

Impairment in insulin secretion without changes in insulin resistance explains hyperglycemia in patients with acromegaly treated by pasireotide LAR

Peter Wolf^{1,2}, Alexandre Dormoy¹, Luigi Maione¹, Sylvie Salenave¹, Jacques Young¹, Peter Kamenický¹, Philippe Chanson¹

1) Service d'Endocrinologie et des Maladies de la Reproduction, Hôpital Bicêtre, Le Kremlin Bicêtre, France
2) Division of Endocrinology and Metabolism, Department of Internal Medicine III, Medical University of Vienna

Objective

Pasireotide is a second line treatment for acromegaly. Apart from the growth hormone (GH) lowering efficacy, clinical use is limited by side effects on glycemic control. The aim of this study was to evaluate longitudinal changes in beta-cell function and insulin sensitivity induced by pasireotide therapy in patients with acromegaly.

Methods

retrospective study in 33 patients (20 ♀):

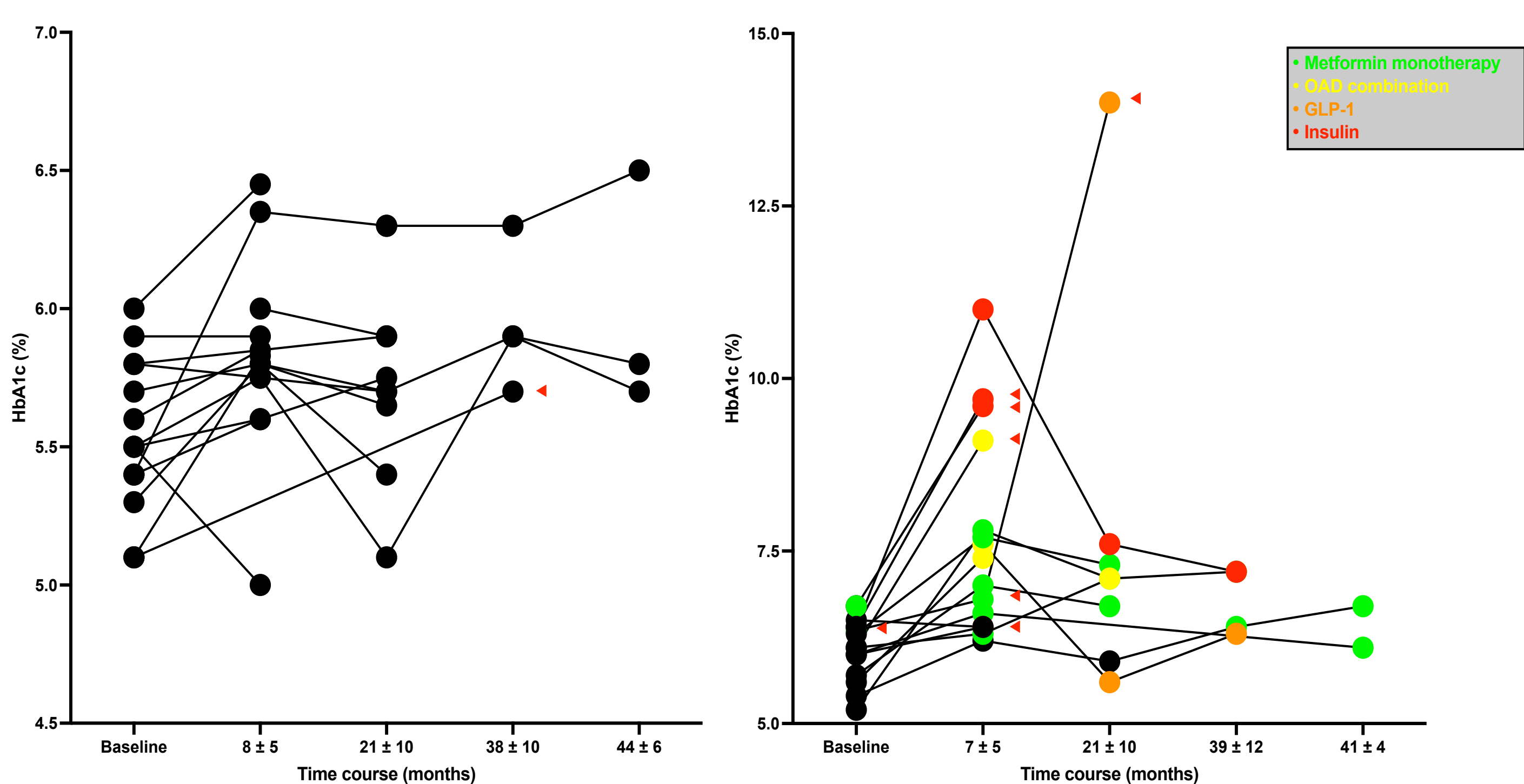
- efficacy: GH/ IGF-I; tumor size
- glucose homeostasis: glucose, HbA1c, antidiabetic treatment

Results

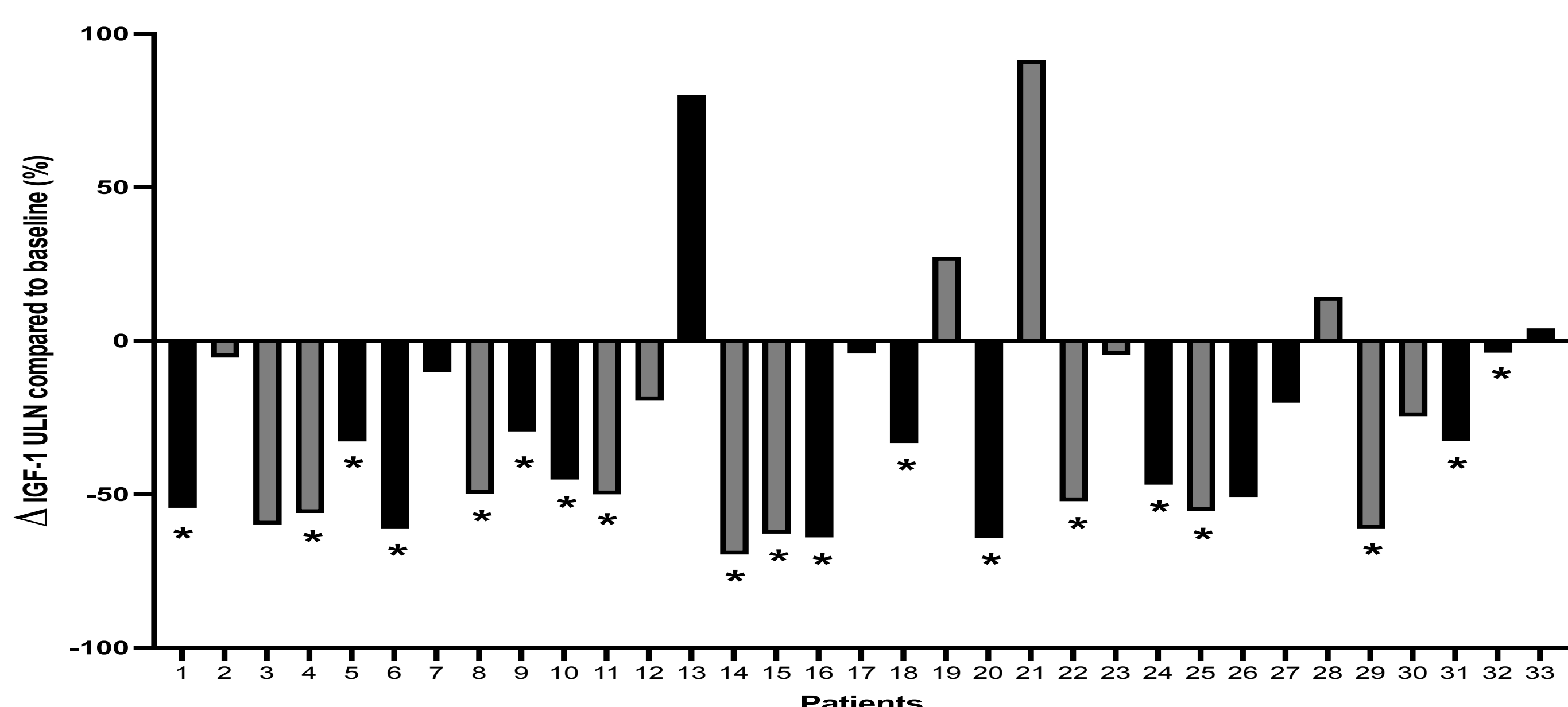
	Baseline	Follow Up	p-value
Follow up period (months)	20 ± 17		
IGF-I (% of ULN)	155 ± 51	106 ± 9	<0.001
GH (ng/ml)	7.8 ± 7.8	3.5 ± 3.4	0.011
Tumor size (mm)	14.7 ± 7.5	14.5 ± 9.4	0.74
≥ 20% reduction (n/%)		2 (10)	
stable (n/%)		17 (85)	
≥ 20 % increase (n/%)		1 (5)	
Prediabetes (n/%)	13 (39)	18 (53)	0.206
Diabetes (n/%)	2 (6)	12 (35)	0.002
HbA1c (%)	5.8 ± 0.4	6.8 ± 1.7	0.001
Diabetes treatment	2 (6)	14 (42)	<0.001

longitudinal data from OGTT in 14 patients:

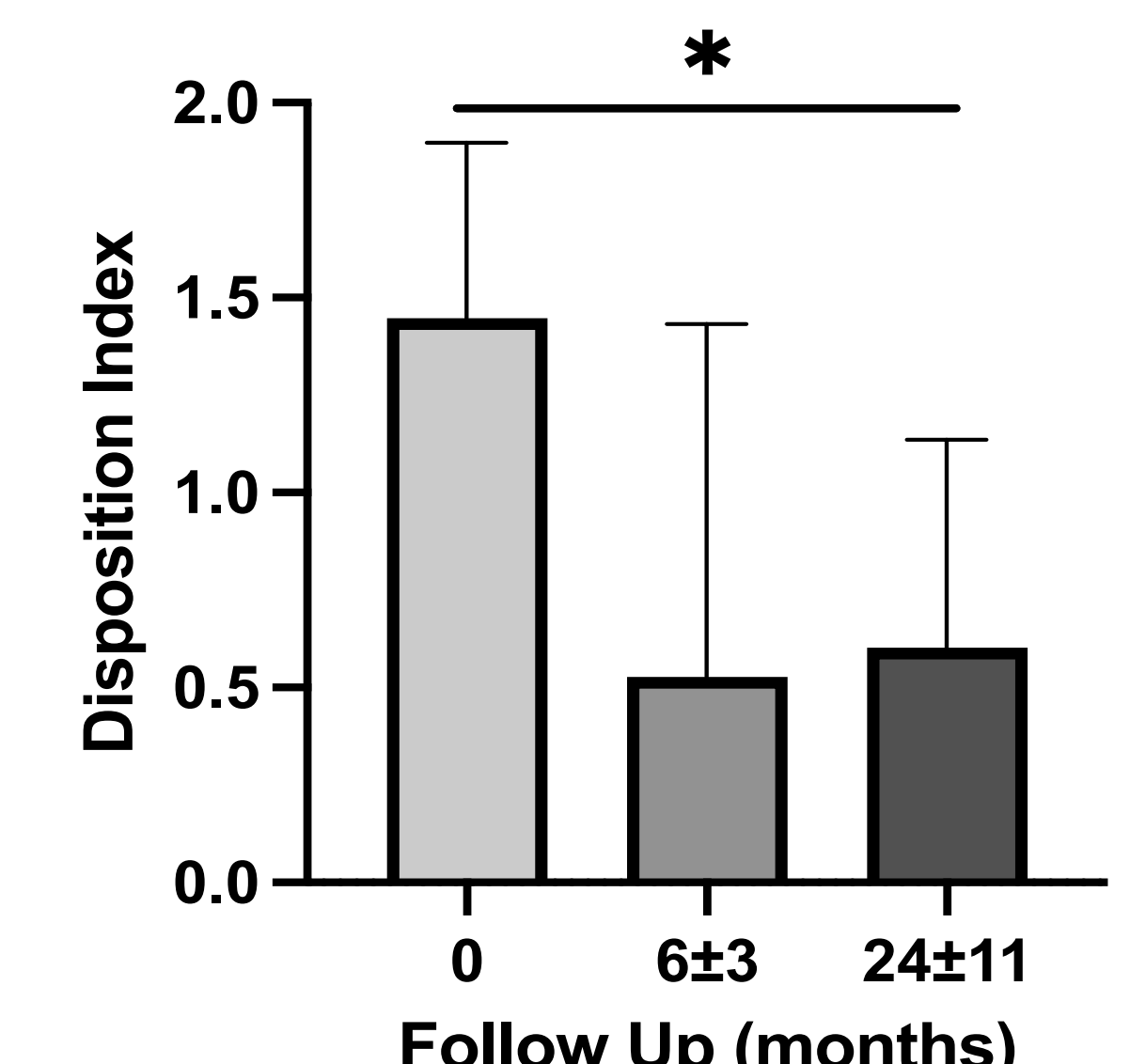
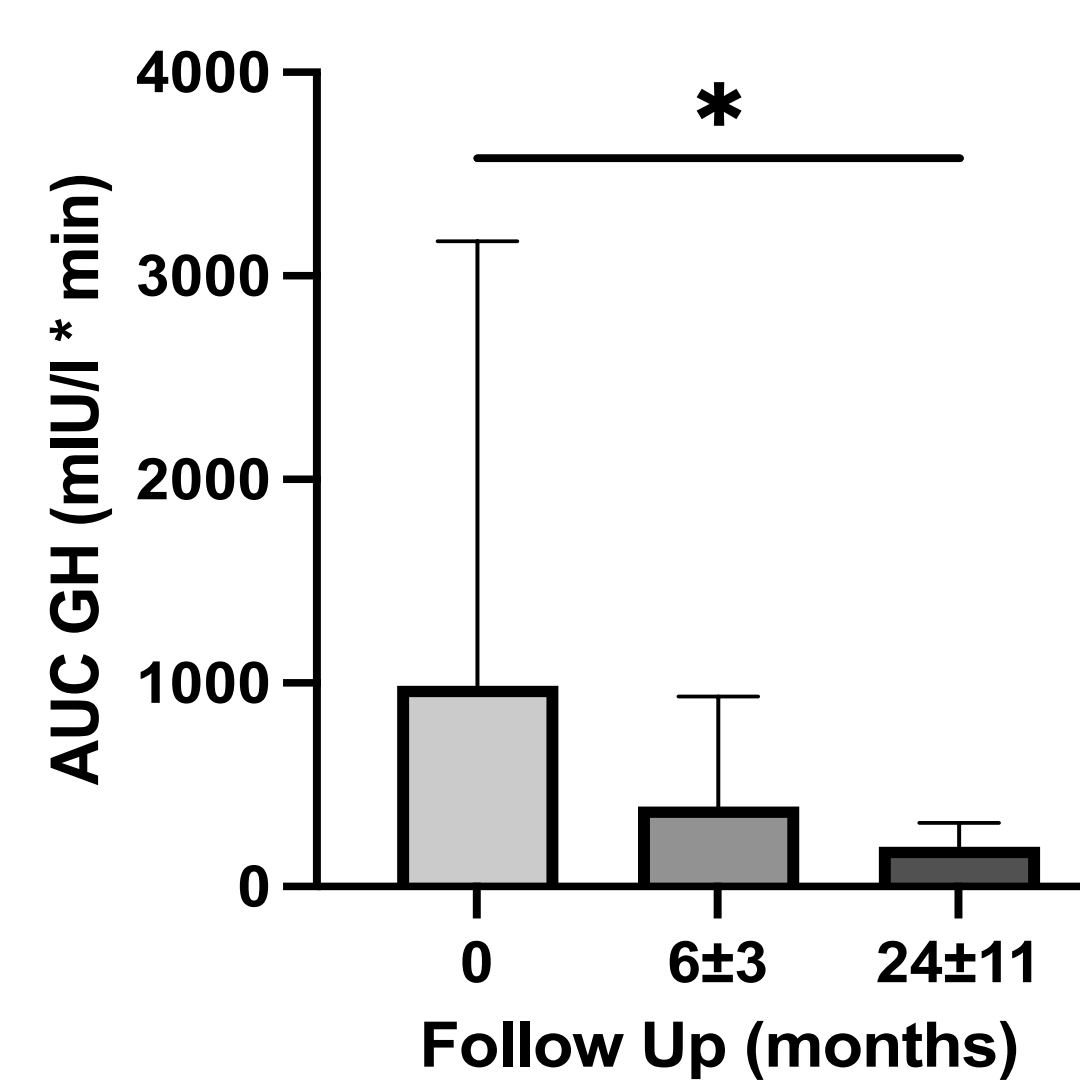
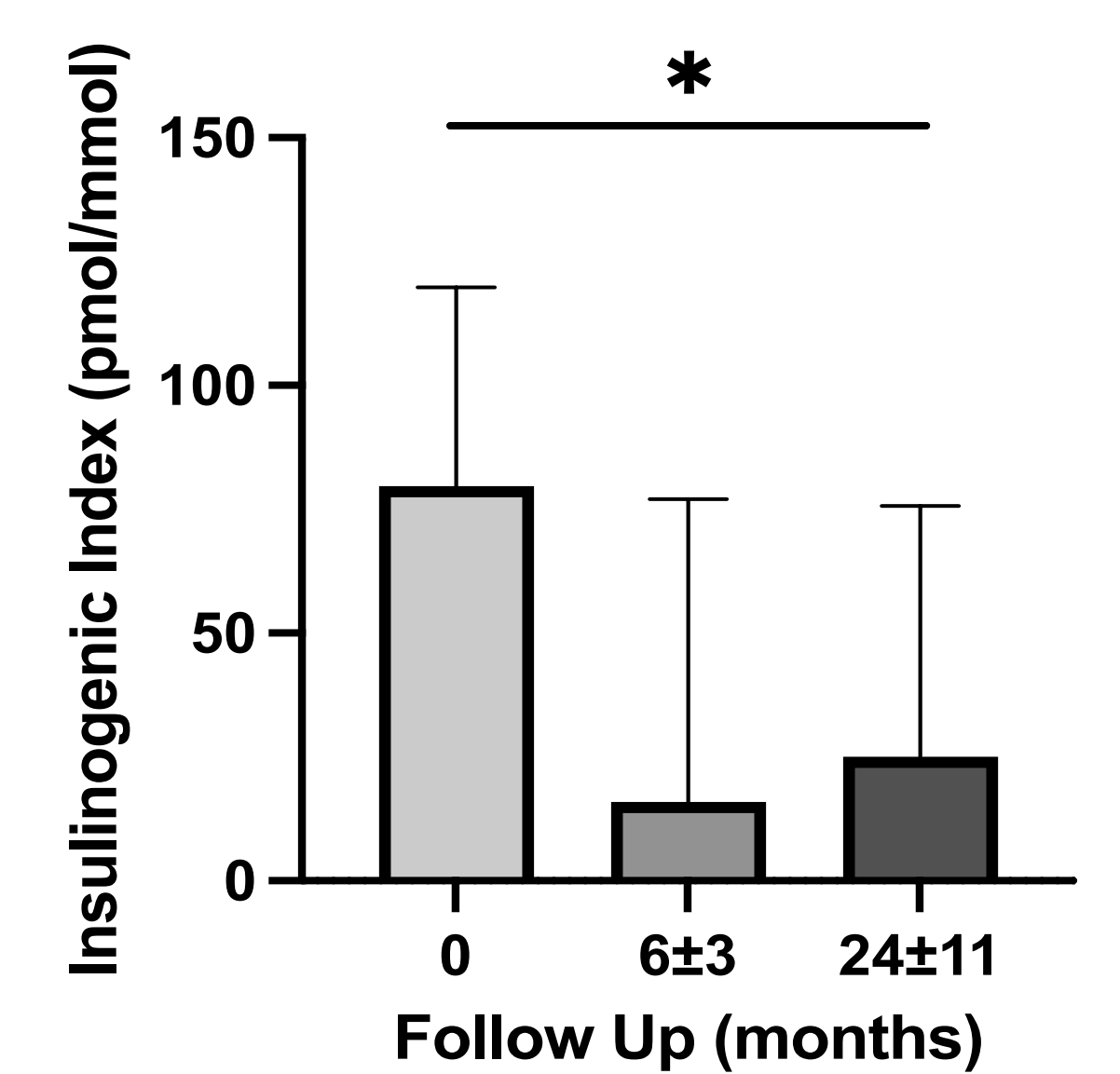
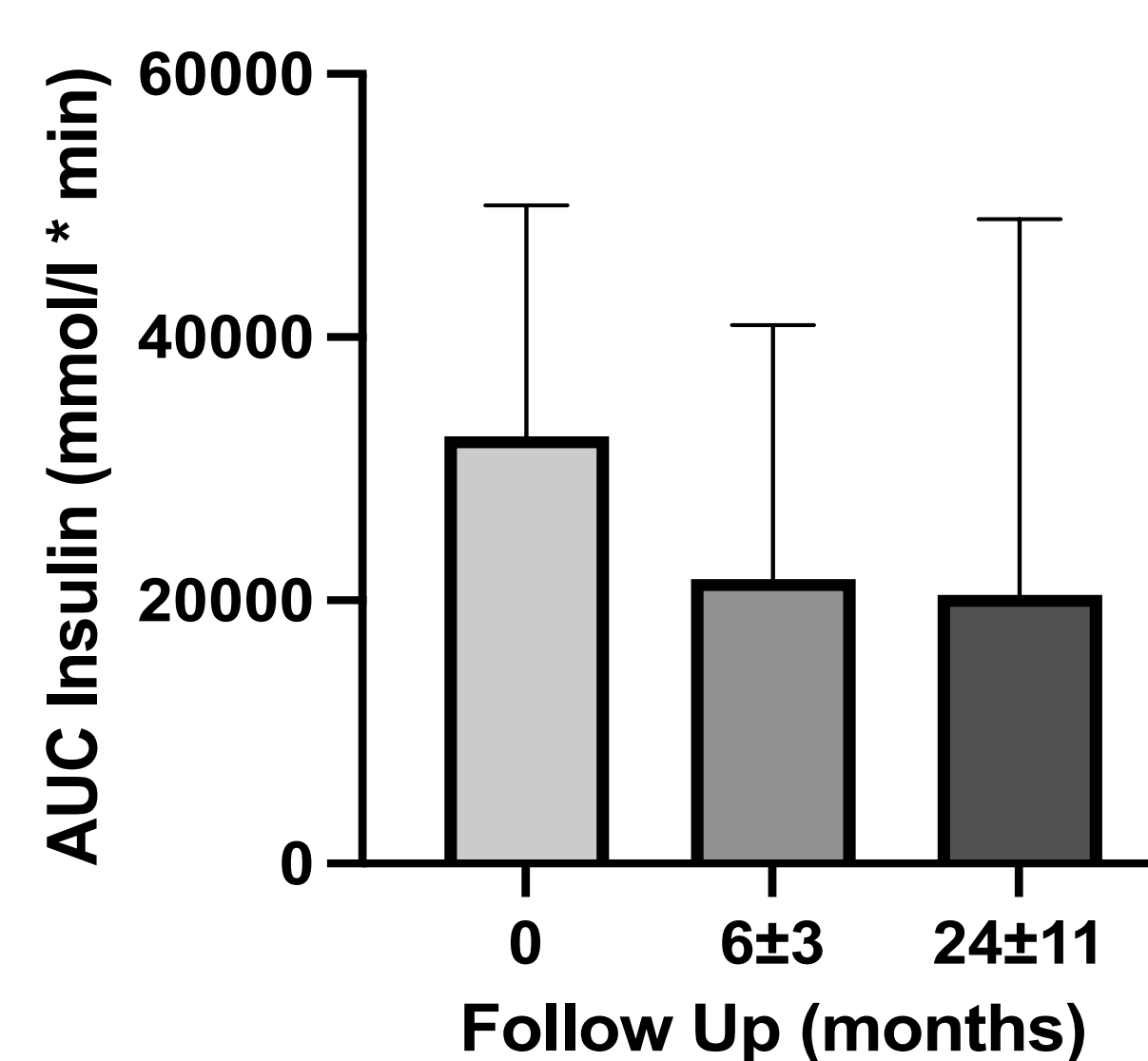
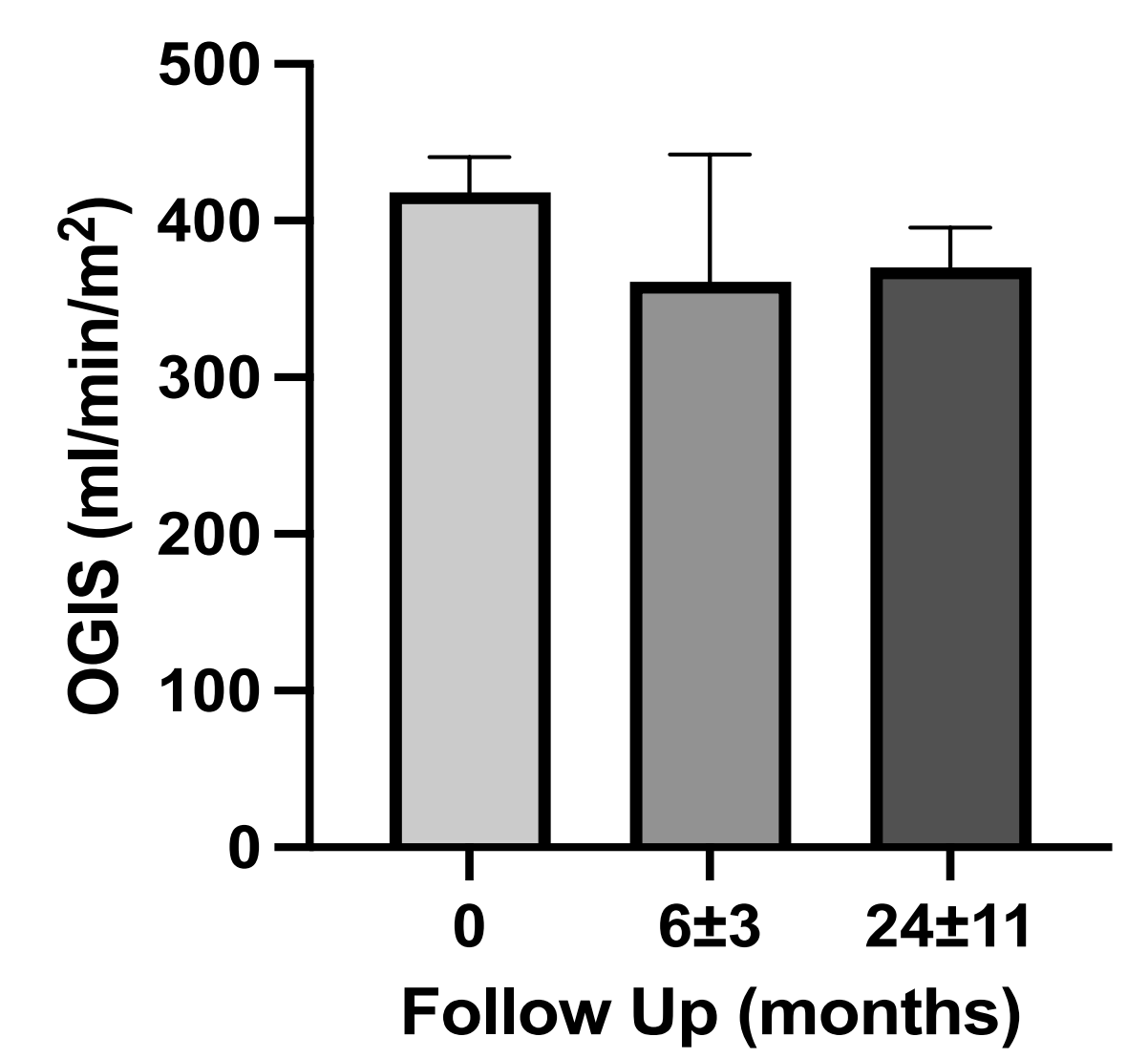
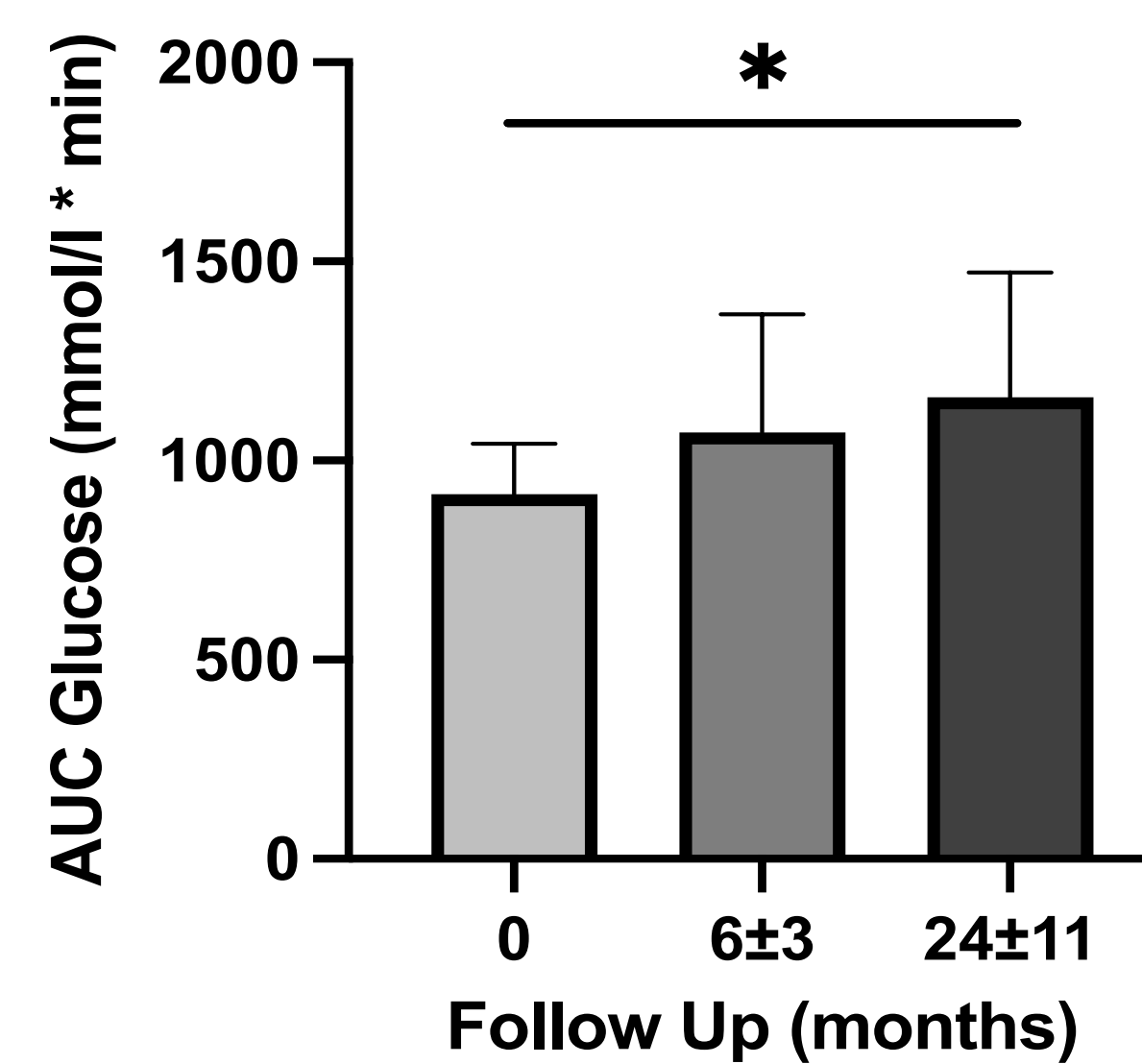
- baseline and follow up after 6.1±3.8 and 24.4±11.1 months
- changes in insulin secretion (insulinogenic index; disposition index) and - sensitivity (HOMA, OGIS)



Changes in HbA1c in patients WITHOUT (left) and WITH (right) antidiabetic treatment during the observation period; different colors highlight different antidiabetic therapies; ◀ indicates a stop of pasireotide because of hyperglycemia



Changes in IGF-I (given as % of ULN); * indicates normalization of IGF-I levels; grey bars indicate antidiabetic treatment



Conclusions:

Worsening of glycemic control during pasireotide therapy is caused by an impaired insulin secretion, whereas insulin sensitivity is not affected.