Prescrire International Editorial

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Margins

Far too many marketing authorisations are based on non-inferiority trials. Two concrete examples are featured in this issue: the oral anticoagulant *rivaroxaban* in patients with atrial fibrillation (see page 257) and the antiretroviral *rilpivirine* as first-line therapy for HIV infection (see page 262).

To conclude that a new drug is "non-inferior" for the primary endpoint, the trial protocol must prespecify the maximum acceptable loss of efficacy with the new drug compared to the standard treatment.

But the selection of the non-inferiority margin varies widely between trials: 46% and 12%, respectively, in the examples reported in this issue.

When interpreting a non-inferiority trial, one should always ask: what is the clinical relevance of the difference tolerated by the trial sponsors? When overall mortality or major outcomes are concerned, 50% is not marginal at all.

"Non-inferiority" is not straightforward. When discussing treatment options with a patient, it is important to assess the risk of lower efficacy to which the new "non-inferior" drug exposes the patient, in comparison with the standard treatment. And it is important to weigh this risk against the new drug's advantages, if any, in terms of a better adverse effect profile or greater convenience.

What patients and healthcare professionals really expect from new drugs is genuine therapeutic progress.

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