Observational study on the prescription of the growth hormone Saizen® in adults in France

MEGHA Study

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Context

- Recombinant growth hormone (r-hGH) Saizen® has pediatric indications but also an indication for GH deficiency in adults.
- On HAS request, Merck Serono made an observatory study to describe prescription and monitoring conditions for patients treated by Saizen® in this indication.
- Included patients are followed-up for 5 years.
  These results describe final analysis.

Results

Included patients characteristics

- 90 GH deficient patients : 45 women ; 49 childhood acquired deficiency (CO group), 41 adulthood acquired deficiency (AO group), mean age :
  31,8±13 years old ; mean BMI (body mass index) : 26,4 kg/m2 (±5.8). Patients were enrolled between December 2003 and October 2007 by 23 French hospitals.
- Patients were followed up 3,3 years (±1,9) on average to a maximum of 5,3 years (time between inclusion and last visit).
- IGF 1 was <-2DS respectively for 62,5 % and 41,7 % of CO and AO patients.
- 95,6 % of patients had at least one associated hypopituitarism deficiency.
- 100 % of AO group patients had at least one dynamic test and 89,8 % of CO group patients (Fig.1).

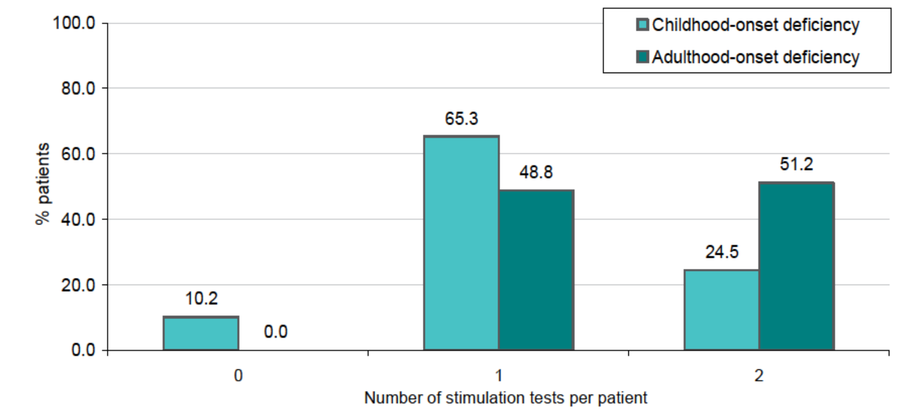
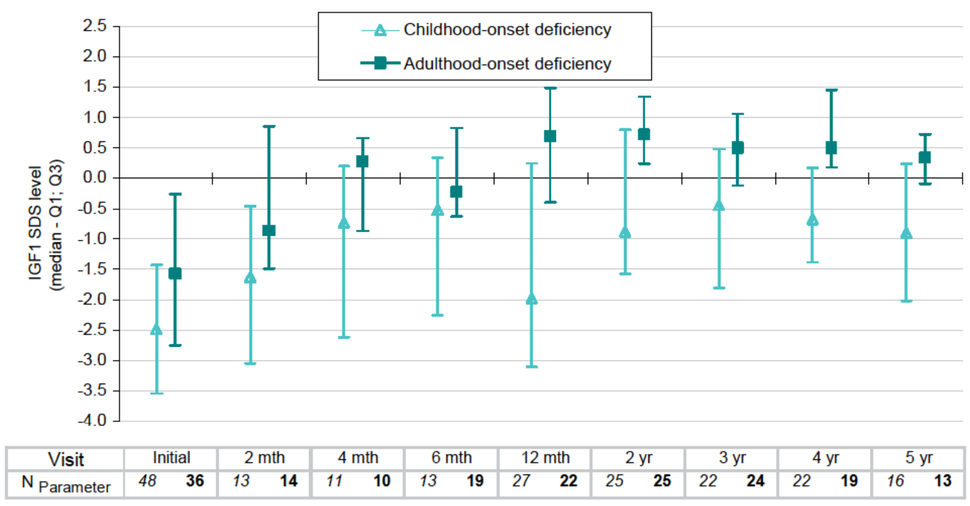


Fig.1 : Distribution of number of GH stimulation tests per patient according to onset of GH deficiency

- Initial GH dose was between 0,15 et 0,3 mg/d for 51,4 % of patients, lower in 27,1 % (median 0,24 mg/d).

Follow-up results

- **IGF-I :**
  One year after inclusion, IGF-I levels remained <-2DS for 48,1% of CO-group patients (4,5 % in AO-group), showing that these patients had not received an adequate GH dose to treat their deficit (Fig.2).



Visit	Initial	2 mth	4 mth	6 mth	12 mth	2 yr	3 yr	4 yr	5 yr
N Parameter	48 **36**	13 **14**	11 **10**	13 **19**	27 **22**	25 **25**	22 **24**	22 **19**	16 **13**

Fig.2 : IGF-I values in SDS (Réf. *Brabant et al. Hormone Research 2003 60 53–60.*)

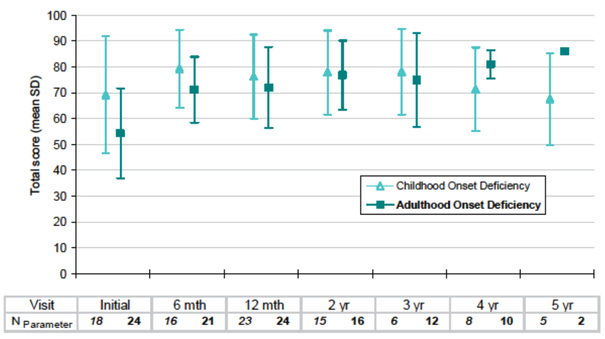
- **BMI, waist/hip ratio (WHR), blood pressure levels, lipid parameters, glycaemia were not significantly changed during follow-up period.**

- **ECGs :** Depending on the follow-up year, 15 to 39 % of patients had at least one ECG performed during the year. ECG result was normal for more than 85 % of the examinations.

- **Imaging examination**
  Depending on the follow-up year, 17 to 27 % of patients had at least one imaging examination performed. The most common examination was an MRI. Analysis of tumor evolution in patients with acquired deficiency showed a stabilization for most of patients and no worsening.

- **Treatment permanent discontinuation**
  Treatment permanent discontinuation was observed for 45 patients (50 % of patients), 24 in CO-group and 21 in AO-group). Patients had discontinued their treatment at a median of 13,0 months after inclusion (Q1=7,0; Q3= 28,0) and discontinuation was asked by the patient in 71,1 % of cases. The main reasons for discontinuation were an AE (9 patients, including 3 patients with a treatment-related AE), injection-related issues (6 patients), lack of efficacy (5 patients) and other non-specified reasons for 21 patients.
  Among these 45 patients, 26 discontinued treatment permanently, 13 took another GH after Saizen® discontinuation and no data were available for 6 patients.

- **Quality of life** (Fig.3)
  Overall, an improved quality of life (PGWB questionnaire) was observed for the first 6 months of treatment with a subsequent stabilization.



Visit	Initial	6 mth	12 mth	2 yr	3 yr	4 yr	5 yr
N Parameter	18 **24**	16 **21**	23 **24**	15 **16**	6 **12**	8 **10**	5 **2**

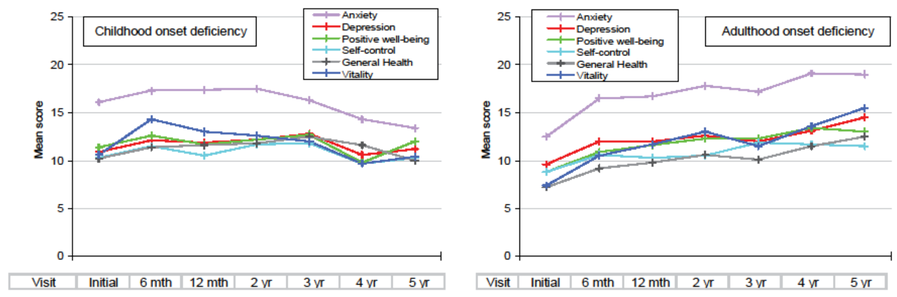


Fig.3 : Scores and subscores of PGWB questionnaires

These analysis results suggest a treatment beneficial effect on patient's quality of life, particularly for those with adulthood GH acquired deficiency.

- **Concomitant treatments**
  Overall, the percentage of patients with at least one concomitant treatment remained stable during follow-up and in similar proportions than those observed at inclusion.

- **Safety**
  The mean duration of treatment exposure was 39,8±22,7 months. Among the 90 included patients, 68 (75,6 %) experienced 278 adverse events (AEs). The most commonly reported AEs were arthralgia (16 patients, 23,5 %), myalgia (9 patients, 13,2 %), asthenia (8 patients, 11,8 %), headaches (7 patients, 10,3 %), depression (7 patients, 10,3 %), and paresthesia (5 patients, 7,4 %).
  No serious adverse event was related to treatment.

Conclusion

In the great majority of cases, prescription recommendations for Saizen® growth hormone in adults are observed. Experienced adverse events confirmed Saizen® safety as described in the Summary of Product Characteristics. However, obtaining earlier an effective dosage and closer monitoring are desirable.

Thanks

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Conflicts of interes

C. Cortet , M. Pugeat , J-L. Sadoul, J.Young, JC. Souberbielle and P. Chanson were investigators of the MEGHA study.

L. Fresneau is employed at Merck Serono S.A.S., Lyon, France.

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