Efficacy of pasireotide LAR for acromegaly: a long-term real-world monocentric study

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PATIENTS

Nineteen acromegalic patients (8 females, 21-69 years-old, with macroadenoma, microadenoma or no evidence of pituitary tumor in 15, 2, 2, respectively) resistant to first generation somatostatin analogs (FG-SA) at high doses and/or intolerant to pegvisomant were switched to pasireotide LAR (PasLAR). Eleven had persistent disease after neurosurgery and two had also undergone radiosurgery (12 and 24 months before starting PasLAR). Six complained of acromegalic headache (symptomatic score was 3/3 in 5 and 2/3 in the other). On FG-SA IGF-1, GH and HbA1c were (mean, range) 193% upper limit normal age-matched range (ULNR) (120-303), 5.2 ng/mL (0.6-25), and 40.6 mmol/mol (29-54), respectively. No patient was taking antidiabetic drugs.

PROTOCOL

PasLAR was injected every 28 days, starting with 40 mg for 3 months, uptitrated to 60 mg if IGF-1 persisted pathologic or downtitrated to 20 mg if IGF-1 was <50% ULNR. GH, IGF-1, HbA1c were assessed at 28, 84 and 168 days after starting protocol. Treatment was withdrawn if IGF-1 remained pathologic after 3 months on 60 mg q 28 days.

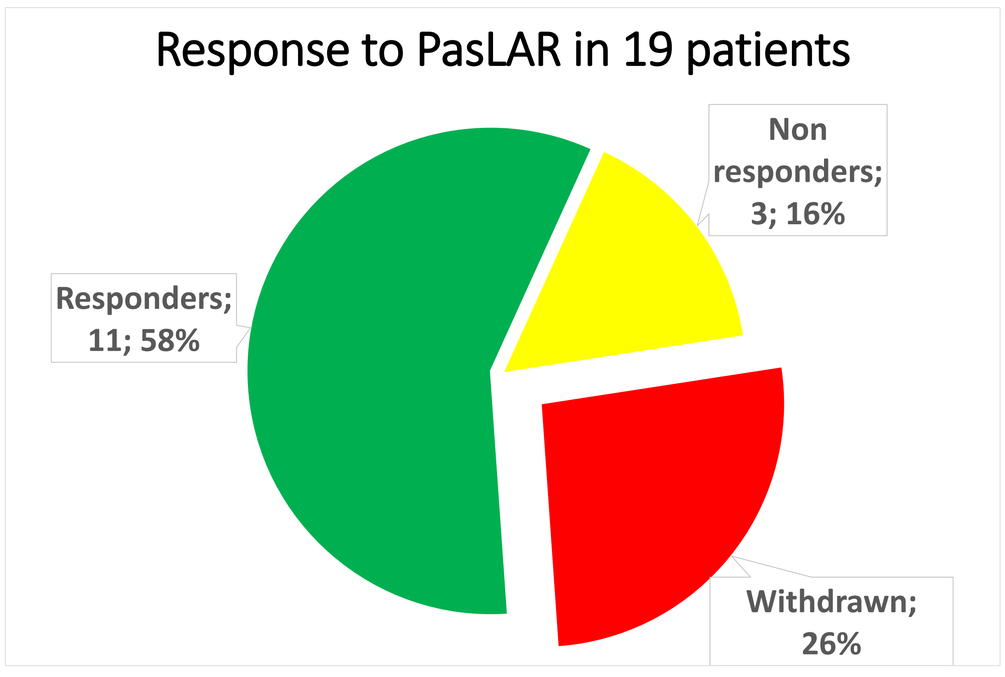
RESULTS

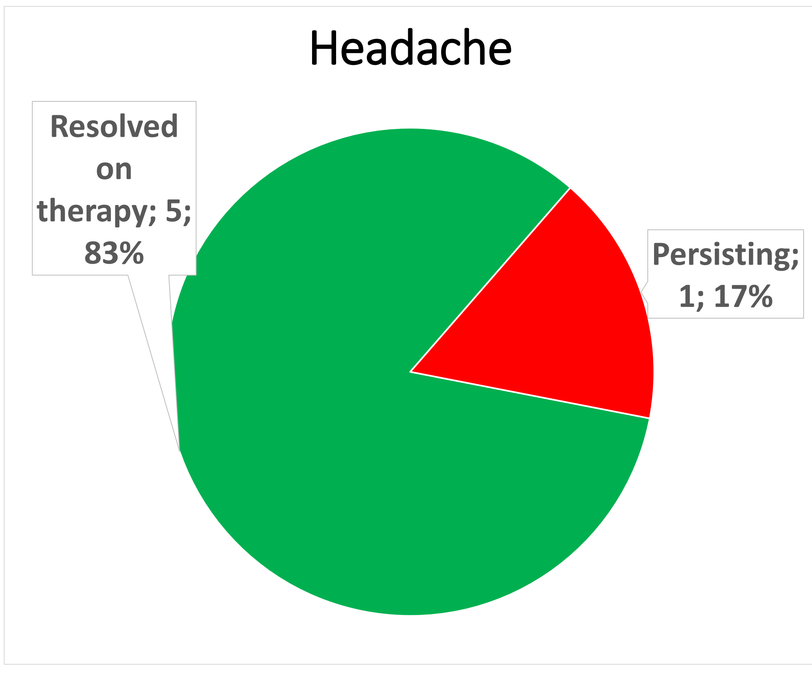
IGF-1 levels: normalized on PasLAR in 10/19 patients after the first injection. Treatment was withdrawn in 5 unresponsive patients at 6 months. After 12 months, IGF-1 was 74% ULNR (29-133, normal in 9/14) and GH 1.2 ng/mL (0.2-3.9). At the last follow-up (mean 26 months, range 6-60, ongoing dose 20 mg in 3, 40 mg in 7 patients, and 60 mg in 4) IGF-1 was 74% ULNR (22-195, normal in 11/14) and GH 0.7 ng/mL (0.1-2.5).

Headache quite disappeared in all patients (in 5/6 after the first injection) and reappeared with pathologic IGF levels after PasLAR withdrawal in one irradiated patient.

Tumor shrinkage (20-35% of basal volume) was observed in 6/7 evaluated patients without previous irradiation at 6-36 months after the start of PasLAR.

Side effects. HbA1c was 43.9 mmol/mol (32-66) at 12 months and 43.3 mmol/mol (29-66) at the last follow-up. Glucose metabolism derangement was observed in 6 patients (until DKA in one). Metformin was started in 4 patients and GLP-1 RA in two (in one coupled with insulin). In two patients PasLAR was withdrawn at 36 and 60 months due to poor compliance in the first and QTc lengthening in the second, who had started amiodarone treatment.





CONCLUSION

Pas-LAR should be considered a second option in patients resistant to FG-SA for its high efficacy and safety. Its quick action allows early identification of responsive patients. Efficacy on severe headache is outstanding.