Pegvisomant

Approved indication: acromegaly

Somavert (Pfizer)

vials containing 10 mg, 15 mg and 20 mg as powder for reconstitution

Australian Medicines Handbook section 10.6

Aust Prescr 2017;40:199
https://doi.org/10.18773/austprescr.2017.065
First published 1 September 2017

Acromegaly is usually the result of an adenoma in the anterior pituitary gland. Although the high concentrations of growth hormone can have direct effects, they also act by increasing production of insulin-like growth factors. A high concentration of insulin-like growth factor type 1 (IGF-1) is a diagnostic feature of acromegaly.

Most patients are treated with surgery, sometimes followed by radiotherapy. Medical treatment may be needed if the surgery is not successful. Giving an analogue of somatostatin (growth hormone inhibiting peptide) is one approach and lanreotide and octreotide have been available for many years.[1]

Pegvisomant offers a different approach. It is an analogue of growth hormone, but it has been genetically engineered to act as a growth hormone receptor antagonist. By binding to the receptor, pegvisomant blocks the binding of growth hormone. This is reflected in reduced concentrations of IGF-1.

The protein is given by subcutaneous injection reaching peak serum concentrations in the next 33–77 hours. As the molecule is pegylated (with polyethylene glycol polymers) its clearance is reduced. The half-life is approximately six days. A daily injection is recommended with the dose adjusted according to the IGF-1 concentration.

A double-blind study compared three different doses of pegvisomant with placebo in 112 patients, 93 of whom had already had surgery for their pituitary adenomas. After 12 weeks the concentration of IGF-1 had significantly declined in the three groups given pegvisomant. Most of the reduction occurred within two weeks.[2]

In an observational uncontrolled longer term follow-up study, 87 out of 90 patients treated for a year had normal IGF-1 concentrations. The concentrations remained low in 39 patients treated for 18 months.[3]

During the long-term follow-up, headaches and infection were the most frequently reported adverse events. Injection-site reactions affected 11% of patients and two people were withdrawn from the study because of increased concentrations of liver enzymes.[3] Hepatic function should therefore be tested before and during therapy.

Blocking the growth hormone receptor may result in increased growth hormone production to overcome the blockade. This is a concern as the patient's tumour may enlarge. In the follow-up study, in patients who had not received radiotherapy, there was an increase in tumour size, however this was not statistically significant.[3]

Pegvisomant was originally approved in Australia more than a decade ago. During this interval more information about the drug has emerged from overseas studies. The postmarketing, open-label ACROSTUDY involved 710 patients followed for up to five years. Most of these patients had received other treatments before starting pegvisomant monotherapy. Although 67.5% of the patients achieved a normal concentration of IGF-1, and 2.6% had a low concentration, it remained elevated in 29.9%. Adverse events affected 345 patients including 133 who had serious adverse events such as increased tumour size. There were liver-related adverse effects in 30 patients,[4] including eight who had transaminase concentration three times the normal limit.[4] Systemic hypersensitivity reactions have also been reported.[4]

Acromegaly is a rare disease so data are still limited. Pegvisomant is only indicated if patients have an inadequate response to surgery, radiation and other drugs. The ACROSTUDY shows that pegvisomant is less effective at normalising IGF-1 than it appeared to be in the original trials.[2,3] This could possibly explain why many patients could not be managed with pegvisomant monotherapy and why the proportion needing higher doses increased during the study. Although there has been research into less frequent dosing, most patients will need daily injections.[4]

T T T manufacturer provided the (2005) clinical evaluation

REFERENCES

1. Lim EM. Drug treatment of pituitary tumours. Aust Prescr 2009;32:19-21. https://doi.org/10.18773/austprescr.2009.010
2. Trainer PJ, Drake WM, Katznelson L, Freda PU, Herman-Bonert V, van der Lely AJ, et al. Treatment of acromegaly with the growth hormone-receptor antagonist pegvisomant. N Engl J Med 2000;342:1171-7. https://doi.org/10.1056/NEJM200004203421604
3. van der Lely AJ, Hutson RK, Trainer PJ, Besser GM, Barkan AL, Katznelson L, et al. Long-term treatment of acromegaly with pegvisomant, a growth hormone receptor antagonist. Lancet 2001;358:1754-9. https://doi.org/10.1016/S0140-6736(01)06844-1
4. Freda PU, Gordon MB, Kelepouris N, Jonsson P, Koltowska-Haggstrom M, van der Lely AJ. Long-term treatment with pegvisomant as monotherapy in patients with acromegaly: experience from ACROSTUDY. Endocr Pract 2015;21:264-74. https://doi.org/10.4158/EP14330.OR

The Transparency Score is explained in New drugs: transparency, Vol 37 No 1, Aust Prescr 2014;37:27.

At the time the comment was prepared, information about this drug was available on the websites of the Food and Drug Administration in the USA, and the European Medicines Agency.