

Stopping The Progression Of Disorder For Acromegaly Sufferers Shows Additional Implications For Breast And Prostate Cancer Patients

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It's easy to hail any cure that relieves the suffering of many, and just as easy to overlook the treatments so crucial to so very few. They call these "orphan drugs" as though these life-saving potions for less than 60,000 or so sufferers have no place in societies with much bigger plagues. But to each individual person so afflicted, "orphan drugs" are life-changing, soul-saving, hope-charged miracles of epic proportions. One such drug is called Somavert and the life-threatening disease it attacks is known as acromegaly.

Acromegaly is a hormonal disorder that results from too much growth hormone (GH) produced by benign tumors on the pituitary gland. If these tumors bloom before the onset of puberty, the victim becomes a giant with myriad health problems. If onset is after puberty, the victim suffers from enlarged limbs and organs, including the heart, and a

variety of related health consequences such as diabetes, debilitating arthritis and cardiovascular disease. Other consequences add insult to injury: bony changes can lead to disfigurement, for example, a huge protruding jaw or super-sized hands and feet, while the skin thickens and exudes excessive perspiration.

“Acromegaly is associated with a proven increased mortality rate,” says Dr. A.J. van der Lely, a clinician in Rotterdam, Netherlands, who, along with Dr. Peter Trainer in Manchester, England, did most of the original work with the GH antagonist—called Pegvisomant and sold as Somavert by Pfizer—in acromegalic patients.

The discovery of Somavert was a huge advancement in the successful treatment of the disease.

“Currently available treatment modalities for acromegaly consist of surgery, radiotherapy and medication,” explains van der Lely. “Unfortunately, surgery cures only 60 percent of patients overall and less than half of patients with macroadenomas, which constitute the majority of patients with acromegaly. The effect of radiotherapy is delayed and variable with poor efficacy and a high incidence of panhypopituitarism. Available medical treatment modalities still leaves at least one third of patients eligible for a more effective medical therapy.”

“In conclusion, Pegvisomant is the most effective medical treatment for acromegaly to date,” he says.

John Kopchick, Ph.D., Goll-Ohio Professor of Molecular Biology and his research team were the first to discover and characterize the molecular aspects of GH antagonists. “Somavert is the first drug of its kind; the very first large molecule antagonist,” he explains.

Kopchick and his team spent 25 years studying growth hormone in mouse models. “We were trying to come up with a more potent agonist, instead we came up with an antagonist—180 degrees from what we were shooting for,” he says.

Ohio University and Kopchick were awarded several U.S. and European patents for the discovery. The drug was approved for use in acromegaly patients in 2003.

Kopchick was instrumental in founding a company, called Sensus, with Rick Hawkins who served as chairman and has since founded an unrelated new company called LabNow. Sensus has since been sold to Pfizer which now distributes and markets Somavert.

“Patients immediately feel better after using Somavert. The letters have poured in from patients and their family members lauding both physical and psychological changes from using Somavert. It’s very satisfying to make a difference in their lives,” says Hawkins.

Hawkins points out that the drug will not reverse bony changes that have already formed, but that it does stop the progression of such changes. “It stops the production of (insulin-like growth factor 1) IGF-1 and normalizes patients,” he says.

As it turns out, Somavert may not be an orphan drug for long. “There is big indication for the drug in the treatment of breast and prostate cancer,” says Hawkins.

van der Lely said that the first association between GH and diabetes was made in 1937 in a showing that anterior pituitary extracts precipitated diabetes in dogs and furthered when Campbell (and others) showed that daily injections of highly purified GH made dogs permanently diabetic. Thirty years ago it was shown that diabetic patients present with GH hypersecretion at about the same time the “GH hypothesis” was launched, suggesting that GH plays an important role in the development of diabetic micro-vascular disease such as retinopathy (damage to the eye’s retina).

Increased circulating GH concentrations are believed to stimulate local IGF-1 concentrations in non-liver tissues, for example, in the kidney, blood vessels and the eye.

“*Researchers believe that suppressing the circulating GH levels will minimize the harmful effects on diabetic metabolic aberration and could prevent long-term diabetic complications.*”

“In this context GHR antagonists are interesting candidates,” says van der Lely. “Experimental data suggest that GHR blockade, by the use of GHR antagonists, may present a new concept in the treatment of diabetic renal complications. Future studies are warranted to fully characterize the clinical potential of GHR antagonists as drugs for treatment of diabetic complications in general.”

The role of GH in a variety of cancers also points to potential successful treatment by Somavert. “A series of epidemiological analyses have linked circulating IGF-1 concentrations, or IGF-1/IGFBP-3 ratios, with the risk of developing several different types of cancer, including prostate, breast and colon cancer,” explains van der Lely. “With respect to modulating tumor growth once neoplastic transformation has occurred, numerous pre-clinical studies have defined IGF-1 as potent growth factor for dozens of different tumor types.”

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