Poster EE27

Cost-effectiveness and Cost-utility Analysis of Somatrogon Once-weekly Injectable vs. Daily Growth Hormones for Treating Pediatric Growth Hormone Deficiency

Simone Rivolo[1], Jane Loftus[2], Balazs Peter[3], Marion Fahey[4], Samira Toghanian[5], Carmen Peral[6], Cynthia Khanji[7], Michelle Stewart[8], Thitima Kongnakorn[9]

[1]Evidera, Inc. Milan, Italy, [2]Pfizer Ltd Walton Oaks, Tadworth, UK, [3]Evidera, Inc. Budapest, Hungary, [4]Pfizer Ireland, [5]Pfizer Sweden, [6]Pfizer Spain, [7]Pfizer Canada, [8]Pfizer, Inc., Groton, CT, USA, [9]Evidera, Inc. London, UK.

Objective

To evaluate cost-effectiveness and cost-utility of somatrogon (once-weekly injectable long-acting human growth hormone) vs daily injectable growth hormones across 5 countries (United States, Canada, Spain, Sweden, Ireland)

Conclusion

Somatrogon weekly injections were estimated to result in higher near adult height (NAH), higher quality-adjusted life years (QALYs) and favourable cost-effectiveness vs. human growth hormone (dGHs), in growth hormone deficiency (pGHD).

Background

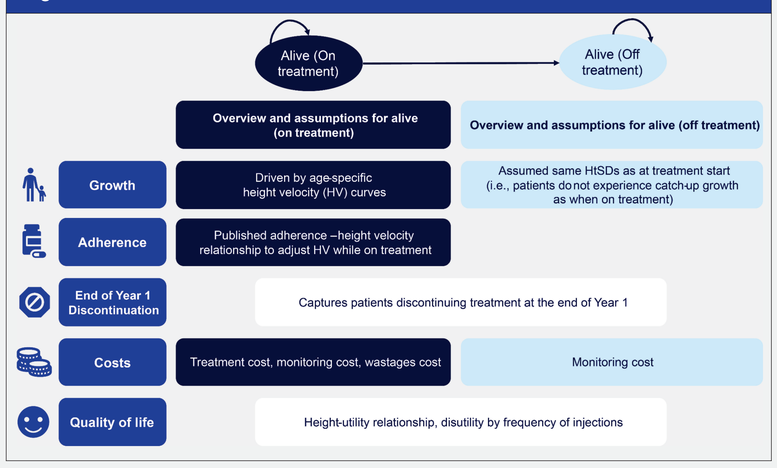
- Paediatric growth hormone deficiency (pGHD) is defined as growth failure associated with inadequate growth hormone (GH) production. Daily injections of recombinant human GH (dGH) [somatropin] is the current standard of care, which has been shown to be safe and effective.[1]
- However, dGHs are associated with key drivers suboptimal adherence (5%-82% non-adherence prevalence)[2], with one of the key driver being exhaustion from the daily burden of long-term injections.[3] Suboptimal adherence is associated with reduced dGHs effectiveness, leading to lower yearly growth[4-6] and reduced near adult height (NAH) achieved.
- Somatrogon, a once-weekly injectable long-acting human GH, has demonstrated clinical non-inferiority[7] and significantly lower life interference vs. somatropin[8]. Therefore, Somatrogon weekly injection schedule has the potential to increase patients' adherence and improve patients QoL, in turn leading to improved final adult height vs. dGHs over the long term.

Methods

MODEL DESCRIPTION

- A Markov model (**Figure 1**) was developed in Microsoft Excel® to simulate patients starting somatrogon or dGHs treatment at 3-12 years of age. The model consists of two health states: 1] Alive on-treatment and 2] Alive off-treatment, with the modelled time horizon up to 18 years of age.
- Patients' growth was modelled for each age band separately, through age- and gender-specific height velocity (HV) curves. Patients could discontinue at end of Year 1, with all other patients assumed to remain on-treatment until the end of the model time horizon.
- Treatment-specific adherence was captured while patients remained on treatment, with adherence-HV published relationships used to account for the decline in growth due to lack of adherence.
- Height-specific utilities (as in previous economic models[9,10]) and disutilities due to frequency of injections were considered to capture the impact of GH therapy on patients QoL.
- Treatment costs (while on treatment) and monitoring costs (on/off treatment) were considered in the model. The model was also designed to capture up to 5 different types of wastages caused by 1] product losses during injection preparation or device setting; 2] remaining product in the cartridge not large enough to warrant two injections thus not administered; 3] device setting dosing increments providing a larger dose than required; 4] storage wastage due to the product expiration (commonly after 21-28 days); 5] adherence wastage for the number of doses missed.

Figure 1: Model structure overview



MODEL ASSUMPTIONS

- Given the paediatric population, the time horizon limited to 18 years of age and that neither the disease[11] nor the treatment are associated with excess mortality (vs. the general population), the model does not capture death.
- HV from Year 2 onwards was extrapolated using the yearly decrease in height standard deviation (ΔHtSDs) gain observed in the literature[12,13], assumed to be constant over time and equal across age bands.
- The same adherence-HV relationship was applied across the comparators, due to the lack of treatment-specific relationships available in the literature.
- Patients may discontinue at the end of the first year and instead move to 'Alive (off treatment)' health state, where they remain until the end of the time horizon.
- Patients off-treatment after Year 1 were assumed to maintain the HtSDs at diagnosis, thus still experiencing growth, albeit limited (i.e. no catch-up growth to reduce the initial HtSDs deficit vs. the general population).

MODEL INPUTS

Clinical Inputs

- The clinical inputs are summarised in **Table 1**, with the cohort baseline characteristics and Year 1 HV (age specific) derived from the somatrogon trial[7].
- The HV from Year 2 onwards was extrapolated using country specific growth charts and the decline in HtSDs observed in the literature[12,13] (with the resulting somatrogon age-specific HV curves for US shown in **Figure 2**, as an example).
- Higher adherence of 4%-5% for somatrogon vs. dGHs in Year 1, tapering over time, was based on clinical consultation.
- Patients' QoL was captured based on 1] the height-utility relationship available in the literature[9,10], and 2] QoL decrement due to injection frequency from a study in diabetic patients, due to the lack of pGHD specific data (-0.023 for once-weekly vs. daily and -0.062 for off-treatment vs. daily[13]).

Figure 2: Somatrogon HV by age (US)

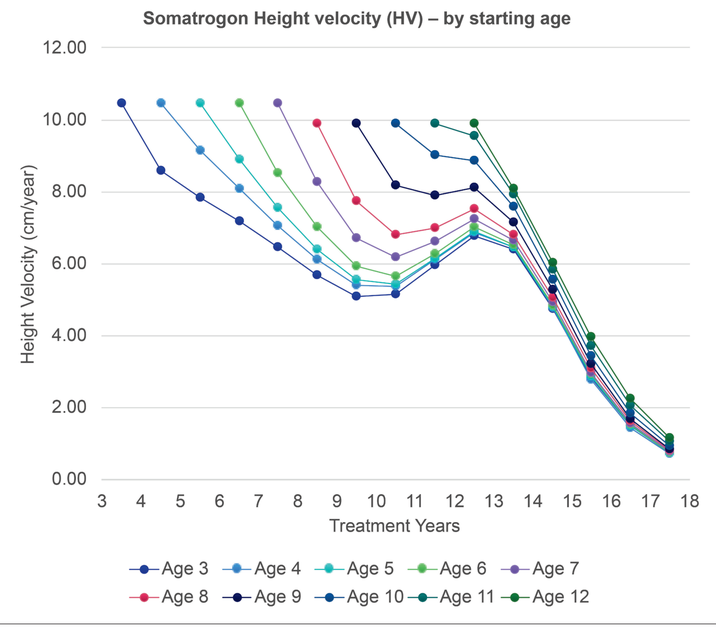


Table 1: Summary of key model inputs

Parameter	US	Canada	Spain	Sweden	Ireland	Source
Cohort	3-12 years old based on Somatrogon trial (baseline ΔHtSDs: -2.86, proportion of male: 71.9%)					Somatrogon trial[7]
Height velocity dGH – Year 1	Age 3-7:10.29 cm/year* Age 8-12: 9.35 cm/year*					Somatrogon trial[7]
Height velocity Somatrogon – Year 1	Age 3-7: 10.45 cm/year Age 8-12: 9.91 cm/year					Somatrogon trial[7]
ΔHtSDS decline from Year 2	40.54% for US and Canada		40.05%	40.54% for Sweden and Ireland		Ranke 2010[12], Luzuriaga Tomas 2016 [13]
Discontinuation at the end of Year 1	20.4%	20.4%	0%	20.4%	4%	Pfizer data on file[15], Spain: assumption Spandonaro 2013[16]

*Same Year 1 HV between dGHs and Somatrogon evaluated as scenario

Cost and Resource Use Inputs

- Treatment costs and monitoring costs were sourced from local data (**Table 1**), with the wastage costs driven by the device characteristics available on the markets. The dGHs were modelled as a basket of available brands and devices (with the same efficacy assumed since they are all somatropin formulations).
- The resource use frequencies associated with each health state are based on a previous dGHs NICE (National Institute for Health and Care Excellence) technical appraisal[10] or clinical experts' consultation, with the resulting monitoring costs summarised in **Table 3**.

Table 2: Dosing and drug acquisition costs (price per mg)

Description	US	Canada	Spain	Sweden	Ireland
Source of drug acquisition cost of dGHs	IBM Micromedex® RED BOOK®	Saskatchewan Drug Plan e-Formulary and Ontario EAP e-Formulary	BOT PLUS web (botplusweb.farmaceuticos.com)	tlv.se	HSE, 2022. October 2022 HT List of reimbursable items. PCRS Online Services - HSE.ie
Somatrogon drug acquisition cost scenarios (price per mg per week)	0% - 15% higher weekly cost vs. dGHs weekly cost based on dGHs country-specific market shares				
dGH dosing	0.24 mg/kg/week	0.18-0.24 mg/kg/week	0.21 mg/kg/week	0.24 mg/kg/week	0.21 mg/kg/week
Somatrogon dosing	0.66 mg/kg/week				
Adherence for dGH	88.7%-58.5% (Year 1 – Year 15) for dGHs	88.7%-82.2% (Year 1 – Year 15) for dGHs	93.9% - 95.9% (Year 1 – Year 4) from Arnao[6]. 2.16% yearly decrease Year 4+ from Maggio[4]	88.7%-58.5% (Year 1 – Year 15) for dGHs	95.3%-65% (Year 1 – Year 15) for dGHs from Maggio[4]
Adherence – HV relationship	Decline in HV with a decrease in adherence from Maggio 2018[4]	Decline in HV with a decrease in adherence from Maggio 2018[4]	Decline in HV with a decrease in adherence from Maggio 2018[4]or Arnao 2019[6]	Decline in HV with a decrease in adherence from Maggio 2018[4]	Decline in HV with a decrease in adherence from Maggio 2018[4]
Types of wastages	last dose, device setting, storage, preparation, adherence wastage	last dose, device setting, storage, preparation, adherence wastage	-	adherence wastage	device setting wastage, adherence wastage

Table 3: Summary of resource use yearly frequencies and unit costs

Resource frequency and unit cost	US	Canada	Spain	Sweden	Ireland
Endocrinologist visit	On-treatment: 3.5 Off-treatment: 2 ($ 206.50/visit)	On-treatment: 3 Off-treatment: 2 ($ 165.5/visit)	On-treatment: 4.5 Off-treatment: 1.5 (€ 108/visit)*	On-treatment: 3.5 Off-treatment: 2 (Kr 1,707.00/visit)	On-treatment: 3.5 Off-treatment: 2 (€ 414.00/visit)
Blood tests	On-treatment: 1 Off-treatment: 1 ($ 43.00/visit)	On-treatment: 1 Off-treatment: 1 ($ 3.98/visit)	On-treatment: 1.5 Off-treatment: 0.5 (€ 4/visit)	On-treatment: 1 Off-treatment: 1 (Kr 253.00/visit)	On-treatment: 1 Off-treatment: 1 (€ 25.00/visit)
Hand X-Ray	On-treatment: 1 ($ 125.50/visit)	On-treatment: 1 ($ 21.30/visit)	On-treatment: 0.5 Off-treatment: 0.5 (€ 55/visit)	On-treatment: 1 (Kr 720.00/visit)	On-treatment: 1 (€ 93.33/visit)
Pituitary Function Test**	On-treatment: 0.2 ($ 1,310.00/visit)	On-treatment: 0.2 ($ 93.90/visit)	On-treatment: 1.16 Off-treatment: 1.03 (€ 164/visit)	On-treatment: 0.2 (Kr 488.00/visit)	On-treatment: 0.2 (€ 109.98/visit)
General biochemistry	-	-	On-treatment: 0.5 Off-treatment: 0.5 (€ 31/visit)	-	-
Sources	Frequency: Christensen, 2010[8]; TA188[9] Cost: InHealth Professional Services. 2020 Physicians' Fee and Coding Guide (Payment Range). ISBN 978-1-60099-108-9	Frequency: Christensen, 2010; TA188 Cost: Ontario Schedule of Benefits Physician Services	Frequency: expert opinion Cost: Libro De Tarifas 2021	Frequency: Christensen, 2010[9]; TA188[10] Cost: local sources***	Frequency: Christensen, 2010[9]; TA188[10] Cost: local sources****

*Endocrinologists visit for Spain consists of four items (visita endocrinologo, fondo de ojo, auxologia complete, consulta al Sº de farmacia)
**Pituitary function test includes hormones prolactin, LH, FSH, TSH, Free T4, ACTH, cortisol, GH, IGF-1
***Hand X-Ray, pituitary function test: https://vardgivare.skane.se; endocrinologist visit, blood tests p46: https://sodrasjukvardsregionen.se
****Cost: Endocrinologist visit: K64B- Endocrine Disorders, MINC, ABF 2020. https://www.hpo.ie/abf/ABF2020AdmittedPatientPriceList.pdf; Blood tests: https://fola.care/prices; Hand X-Ray: https://www.affidea.ie/prices; Pituitary Function Test: https://www.thegpsurgery.co.uk/blood-test/endocrinology

Results

- Treating with somatrogon led to 1.71-4.11 cm near adult height (NAH) gain and 0.19-0.43 higher quality-adjusted life years (QALY) vs. dGHs, across the 5 countries considered, as summarised in **Figure 3**.
- Somatrogon was generally cost-effective vs dGHs, with dGH dosing, injection frequency disutility, dGHs unit costs and somatrogon adherence being the key cost-effectiveness drivers, across all countries (based on scenario analysis and deterministic sensitivity analysis).

Figure 3: Results overview across countries

	US	Canada	Spain	Sweden	Ireland
Health outcomes	**1.87 cm gain and 0.24 QALYs gain vs. dGHs**	**1.71-2.28 cm gain and 0.25-0.30 QALYs gain vs. dGHs**	**4.11 (4.08-4.12) cm gain and 0.33-0.34 QALYs gain vs. dGHs** ranges based on 1,000 PSA run	**2.13 cm gain and 0.25 QALYs gain vs. dGHs** 0.19-0.39 QALYs across scenarios	**2.85 cm gain and 0.27 QALYs gain vs. dGHs** 1.84-3.66 cm gain and 0.24-0.43 QALYs across scenarios
Cost-effectiveness	**Cost-effective at the WTP of $150,000** **Cost-effective at the WTP of $150,000 across most of the scenarios explored**	**Cost-effective vs. dGHs if 0.18 mg/Kg/week used and list price not higher than dGHs** **Dominant (meaning lower costs and higher QALYs thus cost-effective) vs. dGHs if 0.24 mg/Kg/week used**	**Dominant (meaning lower costs and higher QALYs thus cost-effective) vs. dGHs**	**Dominant (meaning lower costs and higher QALYs thus cost-effective) vs. dGHs**	**Cost-effective at the WTP of €20,000** Cost-effective at the WTPs of €20,000-€45,000 across all of the scenarios explored

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