

Safety and efficacy of treatment with long-acting lanreotide autogel® in early infancy in patients with congenital hyperinsulinism

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Background

Long-acting somatostatin analogues have been reported to be an effective treatment option to prevent hypoglycaemia in children with severe diffuse congenital hyperinsulinism (CHI). To date, only somatostatin or long-acting somatostatin analogue octreotide have been used in early infancy, requiring either continuous i.v. or s.c. infusion or multiple daily injections. Long-acting lanreotide autogel® (LAN-ATG), that has to be applied only once a month, has not been reported as a treatment option in early infancy (< 6 month of age).

Methods

We report the off-label use of LAN-ATG (5 - 10 mg/kg body weight) in four infants with CHI at an age of 2-3 month. CHI was due to homozygous ABCC8 gene mutations (c.563A>G; c.1176G>C) (patients 1 and 2) and in the context of Beckwith-Wiedemann syndrome (BWS) (UDP11 mosaic) (patients 3 and 4). Blood glucose concentrations, incidence of hypoglycaemia and the need of concomitant drugs and feeding before and after LAN-ATG treatment, as well as side effects were evaluated.

Results

Mean blood glucose concentrations 7 days before compared to 7 days after the first LAN-ATG administration increased by 0.75 mmol/L (range 0.39 – 1.19 mmol/L) (Fig. 1). Frequency of hypoglycaemia < 3.33 mmol/L decreased by 13% (range 0.1 - 27%) and of hypoglycaemia < 2.78 mmol/L by 7.7% (range 1.7 – 14.81%) (Fig. 2). Glucose infusions, octreotide, and glucagon treatment could be successfully stopped in all cases 3 - 20 days after the first LAN-ATG injection. In 3 patients with an increased carbohydrate intake, this could be normalized (average reduction of 7 g/kg body weight/d (range 1.75 - 12.8 g/kg body weight/d) (Fig. 3). Over a total of 40 treatment months, no serious adverse effects occurred. One patient had developed asymptomatic cholecystolithiasis while under subcutaneous octreotide therapy before the first LAN-ATG injection, which was treated with ursodesoxycholic acid, 3 developed subcutaneous nodules, which regressed spontaneously and showed no signs of inflammation (Fig. 4 and 5). On the day of the administration of LAN-ATG, all patients showed at least 2 hyperglycaemic blood glucose levels (> 8.33 mmol/L).

Conclusion

During treatment of CHI with LAN-ATG in early infancy in our cohort, no severe side effects, such as necrotizing enterocolitis, were observed. Treatment allowed return to an age-appropriate carbohydrate intake and resulted in improved glucose control. LAN-ATG might be a treatment option in patients < 6 month of age, not responding to current treatment regimens, as an alternative to surgery. It seems advisable to evaluate tolerability of somatostatin analogues using shorter acting octreotide for at least several days with slowly increasing dosages prior to first LAN-ATG injection. With only one injection per month it provides a higher flexibility in everyday life than octreotide. As there is still only limited data on the efficacy, dosage and safety especially in early infancy, LAN-ATG treatment remains an individual off-label approach after careful consideration of all available options and counseling of the parents.

Literature:

1 Kühnen P, Marquard J, Ernert A, Meissner T, Raile K, Wannemacher G, Blankenstein O: Long-term lanreotide treatment in six patients with congenital hyperinsulinism. *Horm Res Paediatr* 2012;78:106-112.

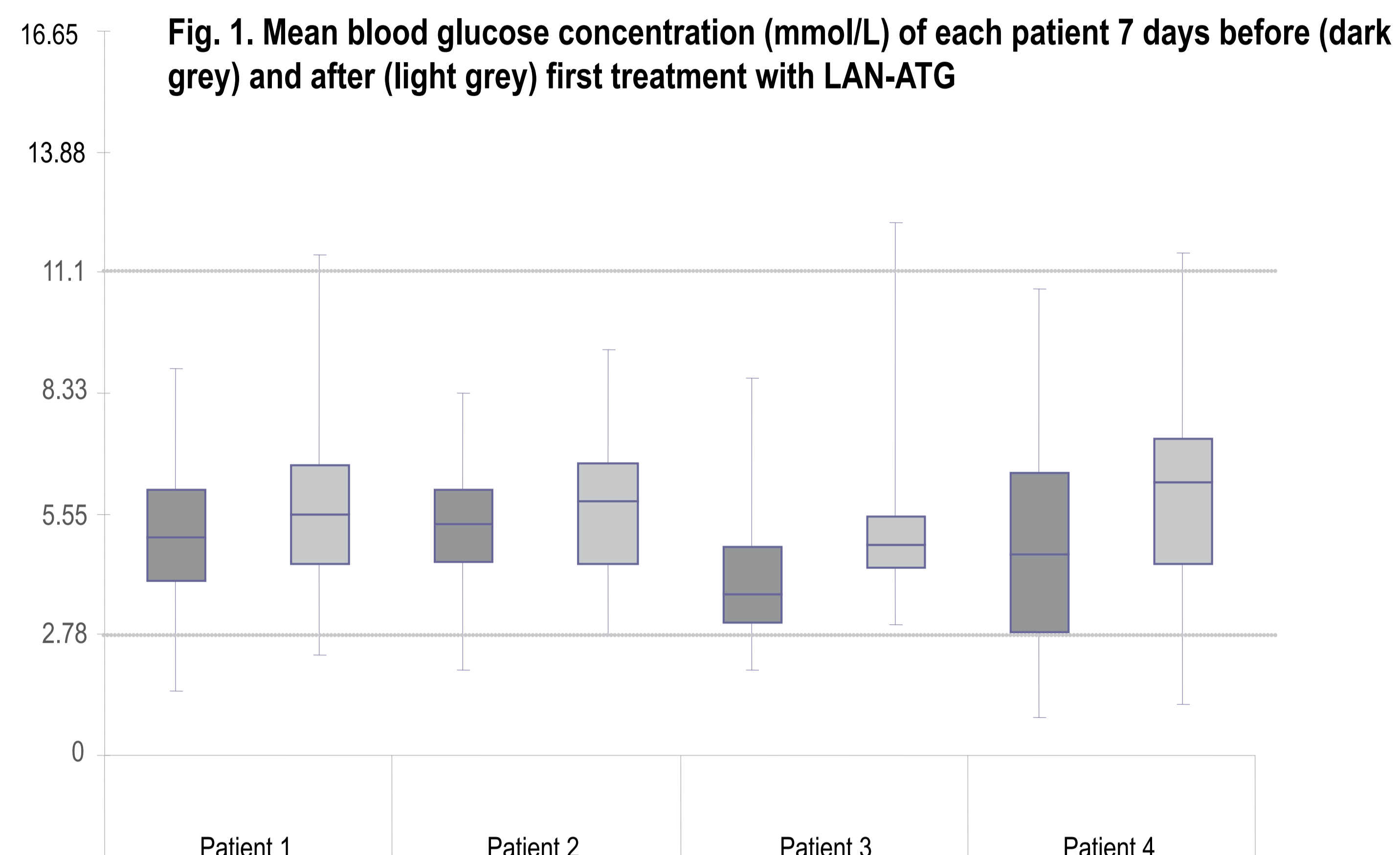


Fig. 1. Mean blood glucose concentration (mmol/L) of each patient 7 days before (dark grey) and after (light grey) first treatment with LAN-ATG

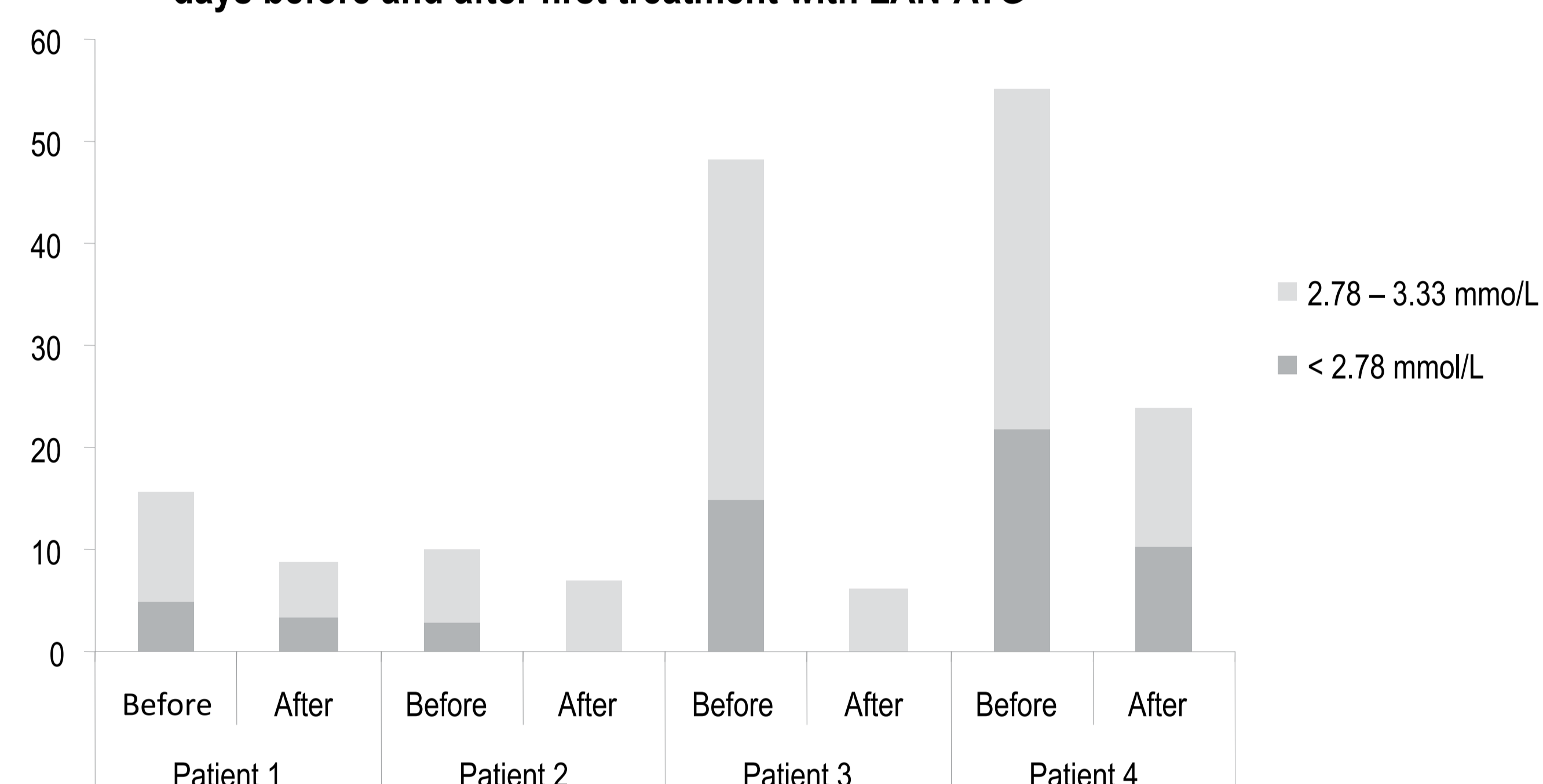


Fig. 2. Occurrence of hypoglycaemic episodes (% of recorded blood glucose values) 7 days before and after first treatment with LAN-ATG

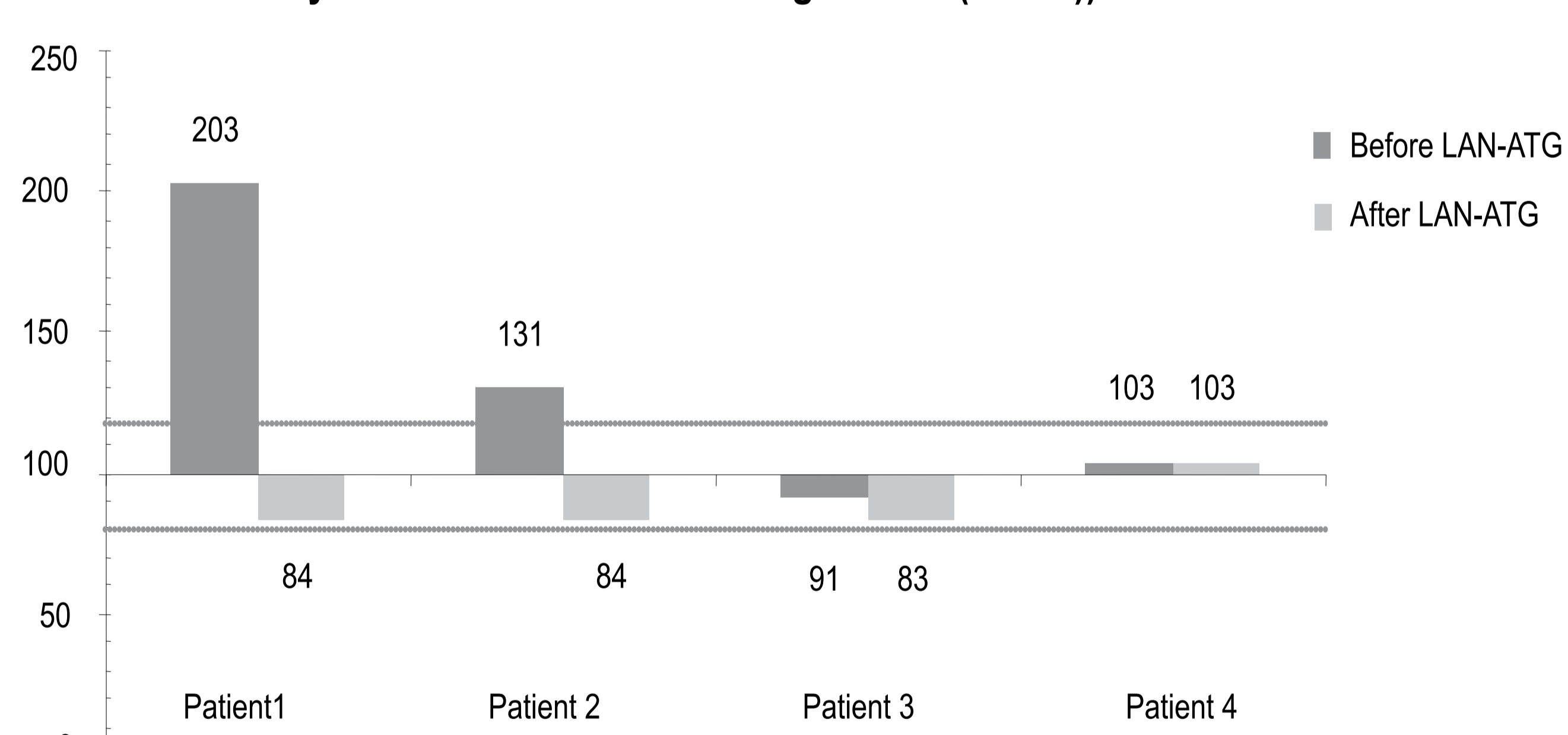
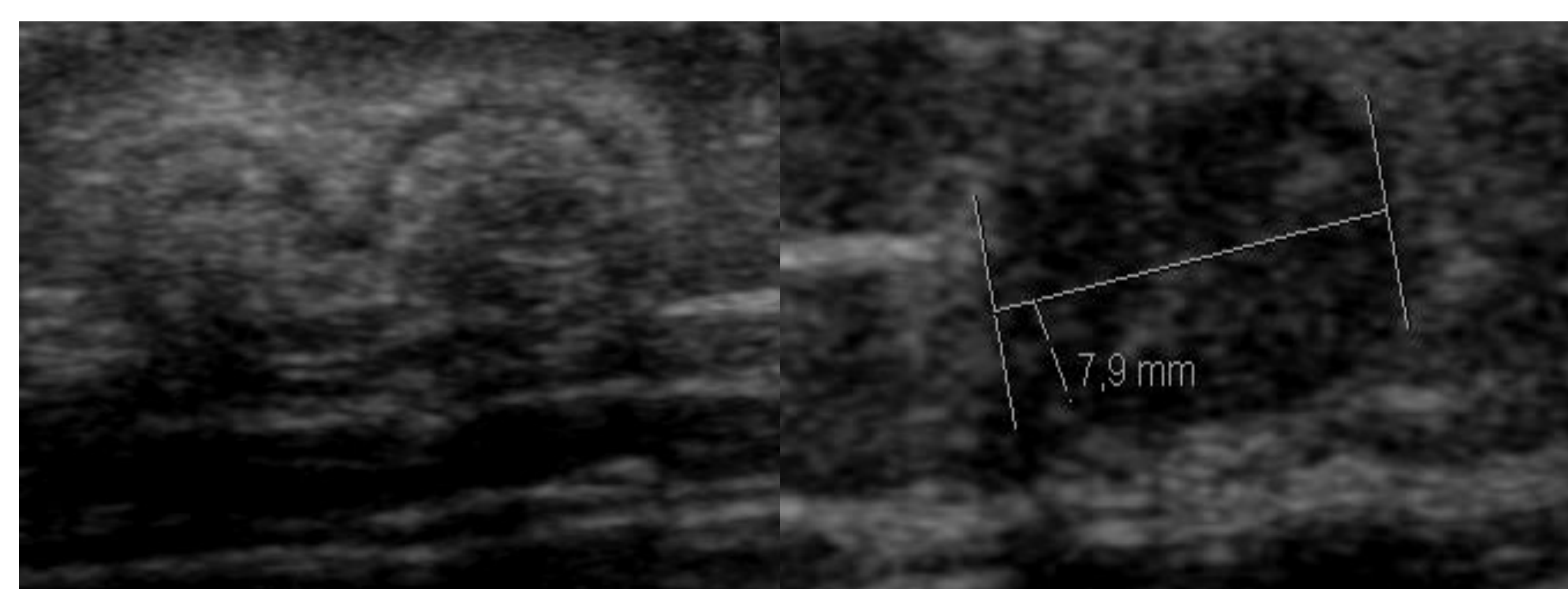


Fig. 4 and 5. Subcutaneous nodules



Disclosure Statement: H.C. has received financial support for congress participation from Merck Serono. S.K. has received financial support for congress participation from Ipsen Pharma and Merck Serono. T.M. has received financial support for congress participation from Ipsen Pharma, Merck Serono, Milupa metabolics and Novo Nordisk.

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