Brand Name: Sogroya

Generic Name: Somapacitan-beco

Manufacturer: Novo Nordisk Inc.

Drug Class: Growth hormone replacement

Uses:
Labeled: Replacement of endogenous growth hormone in adults with growth hormone deficiency (GHD).

Mechanism of Action: Sogroya binds to growth hormone (GH) receptors in the targeted cells producing a signal to cause the pharmacodynamic effects. Some of these effects are mediated through insulin-like growth factor 1, and others are caused directly by the drug.

Pharmacokinetics

Tmax	4-24 hours
Volume of Distribution	~14.6 L
Half life	~2-3 days
Clearance	0.268 $\pm$ 0.03 mg/h
Protein Binding	99% protein bound
Bioavailability	100%

Metabolism: Proteolytic cleavage of the linker sequence between the peptide and albumin without an active metabolite.

Elimination: ~81% of the dose is eliminated renally and ~13% is eliminated through feces. There is no intact somapacitan excreted renally or fecally.

Efficacy:

Citation: Johannsson G, Feldt-Rasmussen U, Håkonsson IH, et al. Safety and convenience of once-weekly somapacitan in adult GH deficiency: a 26-week randomized, controlled trial. Eur J Endocrinol. 2018;178(5):491-499.

Study Design: A randomized, open-label, active controlled study comparing once weekly somapacitan with once daily Norditropin.
Description of Study: This trial included male and female patients, aged 17-79, with adult growth hormone deficiency treated with once daily growth hormone (GH) for greater than 6 months. Patients were randomized into two groups receiving either somapacitan (n=61) or once daily norditropin (n=31) both administered by subcutaneous pen. Both treatments were titrated as necessary over 8 weeks then given the fixed dose for another 18 weeks. The key outcomes were the occurrence of adverse events (AE) and convenience score (using the Treatment Satisfaction Convenience Questionnaire for Medications-9 (TSQM-9)). The study found that AE's were mostly mild and transient in

patients, with the most common being nasopharyngitis, headache, and fatigue. There were no clinically significant injection site reactions after giving over 1500 shots and the TSQM-9 score in the somapacitan group was significantly more increased.
Limitations: Statistical analyses were not provided for comparing the rates of the adverse events. The 26-week trial period was a very short trial time for these drugs. The sample sizes were fairly small for each group (somapacitan n=61; Norditropin n=31.) The study was also open-label which could lead to possible bias.
Conclusions: This study shows that the adverse events may be similar between the once daily GH and the once weekly. Due to its once weekly dosing patients found somapacitan to be more convenient and had a higher overall treatment satisfaction. More well-designed studies should be done to show any statistical differences in AE rates and to determine if there was a difference in efficacy.

Citation: Johannsson G, Gordon MB, Højby Rasmussen M, et al. Once-weekly Somapacitan is Effective and Well Tolerated in Adults with GH Deficiency: A Randomized Phase 3 Trial. J Clin Endocrinol Metab. 2020;105(4):e1358-e1376.

Study Design: Randomized, parallel, double blinded and open label, placebo and active controlled
Description of Study: This clinical trial included male and female patients, aged 23-79, with a diagnosis of adult or childhood-onset growth hormone deficiency who were treatment naïve for > 180 days. They were randomized to receive either once weekly somapacitan (n=121), once weekly placebo (n=61), or once daily growth hormone (GH) (n=119). The study was double blind between the somapacitan and the placebo group but open-label for the GH group. There was an 8-week titration period, followed by a 26-week fixed dose treatment. The primary outcome was to show there is a treatment difference between somapacitan and placebo in truncal fat percentage. The researchers found that somapacitan significantly reduced truncal fat percentage (-1.53% [-2.68, -0.38] p=0.009). Additionally, they found that improvements were maintained at 86 weeks with both the somapacitan group and the daily GH group.
Limitations: No statistical tests were utilized to assess differences between the two active groups' efficacy measures or AE rates. The patients who received the daily GH were unblinded due to the fact that they got treatment every day and the other two groups got treatment once a week.
Conclusions: The study showed that somapacitan was more efficacious than placebo at reducing truncal fat percentage. However, the study should have statistically analyzed efficacy results between the two active treatment groups. Without statistical analysis, this study cannot show that the once weekly somapacitan should be used over an older treatment like once daily GH.

Citation: Otsuka F, Takahashi Y, Tahara S, Ogawa Y, Højby Rasmussen M, Takano K. Similar safety and efficacy in previously treated adults with growth hormone deficiency randomized to once-weekly somapacitan or daily growth hormone [published online ahead of print, 2020 Jun 30]. Clin Endocrinol (Oxf). 2020;10.1111/cen.14273.

Study Design: Randomized, parallel, open-label, active control trial

Description of the Study: Participants in this study were Japanese patients, aged 18-79 years old, with a diagnosis of adult or childhood-onset growth hormone deficiency for at least 6 months. Patients were randomly assigned to two groups, either somapacitan once weekly (n=46) or daily growth hormone (GH) (n=16), and the treatments were open label. Patients had their doses titrated over the first 20 weeks, then continued their final dose for another 36 weeks. The primary endpoint was incidence of adverse events (AE). Researchers found that rates of AEs/100 patient years were similar between the two groups (somapacitan (312.7); daily GH (309.8)). They also found no difference between the two groups in change from baseline to week 52 in visceral, subcutaneous, and total adipose tissue.
Limitations: The study was funded by the manufacturer of somapacitan. The study population were only Japanese ethnicity which would make it hard to extrapolate to other ethnicities. The sample sizes were small (somapacitan n=46, Daily GH n=16). The study was open label which could result in bias.
Conclusion: This study showed that daily GH and once weekly somapacitan had no significant difference in efficacy at reducing adipose tissue. This study can also be used to show that there are similar AE rates per 100 patient years between the two drugs, even with the different administration times. This could be used to support the use of once weekly somapacitan instead of daily GH due to reduced patient burden.

Contraindications: Acute critical illness, active malignancy, hypersensitivity to Sogroya, and active proliferative or severe non-proliferative diabetic retinopathy.

Precautions: Increased mortality in patients with acute critical illnesses; increased risk of neoplasms; glucose intolerance and diabetes; intracranial hypertension; severe hypersensitivity; fluid retention; hypoadrenalism; hypothyroidism; pancreatitis; lipohypertrophy/lipoatrophy; laboratory tests. (Inorganic phosphates, alkaline phosphates, and parathyroid hormone may increase)

Adverse effects: Back pain (10%), arthralgia (6.7%), dyspepsia (5%), sleep disorder (4.2%), dizziness (4.2%), tonsilitis (3.3%), peripheral edema (3.3%), vomiting (3.3%), adrenal insufficiency (3.3%), hypertension (3.3%), blood creatinine phosphokinase increase (3.3%), weight increase (3.3%), and anemia (2.5%)

Drug Interactions:
Replacement Glucocorticoids: Patients treated with glucocorticoid replacements may require an increase in their maintenance and/or acute dose due to Sogroya's inhibition of the enzyme 11ßHSD-1.
CYP450 Metabolized Drugs: Limited data indicates that Sogroya may increase the clearance of CYP450 mediated antipyrine clearance.
Oral Estrogen: May reduce the serum IGF-1 which would necessitate a possible need to increase the Sogroya dose
Insulin and/or Hypoglycemic Agents: Sogroya may decrease insulin sensitivity so dose of insulin and other hypoglycemic agents may need adjusted

Dosing/Administration

Usual Dose: Initiate with a dose of 1.5mg subcutaneously once a week. Dose can be increased by 0.5mg – 1.5mg every 2 – 4 weeks until desired response is achieved. Dosage should also be titrated based on insulin-like growth factor serum concentrations taken 3 – 4 days after the prior dose. The maximum recommended dosage is 8mg once weekly.
Geriatric Dose: Initiate at a dose of 1mg subcutaneously once a week and use smaller dosage increase than the adjustments above.
Pediatric Dose: N/A
Renal Impairment Dose: N/A
Hepatic Impairment Dose: There is no specific dosage adjustment needed. In moderate impairment start at 1 mg a week with smaller dosage impairment with a maximum of 4 mg. Not recommended in patients with severe hepatic impairment.
When Taking with Oral Estrogen: Initiate with a dose of 2 mg per week. Titrate by 0.5 – 1.5 mg every 2 – 4 weeks as needed for a therapeutic response.

Special circumstances:
Immunogenicity: As with any therapeutic protein, there is a risk for immunogenicity with Sogroya. Immunogenicity has not been seen in any patient in the clinical trials with GHD, but there is always a risk.
Pregnancy: There is no data associated with Sogroya in pregnant women. Studies have been published with recombinant growth hormone not causing any kind of birth defects over several decades. In animal studies, Sogroya did not show any teratogenicity in rats and rabbits at 12 times the clinical exposure recommended in humans.
Lactation: There is no information available on the presence of Sogroya in human milk, the effects on infants, or the effects on milk production. Sogroya related material was found in the milk of rats, which means it is likely that it will also be in human milk. Published data available on recombinant growth hormone administered 7 days before lactating did not increase the normal breast milk concentration of GH in the breast milk. The risks vs. benefits should be weighed when deciding whether to breastfeed while on this medication.

Conclusion: Somapacitan appears to have similar efficacy to other growth hormone therapies that are currently used. Somapacitan is formulated to be a once a week injection as opposed to once a day like other growth hormone formulations. This factor may reduce patient burden compared to once daily administration of current growth hormone therapies and may increase patient satisfaction. This drug can be used to replace traditional growth hormone replacement therapies as a more convenient, but still efficacious option if cost differences are not prohibitive.

References:

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