

# Long Acting Somatostatin Analogue (Lanreotide) therapy in Congenital Hyperinsulinism – Pharmacokinetics and long term follow-up study

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## Background

- Congenital hyperinsulinism (CHI) causes severe hypoglycaemia in children.
- Diazoxide and daily octreotide injections are first and second-line of treatment for CHI respectively.

## Objective and hypotheses

- To evaluate the efficacy, safety and pharmacokinetics of long acting somatostatin analogue (Lanreotide) therapy in CHI patients.

## Results

- 31 children were commenced on Lanreotide and 5 had to stop treatment. Out of 26 children, 18 were on daily octreotide and 8 on diazoxide.
- Pharmacokinetic data on 21 children showed highest median value (25<sup>th</sup>-75<sup>th</sup> interquartile range) of Lanreotide concentration was 14.93ng/ml (4.39-31.6) at +4 hours of 1<sup>st</sup> dose (figure 1).
- The median values (25<sup>th</sup>-75<sup>th</sup> interquartile range) prior to 2<sup>nd</sup>, 3<sup>rd</sup>, 4<sup>th</sup>, 5<sup>th</sup>, 6<sup>th</sup> and 12<sup>th</sup> doses were 0.88ng/ml (0.66-1.32), 1.09ng/ml (0.89-1.35), 1.21ng/ml (0.87-1.49), 0.79ng/ml (0.67-1.55), 1.35ng/ml (1.19-1.86) and 1.44ng/ml (1.08-2.18) respectively (figure 2).
- PedsQL showed significant change in total health and psychosocial score and significant reduction in overall stress in the SDQ after 1-year post-Lanreotide (p<0.05).
- CGMS on 15 children showed significant reduction in hypoglycaemic episodes after 1 year of therapy (p=0.012) (figure 3).

## Conclusion

- This study demonstrates lanreotide is safe and effective alternative to diazoxide and octreotide therapy in CHI patients with a significant improvement in blood glucose control and quality of life.
- There is cumulative effect in Lanreotide concentration after each dose. Our 2.5 years follow-up data shows no adverse effects on growth.
- However also to note that not all patients with CHI will response to Lanreotide and they need close monitoring when assessing the response of Lanreotide.

## Methods

- Patients >6 months of age either on high dose diazoxide (causing side effects), or daily octreotide were started on 30mg Lanreotide every 4-weeks.
- Children >3 years of age had Paediatric Quality of Life (PedsQL) with Strengths and Difficulties questionnaires (SDQ) and continuous glucose monitoring (CGMS) pre and 1-year post-Lanreotide.
- Plasma Lanreotide concentrations measured by radioimmunoassay (>3 years of age) at different time points after first dose and subsequently prior to each dose for 6 months.

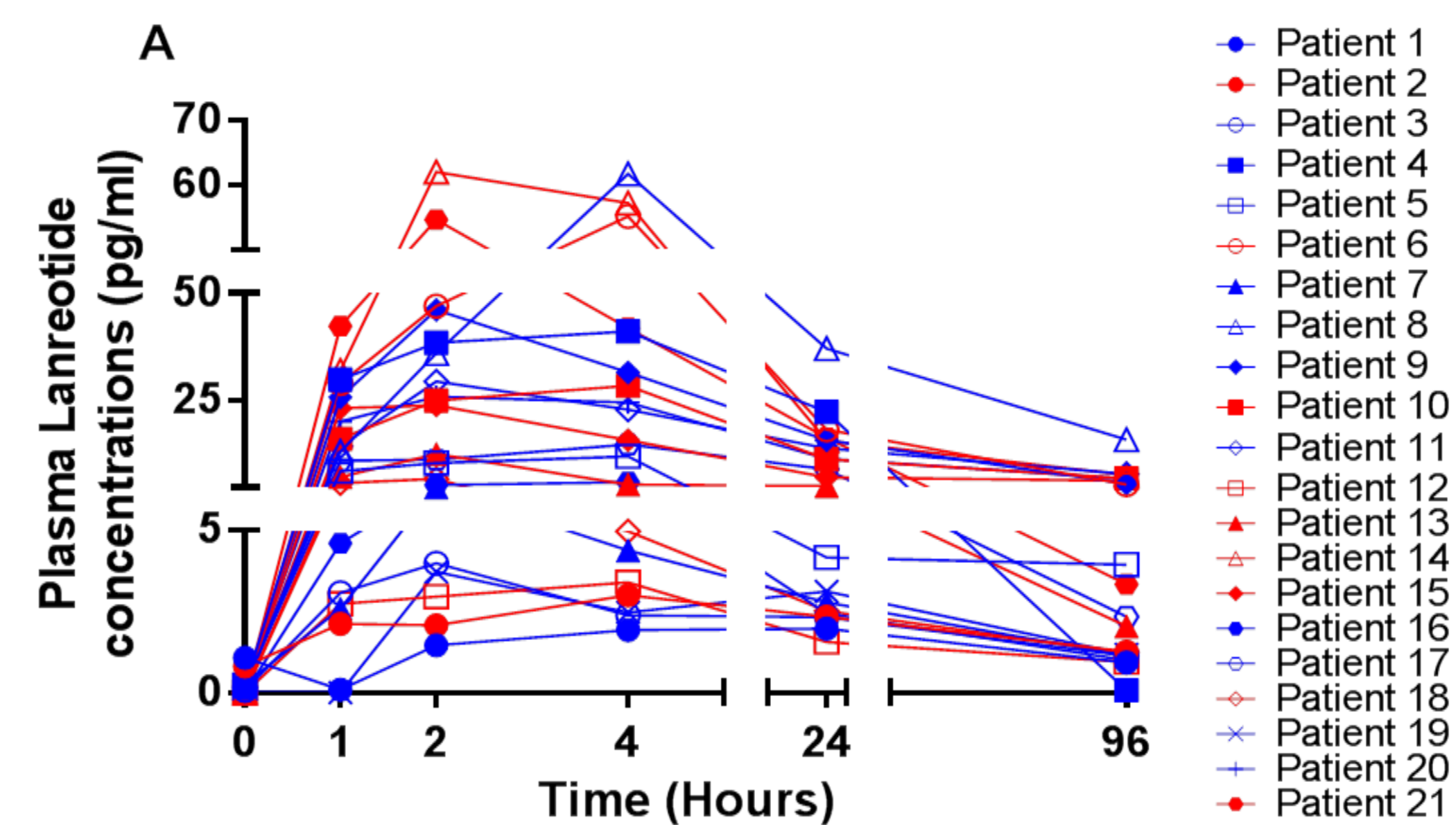


Figure 1: Comparative plasma profile of Lanreotide following the first of a 4-weekly injection of Lanreotide Autogel at 30 mg dose. Pharmacokinetic profile of Lanreotide in patients with CHI. Mean and standard error of mean (SEM) is plotted for individual CHI patients recruited.

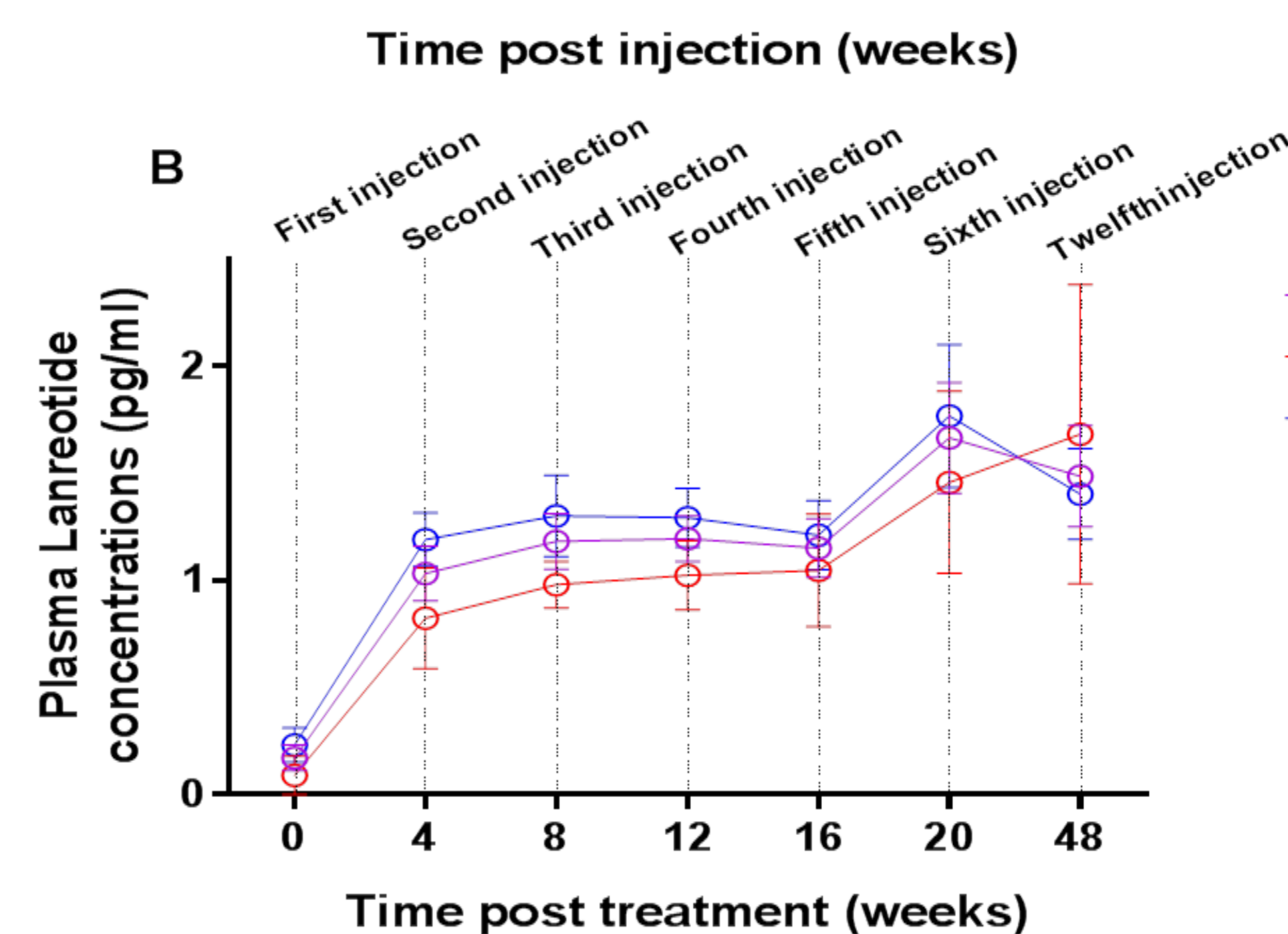


Figure 2: Comparative plasma profile of Lanreotide prior to the first and then subsequent series of a 4-weekly injection of Lanreotide Autogel. Pharmacokinetic profile of Lanreotide in patients with CHI. Mean and standard error of mean (SEM) is plotted on all patients with CHI (purple, n=21), those previously on diazoxide (DZX: red) and those originally on octreotide treatment (OCT: blue).

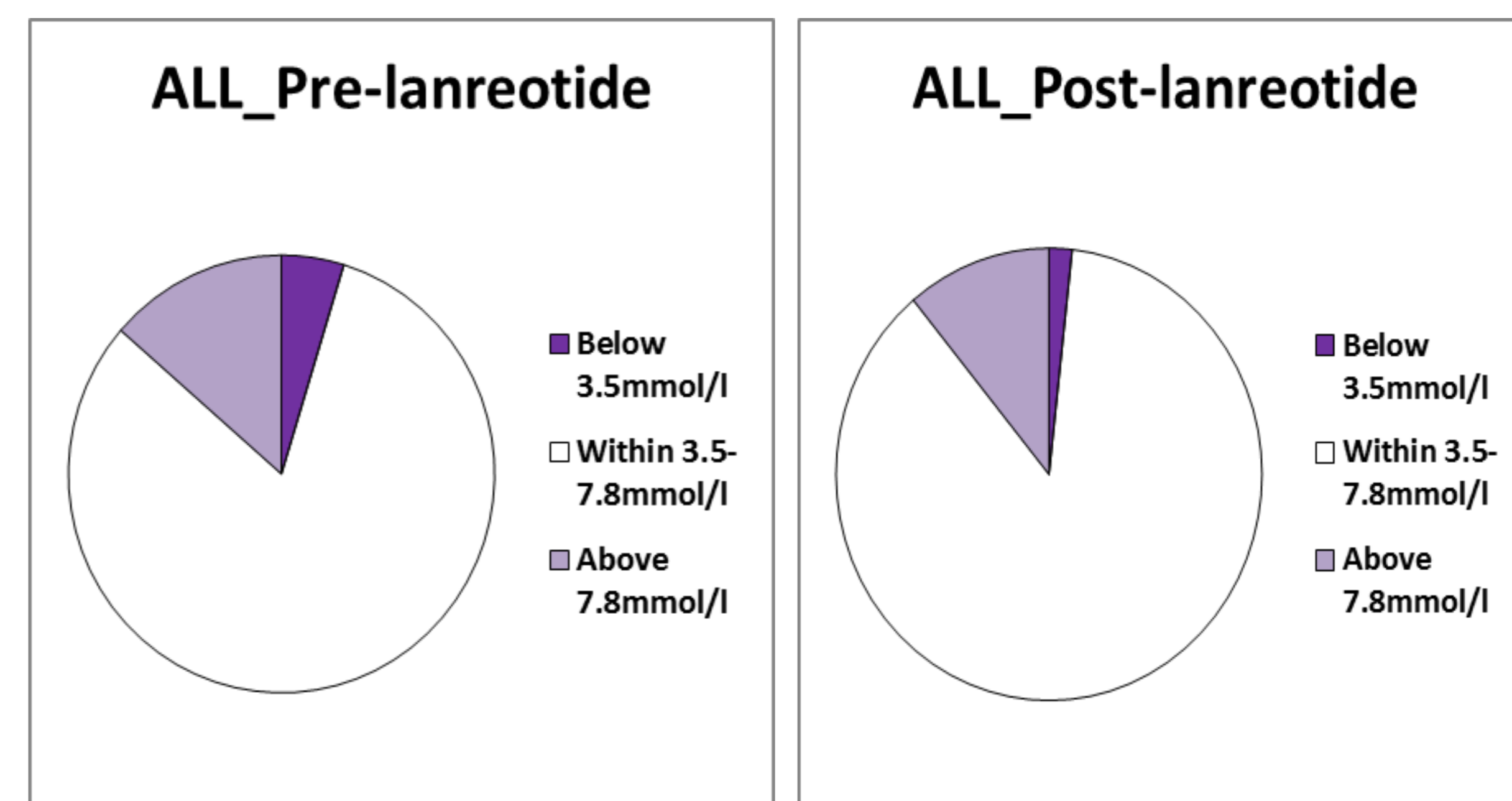


Figure 3: Weekly distribution of blood glucose averages as a % of pre- and 1 year post-Lanreotide treatment (purple) in all patients and those patients originally on diazoxide treatment octreotide treatment (N=15). Values as mean and SD: Standard deviation. P< 0.05 is deemed significant.

BM	% Pre-Lanreotide		% Post-Lanreotide		N	p-value
	Mean	SD	Mean	SD		
Below 3.5 mmol/l	4.7	4.4	1.7	2.3	15	0.012
Within 3.5-7.8 mmol/l	81.7	11.9	87.3	10.8	15	0.074
Above 7.8 mmol/l	13.6	10.9	11.0	9.1	15	0.328