EDITORS' OPINION

Failure to demand solid evidence for marketing authorisation spells danger for patients

In order to minimise the dangers of drugs, marketing authorisation should be granted on the basis of a rigorous evaluation, which in most cases will involve double-blind randomised trials comparing the drug against a standard treatment, showing that the drug represents a tangible therapeutic advance for patients. And at least two trials are required to ensure that the findings are reproducible (1,2).

Unfortunately, in 2020, it is clear that pharmaceutical companies generally do not respect these requirements, and the European Medicines Agency (EMA) does not insist that they do so. Consequently, most applications are based on a single clinical trial.

The application to extend *dasatinib*'s indications to include children with acute lymphoblastic leukaemia illustrates this issue: the extension of indication was approved on the basis of non-comparative data alone, without the EMA demanding more information (see "Dasatinib in children with acute lymphoblastic leukaemia" p. 12).

In certain very specific situations, non-comparative data are sometimes acceptable, for example in a condition for which an urgent, unmet medical need exists or a serious condition that is so rare that it is impossible to recruit enough patients for a comparative trial (1). The use of *dasatinib* in children with acute lymphoblastic leukaemia does not meet these criteria. A treatment of the same type with a favourable harm-benefit balance is already available for these children. Furthermore, a randomised comparative trial versus *imatinib* has now been conducted. Its results were published just a few months after *dasatinib* was granted marketing authorisation in this situation, thus proving that a comparative evaluation would have been feasible (3).

In March 2020, the EMA rightly urged the scientific community to conduct randomised comparative trials designed to generate robust evidence on covid-19 (4). It would be helpful if the EMA adopted the same attitude towards other clinical situations, to better serve patients and build confidence in its work.

▶ Translated from *Rev Prescrire* **October 2020**
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1- Prescrire Editorial Staff "Adaptive pathways: EMA's dangerous plan" *Prescrire Int* 2016; **25** (174): 223.
2- Prescrire Rédaction "Évaluer le progrès thérapeutique: avec méthode, au service des patients" *Rev Prescrire* 2015; **35** (382): 565-569.
3- Shuhong S et al. "Effect of dasatinib vs imatinib in the treatment of pediatric Philadelphia chromosome-positive acute lymphoblastic leukemia. A randomized clinical trial" *JAMA Oncol* 2020; **6** (3): 358-366 + supplementary material: 53 pages.
4- Prescrire Editorial Staff "Evidence required: for covid-19 too" *Prescrire Int* 2020; **29** (218): 199.

risankizumab (SKYRIZI°) and plaque psoriasis

NOTHING NEW

According to several clinical trials in patients with moderate to severe plaque psoriasis, *risankizumab* (an interleukin-23 inhibitor) was more effective in reducing lesions than *adalimumab* (a TNF-alpha inhibitor), *ustekinumab* (an interleukin-12 and interleukin-23 inhibitor) and *secukinumab* (an interleukin-17A inhibitor). However, given the limited experience with use of *risankizumab*, it is preferable to initially use a TNF-alpha inhibitor. And when such a drug fails, the efficacy and adverse effect profile of *risankizumab* seem similar to those of *guselkumab* (another interleukin-23 inhibitor), even though *risankizumab*'s evaluation is more extensive. In summary, *risankizumab* does not provide a therapeutic advance for patients.

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romiplostim (NPLATE°) and chronic immune thrombocytopenia from one year of age

NOTHING NEW

Like *eltrombopag*, *romiplostim* increases platelet counts in the short term in children after standard treatments have failed, but with no demonstrated effect in reducing the number of bleeding episodes. Its adverse effect profile in children is similar to that in adults, and additionally includes oropharyngeal and abdominal pain, and rhinitis. There is a risk of error when preparing the drug for administration.

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