Transsphenoidal surgery (TSS) of the pituitary is the standard treatment for Cushing disease. Adrenocorticotropic hormone (ACTH) levels did not fluctuate and remained consistent with hypercortisolism during the treatment with relacorilant. At the conclusion of the study, patients underwent scheduled TSS surgeries.

Relacorilant demonstrates similar glucocorticoid receptor antagonistic effects as mifepristone in vitro, but without the anti-progesterone effects (abortifacient, endometrial thickening, vaginal bleeding) or mineralocorticoid effects (hypokalemia) of mifepristone. Results from an open-label phase 1 study (NCT03469470) indicated that relacorilant improved glycemic and blood pressure control in patients with endogenous hypercortisolism:

- In the high-dose (4 to 40 mg/day) relacorilant cohort, 50% of patients with hyperglycemia achieved improved glycemic control, as shown by ≥0.5% decrease in HbA1c, normalization or ≤30 mg/dL decrease in 2-hour oral glucose tolerance test (OGTT) glucose, or decrease in total daily insulin (≥25%) or sulfonylurea dose (≥50%).
- 20% of patients with uncontrolled hypertension achieved a ≥15-mmHg decrease in mean arterial and diastolic blood pressure, as measured by 24-hour ambulatory monitoring.

Here we describe two patients with CD who were treated with relacorilant in the phase 2 study and who showed evidence of tumor shrinkage on posttreatment magnetic resonance imaging (MRI) performed after complete surgery.

**Case Presentation**

- Two patients with the ronivod Cushing disease to a macroadenomas were enrolled in the phase 2, multicenter, open-label, 12-week study of relacorilant for preoperative management.
  - At the conclusion of the study, patients underwent scheduled TSS surgeries.
  - Eligibility for the study included:
    - Patients aged 18 to 65 years with confirmed endogenous hypercortisolism as evidenced by ≥2 of the following:
      - 24-hour urinary free cortisol (UFC) above the upper limit of normal (ULN)
      - Late-night salivary cortisol ≤2.5 nmol/L
      - Normal laboratory ranges: ACTH, 1.3 to 11.1 pmol/L; late-night salivary cortisol, ≤2.5 nmol/L; urinary free cortisol, 111 to 483 nmol/24 h.

**MRI Results**

- Both patients showed radiographic tumor shrinkage at several time points:
  - Weeks 1 to 4: 100 mg/day
  - Weeks 5-8: 150 mg/day
  - Weeks 9-12: 200 mg/day
- After completing the 3-month study, preoperative MRI revealed shrinkage in the size of their tumors:
- MRI of the hypophysis obtained 6 months later (right image) showed a reduction in size of the macroadenoma (21 x 22 x 19 mm).
- The reduction in the size of the macroadenomas may potentially be attributable to endogenous (hormonal) stimulation via upregulation of somatostatin receptors type 2 (SSTR2), which are downregulated in patients with hypercortisolism.
- This finding is confirmed, it may support the role of relacorilant as an alternative treatment for patients with CD and invasive macroadenomas.

**Patient History and Baseline Characteristics**

<table>
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<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age</th>
<th>Weight, kg</th>
<th>Body mass index, kg/m²</th>
<th>ACTH, pmol/L</th>
<th>Biochemical findings</th>
<th>Hypertension</th>
<th>Diabetes</th>
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</table>

**REFERENCES**


**CONCLUSIONS**

- This open-label, phase 2 study enrolled two patients with Cushing disease who were treated with relacorilant for preoperative management.
- After completing the 3-month study, preoperative MRI revealed shrinkage in the size of their tumors:
- This finding is confirmed, it may support the role of relacorilant as an alternative treatment for patients with CD and invasive macroadenomas.

**DISCLOSURES**

- The authors report no conflicts of interest.