Evaluation of MRI T2-signal intensities of GH-secreting pituitary macroadenoma in treatment-naive acromegalic patients receiving primary treatment with lanreotide Autogel 120 mg

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Introduction and objectives

- Acromegaly is a chronic condition characterized by excess growth hormone (GH) secretion, which is caused, in the majority of cases, by a pituitary adenoma. Long-acting somatostatin analogues (SSAs) are well established treatments for acromegaly after unsuccessful surgery, and are also used as first-line treatment if surgery is refused, contra-indicated or unlikely to be successful.

- In a previous study, the hypointense T2-signal of GH-secreting pituitary adenomas on magnetic resonance imaging (MRI), which reflects various tissue properties, predicted the biochemical outcome of pituitary SSA therapy.

- However, the definition of T2 hypointensity of GH-secreting adenomas varies between studies. We hypothesise that different definitions of T2 hypointensity and hypointensities lead to differences in perceived distributions of GH-secreting adenomas, and therefore to differences in reported outcomes after SSA treatment.

- Here, we investigate three methods for evaluating the T2-signal intensity of pituitary macroadenomas, and the extent to which they predict the response to SSA treatment, using additional post hoc analysis of data from the PRIMARYS study (EudraCT:2007-000253-33; NC:10006096).

Methods

- PRIMARYS was an open-label study in which 90 patients with acromegaly received primary medical treatment with the long-acting SSA, lanreotide Autogel (Depot) in the USA, at a fixed dose of 120 mg every 4 weeks for 1 year. The study was conducted to evaluate the tumour volume reduction in patients with macroadenomas (diameter ≤ 20 mm) via standardized MRI readings. Patients were eligible for inclusion if they were treatment naïve and had no visual field defects.

- In the current analysis, each MRI was read by a single neuroradiologist to determine T2-signal intensity, using one qualitative method based on visual assessment (as per daily routine practice) and two quantitative methods, the Heck method1 and a method using the signal intensity ratio of the adenoma over the grey matter (Figure 1).

- For each method, intensities were rated as hypointense, isointense or hyperintense, as defined in Figure 1.

- The reader was blinded to the identity of the subject and the status of hormonal control and tumour response.

- For each of the three methods, signal intensities at baseline were summarized in the overall population and according to hormonal control and tumour response (endpoints of the PRIMARYS study).

- Hormonal control was defined as GH levels ≤2.5 ng/mL and normalized insulin-like growth factor (IGF-1).

- Tumour response was defined as a reduction in tumour volume ≥20% between baseline and the patient’s last visit during the study.

- Multivariate analyses were conducted to evaluate whether, after controlling for other baseline characteristics, baseline T2-signal intensities were associated with the change in GH and IGF-1, hormonal control and tumour response at last visit study available (EUDAT).

Results

- Baseline T2 signal intensity data were available for 85 patients, of whom 50 achieved hormonal control and 53 achieved tumour response at both.

- Overall, more adenomas were classified as hypointense using the visual assessment method (59%) than using either of the quantitative methods (signal ratio method, 36%; Heck method, 20%) (Table 1).

- Figure 2 shows an MRI scan of a patient classified as hypointense using both the visual assessment and the signal ratio methods, but isointense using the Heck method.

- Patients achieving hormonal control or tumour response were more often classified as hypointense according to the visual assessment method than with the quantitative methods (Figure 3 and Figure 4).

- As targeted adenomas appear to be hypointense on T2-weighted images, we arbitrarily selected the visual assessment method, which identified most hypointense adenomas, for further analyses.

- Baseline tumour volumes were lower in the hypointense group than in the isointense and hyperintense groups: median (95% CI) volumes were 1518 (959; 2190) mm³ vs. 2767 (1378; 7239) mm³ and 2013 (1387; 4266) mm³, respectively.

- There was an additional reduction in GH levels of 4.1 µg/L between baseline and IVA for those with hypointense versus isointense tumours (p = 0.0007, F-test).

- Similarly, there was an additional reduction in IGF-1 levels of 45 ng/mL between baseline and IVA for those with hypointense versus isointense tumours (p = 0.0026, F-test).

- No association between the T2-signal intensity and hormonal control was identified. However, the odds of obtaining a tumour response were 6.2 times higher for hypointense versus isointense adenomas (p = 0.013, Wald test).

Conclusions

- These results suggest that clinical visual assessment is preferable for the identification of T2-hypointense, GH-secreting macroadenoma in treatment-naive patients with acromegaly.

- There was a trend towards smaller tumour volumes at baseline in the hypointense group.

- Patients with hypointense lesions have a greater reduction in GH and IGF-1 values compared with those with isointense lesions following primary SSA treatment. In addition, the odds of tumour response are higher.

PRIMARYS Study Group


References