Non-inferiority studies

Recent years have seen a considerable increase in the number of non-inferiority studies. Unlike superiority studies, these studies aim to show that a new drug is not less effective than an existing one. However, the appropriateness of non-inferiority studies is still being debated. Advocates of such studies claim that this type of research is justified in certain situations, for instance when a drug is expected to have the same efficacy but to have fewer side-effects, or to be more convenient to use (e.g. lower dosage frequency) or is cheaper. One may question, however, whether such assumed advantages should not also be examined and proven (in a superiority study). Non-inferiority studies can also be used to expand the range of therapeutic options. For some life-threatening indications it may be sufficient to prove that drugs are not less effective than the standard therapy.

Some opponents regard non-inferiority studies as unethical, as patients taking part in such studies are exposed to potential side-effects while no added benefits are to be expected from the new drug. Nearly all relevant research questions regarding new drugs need to be answered in a superiority study, viz. those to assess whether the new drugs perform better than the current standard therapy. Studies of a new drug whose only purpose is to prove that it does not perform worse than the standard treatment should not be undertaken, for ethical and financial reasons. In other words, researchers will have to clearly justify their decision to start a non-inferiority study in their publications. Medical ethics committees and registration authorities should also assess these studies more critically.

The design and analyses of non-inferiority studies differ from those of superiority studies. There are certain methodological drawbacks to non-inferiority studies, such as the arbitrarily chosen non-inferiority margin (delta: δ or ∆), that is, the maximum negative effect at which a drug can still be regarded as not less effective. The larger this margin, the easier it becomes to establish non-inferiority.

In reading and evaluating publications on non-inferiority studies, doctors, pharmacists and registration authorities should keep the concerns listed in the box on page 33 in mind. If one or more of these requirements are not being met, caution is warranted in interpreting the study results.

References*

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*The literature refers to the Dutch tekst

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