When major trials mean minor efficacy

One of the drugs presented in the current issue has been evaluated in large-scale comparative clinical trials. Mirabegron, a beta-3 adrenoceptor agonist used to treat urge incontinence, was compared with an antimuscarinic drug or placebo in four trials, each including about 1000 to 2000 participants (p. 8-9).

At first glance, trials conducted on such a large number of patients seem to indicate a robust evaluation, based on an impressive body of data concerning both efficacy and adverse effects. But this can be viewed in another light.

When early data suggest that a drug is much more effective than the chosen comparator, there is no need to enrol a large number of patients to obtain a statistically significant result. On the other hand, when the difference in efficacy is expected to be minor, the trial is much less likely to demonstrate a statistically significant difference, unless a large number of patients are recruited.

In fact, clinical trials showed that mirabegron is only slightly more effective than placebo, preventing about one incontinence episode every 2 days…

Large trials can be useful for detecting adverse effects, clarifying the optimal treatment strategy, or demonstrating equivalent efficacy between drugs or efficacy against an uncommon event.

But in practice, do not assume that “major” trials are necessarily a good thing: they can be a sign of minor efficacy.