral arteries atherosclerosis in patients treated with nilotinib. Therefore we provide the evidence of a case of transient retinal ischemia and multiple-vessel stenosis. A larger sample of patients and the comparison with a matched control group are mandatory in order to confirm our data. However a strict monitoring of cerebral and cervical arteries is advisable in patients treated with nilotinib, especially if other risk factors are present.

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