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The sledgehammer

It is important to choose the right tool for the job. There is no need to use a sledgehammer to crack a nut.

The same principle applies in the field of therapeutics.

Osteoporotic fracture prevention in postmenopausal women is primarily based on a healthy lifestyle: consuming an adequate amount of calcium-rich foods, regular physical activity, etc. Drugs come in second place.

Denosumab, a monoclonal antibody, has been developed on the basis of complex pathophysiological hypotheses suggesting that it should act specifically on osteoclasts. Yet this specificity was challenged even at the animal testing stage, which showed effects on lymphocytes and, therefore, on the immune system.

In clinical trials, *denosumab* showed only modest efficacy in postmenopausal women (a few fractures prevented). It is no more effective and probably less so than bisphosphonates. In contrast, numerous potentially serious adverse effects had already been reported, including deep-seated infections (endocarditis, arthritis) and cancers linked to immunosuppression. Long-term risks are obviously unknown.

Thus, the harms associated with *denosumab* far outweigh the expected benefits. And these harms were largely predictable, from the first stages of the drug's development.

One does not use a sledgehammer to crack a nut, nor an immunosuppressive monoclonal antibody to fight osteoporosis.

Prescrire

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