Pegvisomant

Pegvisomant is a protein containing 191 amino acid residues to which several polyethylene glycol polymers have been covalently bound in order to slow clearance from the blood. The protein is a modified version of human growth hormone designed to bind to and block the growth hormone receptor. It is manufactured using genetically modified E. coli bacteria. The polyethylene glycol polymers are subsequently added chemically.

Indications

The FDA approved pegvisomant (Somavert Pfizer), a growth hormone receptor antagonist, for parenteral treatment of acromegaly in patients who are not candidates for or have had an inadequate response to surgery or other treatment [1].

As the only GH receptor antagonist (GHRA) available, pegvisomant has shown its effectiveness in the control of insulin like growth factor IGF-1 [2].

van der Lely et al demonstrated Pegvisomant as an effective medical treatment for acromegaly, because of the patients treated for 12 months or more, 87 of 90 (97%) achieved a normal serum IGF-1 concentration [3].

It is delivered as a powder that is mixed with water and injected under the skin.

Data support a comparable QoL in patients receiving pegvisomant vs. somatostatin analogue, despite the fact that the vast majority receiving pegvisomant did not respond to or were not able to tolerate somatostatin analogs [4].

Despite the more aggressive behavior of GH&PRL-PitNETs compared to Somatotroph pituitary neuroendocrine tumors, there were no significant differences in the rate of IGF-1 control between the two drugs (pegvisomant and pasireotide) in either patient group. Both drugs were effective in controlling IGF-1 and PRL hypersecretion in the tumors studied. The study found that pegvisomant and pasireotide are both effective treatments for controlling IGF-1 and PRL hypersecretion in patients with GH&PRL-Pit-NETs and GH-Pit-NETs, with no substantial differences in efficacy between the two drugs [5].

Side effects

Side effects of Pegvisomant include reactions at the injection site, swelling of the limbs, chest pain, hypoglycemia, nausea and hepatitis.

Blocking of the growth hormone's receptor reduces feedback control of the growth hormone regulation leading to approximately doubled GH levels.

The GH receptor antagonist pegvisomant is increasingly used as therapy in acromegaly.

Combination Therapy

The combination of somatostatin analog SA and pegvisomant in patients who could not achieve IGF-1 normalization was safe and aided improved quality of life in acromegaly [6) 7) 8) 9)].

Further, the combination of pegvisomant and SA could reduce the dose of SA that is required [10)].

There is, however, no evidence adequate to prove the significant benefits obtained from combination [11)].

In Melmed et al's guidelines, such combination is recommended on the condition that patients are resistant to other treatments [12)].

In combination with cabergoline, the combination of SA and cabergoline might provide effective treatment in patients with mixed pituitary neuroendocrine tumors in whom simultaneously elevated prolactin (PRL) and GH are observed [13)], while, in patients who are partially responsive to the maximum SA dose, additive therapy with cabergoline could normalize IGF-1 in about half of the patients, including those without prolactinemia [14)].

Pituitary surgery might be indicated on pegvisomant treatment, due to side effects, adenoma growth or intention to cure after primary treatment.

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