Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.
| Pt no. | Trial Group | Age | Sex  | BMI  | Medical history, 1=yes, 0=no | Tumor maximal diameter, mm | Macroadenoma, 1=yes, 0=no | Caverno-us sinus invasion, 1=yes, 0=no | Tu-mor type | Hypopituita-rism at baseline, 1=yes, 0=no | Gross total resection, 1=yes, 0=no |
|--------|-------------|-----|------|------|-----------------------------|---------------------------|--------------------------|---------------------------------|------------|----------------------------------------|----------------------------------|
| 4      | 1           | 33  | Male | 32.6 | 0                           | 13.0                      | 1                        | 0                               | GH                     | 0                      | 1                  |
| 17     | 1           | 62  | Male | 27.7 | 1                           | 13.0                      | 1                        | 0                               | NF                     | 0                      | 1                  |
| 32     | 2           | 42  | Male | 21.8 | 1                           | 11.0                      | 1                        | 1                               | GH                     | 0                      | 0                  |
| 38     | 2           | 58  | Male | 23.7 | 1                           | 39.0                      | 1                        | 1                               | NF                     | 1                      | 0                  |
| 40     | 1           | 51  | Male | 27.6 | 1                           | 30.0                      | 1                        | 0                               | NF                     | 1                      | 1                  |
| 45     | 2           | 46  | Female | 24.7 | 1                           | 9.4                       | 0                        | 0                               | GH                     | 0                      | 1                  |
| 46     | 1           | 49  | Female | 23.5 | 1                           | 12.0                      | 1                        | 0                               | GH                     | 1                      | 1                  |
| 80     | 1           | 57  | Male | 26.4 | 1                           | 26.0                      | 1                        | 1                               | NF                     | 0                      | 0                  |
| 85     | 1           | 47  | Male | 25.6 | 1                           | 21.0                      | 1                        | 0                               | NF                     | 0                      | 1                  |
| 87     | 2           | 38  | Male | 27.4 | 1                           | 35.0                      | 1                        | 0                               | NF                     | 1                      | 1                  |
| 95     | 1           | 37  | Female | 22.6 | 0                           | 20.0                      | 1                        | 0                               | NF                     | 1                      | 1                  |
| 131    | 2           | 59  | Male | 24.0 | 1                           | 21.0                      | 1                        | 0                               | NF                     | 1                      | 1                  |
| 146    | 2           | 52  | Female | 26.7 | 1                           | 31.0                      | 1                        | 1                               | NF                     | 1                      | 0                  |
| 149    | 2           | 51  | Male | 26.6 | 1                           | 24.0                      | 1                        | 0                               | NF                     | 1                      | 1                  |
| 163    | 1           | 40  | Female | 32.4 | 1                           | 35.0                      | 1                        | 1                               | NF                     | 1                      | 0                  |
| 177    | 1           | 43  | Male | 30.6 | 1                           | 14.0                      | 1                        | 0                               | NF                     | 1                      | 1                  |
| 202    | 2           | 31  | Female | 22.6 | 0                           | 17.5                      | 1                        | 0                               | NF                     | 0                      | 1                  |
| 213    | 1           | 46  | Female | 26.1 | 1                           | 16.0                      | 1                        | 1                               | GH                     | 0                      | 0                  |
| 221    | 2           | 53  | Male | 20.8 | 0                           | 16.0                      | 1                        | 0                               | NF                     | 0                      | 1                  |
| 225    | 2           | 31  | Male | 26.3 | 0                           | 14.0                      | 1                        | 0                               | PRL                    | 1                      | 1                  |
| 229    | 2           | 26  | Female | 23.1 | 0                           | 7.0                       | 0                        | 0                               | PRL                    | 0                      | 1                  |
| 232    | 1           | 37  | Female | 20.3 | 0                           | 9.0                       | 0                        | 0                               | PRL                    | 0                      | 1                  |
| 236    | 2           | 50  | Male | 21.1 | 0                           | 29.8                      | 1                        | 0                               | NF                     | 0                      | 1                  |
| 239    | 2           | 32  | Female | 25.0 | 1                           | 15.0                      | 1                        | 0                               | GH                     | 1                      | 1                  |
| 247    | 2           | 41  | Female | 37.3 | 1                           | 19.0                      | 1                        | 1                               | NF                     | 0                      | 0                  |
| 253    | 2           | 33  | Male | 26.8 | 0                           | 30.0                      | 1                        | 0                               | NF                     | 1                      | 1                  |
| 274    | 1           | 35  | Female | 27.3 | 0                           | 26.8                      | 1                        | 0                               | NF                     | 0                      | 1                  |
| 278    | 2           | 45  | Female | 27.3 | 1                           | 40.3                      | 1                        | 1                               | NF                     | 0                      | 0                  |
| 287    | 2           | 31  | Female | 22.8 | 0                           | 27.0                      | 1                        | 0                               | PRL                    | 1                      | 1                  |
| 301    | 2           | 38  | Female | 23.7 | 1                           | 23.0                      | 1                        | 0                               | NF                     | 1                      | 1                  |
| 303    | 2           | 44  | Female | 24.2 | 0                           | 14.0                      | 1                        | 0                               | PRL                    | 1                      | 1                  |
| 340    | 1           | 34  | Female | 27.9 | 1                           | 18.0                      | 1                        | 0                               | NF                     | 1                      | 1                  |
| 345    | 2           | 55  | Female | 31.2 | 1                           | 30.0                      | 1                        | 1                               | NF                     | 0                      | 0                  |
| 349    | 2           | 31  | Male | 22.0 | 0                           | 27.2                      | 1                        | 1                               | NF                     | 1                      | 0                  |
| 363    | 1           | 18  | Female | 27.7 | 0                           | 15.7                      | 1                        | 0                               | GH                     | 1                      | 1                  |
| 369    | 2           | 57  | Female | 28.3 | 0                           | 14.0                      | 1                        | 0                               | NF                     | 0                      | 1                  |
| 398    | 2           | 65  | Male | 23.8 | 0                           | 19.0                      | 1                        | 0                               | NF                     | 0                      | 1                  |
| 405    | 2           | 62  | Male | 31.0 | 1                           | 35.0                      | 1                        | 1                               | GH                     | 1                      | 0                  |
### eTable 2. List of the Patients With a Secondary Event

| Pt no. | Trial Group | Age | Sex | BMI | Medical history, 1=yes, 0=no | Tumor maximal diameter, mm | Macroadenoma, 1=yes, 0=no | Cavernous sinus invasion, 1=yes, 0=no | Tumor type | Hypopituitarism at baseline, 1=yes, 0=no | Gross total resection, 1=yes, 0=no |
|--------|-------------|-----|-----|-----|-----------------------------|----------------------------|---------------------------|--------------------------------|------------|--------------------------------|--------------------------------|
| 38     | 2           | 58  | Male| 23.7| 1                           | 39.0                       | 1                         | 1                             | NF         | 1                             | 0                     |
| 43     | 1           | 47  | Female| 23.6| 1                           | 7.0                        | 0                         | 0                             | PRL        | 0                             | 1                     |
| 46     | 1           | 49  | Female| 23.5| 1                           | 12.0                       | 1                         | 0                             | GH         | 1                             | 1                     |
| 97     | 2           | 39  | Female| 23.4| 1                           | 25.0                       | 1                         | 1                             | NF         | 1                             | 0                     |
| 127    | 2           | 47  | Female| 23.0| 1                           | 13.0                       | 1                         | 0                             | NF         | 1                             | 1                     |
| 166    | 1           | 37  | Male | 29.7| 1                           | 28.0                       | 1                         | 1                             | NF         | 1                             | 0                     |
| 173    | 1           | 45  | Female| 29.7| 1                           | 36.0                       | 1                         | 0                             | NF         | 1                             | 1                     |
| 199    | 2           | 66  | Female| 26.0| 1                           | 21.0                       | 1                         | 0                             | NF         | 0                             | 1                     |
| 217    | 2           | 30  | Female| 25.2| 1                           | 11.0                       | 1                         | 0                             | PRL        | 0                             | 1                     |
| 240    | 1           | 61  | Male | 25.9| 1                           | 20.0                       | 1                         | 0                             | NF         | 1                             | 1                     |
| 251    | 2           | 27  | Female| 23.7| 0                           | 8.0                        | 0                         | 0                             | PRL        | 0                             | 1                     |
| 268    | 2           | 38  | Female| 25.7| 1                           | 13.0                       | 1                         | 0                             | GH         | 0                             | 1                     |
| 293    | 1           | 69  | Male | 29.7| 1                           | 21.5                       | 1                         | 0                             | NF         | 1                             | 1                     |
| 299    | 1           | 36  | Female| 23.0| 0                           | 22.0                       | 1                         | 1                             | NF         | 0                             | 0                     |
| 369    | 2           | 57  | Female| 28.3| 0                           | 14.0                       | 1                         | 0                             | NF         | 0                             | 1                     |
### Table 3. Subgroup Analyses of the Primary Outcome in the Intention-to-Treat Population

|                                | Hydrocortisone Group | No Hydrocortisone Group | Risk Difference (95% CI) |
|--------------------------------|-----------------------|--------------------------|-------------------------|
| **AI during perioperation (before POD3)** |                       |                          |                         |
| patients with events/total, %, (95% CI) | 14/218, 6.4%, (3.2% to 9.7%) | 24/218, 11.0%, (6.9% to 15.2%) | +4.6% (-0.7% to 9.9%) |
| **Age**                          |                       |                          |                         |
| Age < 45 years (n=214)           | 8/105, 7.6%, (2.5% to 12.7%) | 12/109, 11.0%, (5.1% to 16.9%) | +3.4% (-4.4% to 11.2%) |
| Age ≥ 45 years (n=222)           | 6/113, 5.3%, (1.2% to 9.4%) | 12/109, 11.0%, (5.1% to 16.9%) | +5.7% (-1.5% to 12.9%) |
| **Sex**                          |                       |                          |                         |
| Male sex (n=172)                 | 6/82, 7.3%, (1.7% to 13.0%) | 12/90, 13.3%, (6.3% to 20.4%) | +6.0% (-3.0% to 15.0%) |
| Female sex (n=264)               | 8/136, 5.9%, (1.9% to 9.8%) | 12/128, 9.4%, (4.3% to 14.4%) | +3.5% (-2.9% to 9.9%)† |
| **Body mass index**              |                       |                          |                         |
| Body mass index < 25.5 kg/m² (n=235) | 3/121, 2.5%, (0% to 5.2%) | 14/114, 12.3%, (6.3% to 18.3%) | +9.8% (3.2% to 16.4%)§ |
| Body mass index ≥ 25.5 kg/m² (n=201) | 11/97, 11.3%, (5.0% to 17.7%) | 10/104, 9.6%, (3.9% to 15.3%) | -1.7% (-10.2% to 6.8%)† |
| **Preoperative comorbidities**   |                       |                          |                         |
| Yes (n=318)                      | 9/161, 5.6%, (2.0% to 9.1%) | 13/157, 8.3%, (4.0% to 12.6%) | +2.7% (-2.9% to 8.3%)† |
| No (n=118)                       | 5/57, 8.8%, (1.4% to 16.1%) | 11/61, 18.0%, (8.4% to 27.7%) | +9.3% (-2.9% to 21.4%) |
| **Tumor size**                   |                       |                          |                         |
| Macroadenoma (n=396)             | 13/200, 6.5%, (3.1% to 9.9%) | 22/196, 11.2%, (6.8% to 15.6%) | +4.7% (-0.9% to 10.3%) |
| Microadenoma (n=40)              | 1/18, 5.6%, (0% to 16.1%) | 2/22, 9.1%, (0% to 21.1%) | +3.5% (-12.5% to 19.5%) |
| **Cavernous sinus invasion**     |                       |                          |                         |
| Yes (n=158)                      | 3/76, 3.9%, (0% to 8.3%) | 8/82, 9.8%, (3.3% to 16.2%) | +5.8% (-2.0% to 13.6%) |
| No (n=278)                       | 11/142, 7.7%, (3.3% to 12.1%) | 16/136, 11.8%, (6.3% to 17.2%) | +4.0% (-3.0% to 11.0%) |
| **Tumor types**                  |                       |                          |                         |
| Non-functioning (n=261)          | 9/127, 7.1%, (2.6% to 11.5%) | 16/134, 11.9%, (6.4% to 17.4%) | +4.9% (-2.2% to 11.9%) |
| Functioning (n=175)              | 5/91, 5.5%, (0.8% to 10.2%) | 8/84, 9.5%, (3.2% to 15.8%) | +4.0% (-3.8% to 11.9%) |
| **Preoperative hormone deficiency** |                       |                          |                         |
| Yes (n=234)                      | 7/128, 5.5%, (1.5% to 9.4%) | 13/106, 12.3%, (6.0% to 18.5%) | +6.8% (-0.6% to 14.2%) |
| No (n=202)                       | 7/90, 7.8%, (2.2% to 13.3%) | 11/112, 9.8%, (4.3% to 15.3%) | +2.0% (-5.8% to 9.9%)† |
| **Degree of tumor resection**    |                       |                          |                         |
| Gross-total (n=282)              | 11/146, 7.5%, (3.3% to 11.8%) | 16/136, 11.8%, (6.3% to 17.2%) | +4.2% (-2.7% to 11.1%) |
| Subtotal (n=154)                 | 3/72, 4.2%, (0% to 8.8%) | 8/82, 9.8%, (3.3% to 16.2%) | +5.6% (-2.3% to 13.5%) |

† Indicates that "No Hydrocortisone Group" is non-inferior to "Hydrocortisone Group" if judged by the margin of 0.1.

§ Indicates that "Hydrocortisone Group" is superior to "No Hydrocortisone Group".
AI, adrenal insufficiency; POD3, the 3rd postoperative day; 95%CI, 95% confidence interval.
**eTable 4. Subgroup Analyses of the Secondary Outcome in the Intention-to-Treat Population**

|                                | Hydrocortisone Group | No Hydrocortisone Group | Risk Difference (95% CI) |
|--------------------------------|-----------------------|-------------------------|--------------------------|
|                                | patients with events/total, %, (95% CI) |                          |                          |
| AI from POD3 to POM3           | 7/218, 3.2%, (0.9% to 5.6%) | 8/218, 3.7%, (1.2% to 6.2%) | +0.5% (-3.0% to 3.9%)†   |
| Age                            |                       |                          |                          |
| Age < 45 years (n=214)         | 2/105, 1.9%, (0% to 4.5%) | 4/109, 3.7%, (0.1% to 7.2%) | +1.8% (-2.6% to 6.2%)†   |
| Age ≥ 45 years (n=222)         | 5/113, 4.4%, (0.6% to 8.2%) | 4/109, 3.7%, (0.1% to 7.2%) | -0.8% (-5.9% to 4.4%)†   |
| Sex                            |                       |                          |                          |
| Male sex (n=172)               | 3/82, 3.7%, (0% to 7.7%) | 1/90, 1.1%, (0% to 3.3%) | -2.5% (-7.2% to 2.1%)†   |
| Female sex (n=264)             | 4/136, 2.9%, (0% to 5.8%) | 7/128, 5.5%, (1.5% to 9.4%) | +2.5% (-2.3% to 7.4%)†   |
| Body mass index                |                       |                          |                          |
| Body mass index < 25.5 kg/m²   | 3/121, 2.5%, (0% to 5.2%) | 5/114, 4.4%, (0.6% to 8.1%) | +1.9% (-2.8% to 6.6%)†   |
| Body mass index ≥ 25.5 kg/m²   | 4/97, 4.1%, (0.2% to 8.1%) | 3/104, 2.9%, (0% to 6.1%) | -1.2% (-6.3% to 3.9%)†   |
| Preoperative comorbidities     |                       |                          |                          |
| Yes (n=318)                    | 6/161, 3.7%, (0.8% to 6.7%) | 6/157, 3.8%, (0.8% to 6.8%) | +0.1% (-4.1% to 4.3%)†   |
| No (n=118)                     | 1/57, 1.8%, (0% to 5.2%) | 2/61, 3.3%, (0% to 7.7%) | +1.5% (-4.1% to 7.1%)†   |
| Tumor size                     |                       |                          |                          |
| Macroadenoma (n=396)           | 6/200, 3.0%, (0.6% to 5.4%) | 7/196, 3.6%, (1.0% to 6.2%) | +0.6% (-2.9% to 4.1%)†   |
| Microadenoma (n=40)            | 1/18, 5.6%, (0% to 16.1%) | 1/22, 4.5%, (0% to 13.2%) | -1.0% (-14.7% to 12.7%)  |
| Cavernous sinus invasion       |                       |                          |                          |
| Yes (n=158)                    | 2/76, 2.6%, (0% to 6.2%) | 2/82, 2.4%, (0% to 5.8%) | -0.2% (-5.1% to 4.7%)†   |
| No (n=278)                     | 5/142, 3.5%, (0.5% to 6.6%) | 6/136, 4.4%, (1.0% to 7.9%) | +0.9% (-3.7% to 5.5%)†   |
| Tumor types                    |                       |                          |                          |
| Non-functioning (n=261)        | 5/127, 3.9%, (0.6% to 7.3%) | 5/134, 3.7%, (0.5% to 6.9%) | -0.2% (-4.9% to 4.5%)†   |
| Functioning (n=175)            | 2/91, 2.2%, (0% to 5.2%) | 3/84, 3.6%, (0% to 7.5%) | +1.4% (-3.6% to 6.4%)†   |
| Preoperative hormone deficiency|                       |                          |                          |
| Yes (n=234)                    | 5/128, 3.9%, (0.5% to 7.3%) | 3/106, 2.8%, (0% to 6.0%) | -1.1% (-5.7% to 3.5%)†   |
| No (n=202)                     | 2/90, 2.2%, (0% to 5.3%) | 5/112, 4.5%, (0.6% to 8.3%) | +2.2% (-2.6% to 7.1%)†   |
| Degree of tumor resection      |                       |                          |                          |
| Gross-total (n=282)            | 5/146, 3.4%, (0.5% to 6.4%) | 6/136, 4.4%, (1.0% to 7.9%) | +1.0% (-3.6% to 5.5%)†   |
| Subtotal (n=154)               | 2/72, 2.8%, (0% to 6.6%) | 2/82, 2.4%, (0% to 5.8%) | -0.3% (-5.4% to 4.7%)†   |

† Indicates that "No Hydrocortisone Group" is non-inferior to "Hydrocortisone Group" if judged by the margin of 0.1.

AI, adrenal insufficiency; POD3, the 3rd postoperative day; POM3, the 3rd postoperative month; 95%CI, 95% confidence interval.

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|                        | Patients with Event (n=38) | Patients without Event (n=398) | P Value   |
|------------------------|-----------------------------|-------------------------------|-----------|
| **Sex**                |                             |                               |           |
| Male sex (n=172)       | 18                          | 154                           | Reference |
| Female sex (n=264)     | 20                          | 244                           | 0.296     |
| **Age**                |                             |                               |           |
| Absolute values - year | 43.7 ± 11.3                 | 45.1 ± 13.6                   | 0.474     |
| Age < 45 years (n=214) | 20                          | 194                           | Reference |
| Age ≥ 45 years (n=222) | 18                          | 204                           | 0.647     |
| **Body mass index**    |                             |                               |           |
| Absolute values - kg/m²| 26.1 ± 3.7                  | 25.4 ± 3.7                    | 0.273     |
| Body mass index < 25.5 kg/m² (n=235) | 17                  | 218                           | Reference |
| Body mass index ≥ 25.5 kg/m² (n=201) | 21                  | 180                           | 0.236     |
| **Preoperative comorbidities** |                     |                               |           |
| No (n=118)             | 16                          | 102                           | Reference |
| Yes (n=318)            | 22                          | 296                           | 0.029     |
| Hypertension (n=115)   | 9                           | 106                           | 0.157     |
| Diabetes mellitus (n=44) | 3                    | 41                            | 0.236     |
| Deep vein thrombosis (n=2)       | 0                           | 2                             | 1.000     |
| Bone mineral density loss (n=63) | 5                           | 58                            | 0.260     |
| **Tumor size**         |                             |                               |           |
| Absolute values - mm   | 21.5 ± 9.0                  | 20.5 ± 8.2                    | 0.462     |
| Microadenoma (n=40)    | 3                           | 37                            | Reference |
| Macroadenoma (n=396)   | 35                          | 361                           | 1.000     |
| **Cavernous sinus invasion** |                     |                               |           |
| No (n=278)             | 27                          | 251                           | Reference |
| Yes (n=158)            | 11                          | 147                           | 0.328     |
| **Tumor types**        |                             |                               |           |
| Non-functioning (n=261) | 25                        | 236                           | Reference |
| Functioning (n=175)    | 13                          | 162                           | 0.435     |
| GH-secreting (n=101)   | 8                           | 93                            | 0.623     |
| Prolactin-secreting (n=62) | 5                           | 57                            | 0.712     |
| **Preoperative serum hormone levels** |             |                               |           |
| ACTH - pg/ml           | 31.0 ± 19.5                 | 29.8 ± 19.9                   | 0.720     |
| Cortisol - ug/dl       | 10.4 ± 5.8                  | 13.6 ± 5.6                    | 0.001*    |
| <9.25 ug/dl (n=102)    | 17                          | 85                            | Reference |
| ≥9.25 ug/dl (n=334)    | 21                          | 313                           | 0.001*    |
| **Preoperative hormone deficiency** |               |                               |           |
| No (n=202)             | 18                          | 184                           | Reference |
| Yes (n=234)            | 20                          | 214                           | 0.893     |
| Condition                  | Reference | Count | Total | P-value |
|----------------------------|-----------|-------|-------|---------|
| Hypothyroidism (n=139)     |           | 11    | 128   | 0.764   |
| Hypogonadism (n=135)       |           | 13    | 122   | 0.823   |
| GH deficiency (n=20)       |           | 5     | 15    | 0.062   |
| **Degree of tumor resection** |   |       |       |         |
| Subtotal (n=154)           |           | 11    | 143   | Reference |
| Gross-total (n=282)        |           | 27    | 255   | 0.390   |

* Indicates statistically significant differences after being justified by the FDR algorithm, used to control the chance of generating false positives during multiple comparisons.

ACTH, adrenocorticotropic hormone; GH, growth hormone.
Table 6. Prognostic Factors Associated With a Secondary Event in 436 Patients

|                      | Patients with Event (n=15) | Patients without Event (n=421) | P Value |
|----------------------|-----------------------------|-------------------------------|---------|
| **Sex**              |                             |                               |         |
| Male sex (n=172)     | 4                           | 168                           | Reference |
| Female sex (n=264)   | 11                          | 253                           | 0.303   |
| **Age**              |                             |                               |         |
| Absolute values - year | 47.1 ± 12.9              | 44.9 ± 13.4                     | 0.538   |
| Age < 45 years (n=214) | 6                           | 208                           | Reference |
| Age ≥ 45 years (n=222) | 9                           | 213                           | 0.474   |
| **Body mass index**  |                             |                               |         |
| Absolute values - kg/m2 | 25.6 ± 2.6              | 25.4 ± 3.7                     | 0.859   |
| Body mass index < 25.5 kg/m2 (n=235) | 8                           | 227                           | Reference |
| Body mass index ≥ 25.5 kg/m2 (n=201) | 7                           | 194                           | 0.964   |
| **Preoperative comorbidities** |               |                               |         |
| No (n=118)           | 3                           | 115                           | Reference |
| Yes (n=318)          | 12                          | 306                           | 0.531   |
| Hypertension (n=115) | 2                           | 113                           | 1.000   |
| Diabetes mellitus (n=44) | 0                           | 44                           | 0.563   |
| Deep vein thrombosis (n=2) | 0                           | 2                            | 1.000   |
| Bone mineral density loss (n=63) | 3                           | 60                           | 0.720   |
| **Tumor size**       |                             |                               |         |
| Absolute values - mm | 19.4 ± 9.6                  | 20.6 ± 8.2                     | 0.565   |
| Microadenoma (n=40)  | 2                           | 38                            | Reference |
| Macroadenoma (n=396) | 13                          | 383                           | 0.910   |
| **Cavernous sinus invasion** |               |                               |         |
| No (n=278)           | 11                          | 267                           | Reference |
| Yes (n=158)          | 4                           | 154                           | 0.433   |
| **Tumor types**      |                             |                               |         |
| Non-functioning (n=261) | 10                          | 251                           | Reference |
| Functioning (n=175)  | 5                           | 170                           | 0.584   |
| GH-secreting (n=101) | 2                           | 99                            | 0.579   |
| Prolactin-secreting (n=62) | 3                           | 59                           | 0.997   |
| **Preoperative serum hormone levels** |               |                               |         |
| ACTH - pg/ml          | 24.5 ± 15.5                 | 30.1 ± 20.0                    | 0.285   |
| Cortisol - ug/dl     | 7.7 ± 5.5                   | 13.5 ± 5.6                     | <0.001* |
| <8.8 ug/dl (n=96)    | 10                          | 86                            | Reference |
| ≥8.8 ug/dl (n=340)   | 5                           | 335                           | <0.001* |
| **Preoperative hormone deficiency** |               |                               |         |
| No (n=202)           | 7                           | 195                           | Reference |
| Yes (n=234)          | 8                           | 226                           | 0.979   |
| Condition                  | Count | Reference | p-Value |
|---------------------------|-------|-----------|---------|
| Hypothyroidism (n=139)    | 7     | 132       | 0.473   |
| Hypogonadism (n=135)      | 3     | 132       | 0.740   |
| GH deficiency (n=20)      | 4     | 16        | 0.011   |

**Degree of tumor resection**

| Method         | Count | Reference | p-Value |
|----------------|-------|-----------|---------|
| Subtotal (n=154)| 4     | 150       | Reference |
| Gross-total (n=282)| 11   | 271       | 0.475   |

* Indicates statistically significant differences after being justified by the FDR algorithm, used to control the chance of generating false positives during multiple comparisons.

ACTH, adrenocorticotropic hormone; GH, growth hormone.
eTable 7. Adjusted Incidence Rate Difference and 95% CI for the Primary Outcome

|                               | No-Hydrocortisone Group | Hydrocortisone Group | Risk Difference (95% CI) |
|-------------------------------|-------------------------|----------------------|--------------------------|
|                               | patients with events/total, %, (95% CI) |                       |                          |
| Unadjusted Primary Outcome    |                         |                      |                          |
| New-onset AI during perioperation | 24/218, 11.0%, (6.9%, 15.2%) | 14/218, 6.4%, (3.2%, 9.7%) | +4.6% (-0.7%, 9.9%) † |
| BMI<25.5 kg/m²                 | 14/114, 12.3%, (6.3% to 18.3%) | 3/121, 2.5%, (0% to 5.2%) | +9.8% (3.2% to 16.4%) § |
| BMI≥25.5 kg/m²                 | 10/104, 9.6%, (3.9% to 15.3%) | 11/97, 11.3%, (5.0% to 17.7%) | -1.7% (-10.2% to 6.8%) † |
| Adjusted Primary Outcome #    |                         |                      |                          |
| New-onset AI during perioperation | -                     | -                    | +4.4% (-0.8%, 9.8%) †    |

† Indicates that "No-Hydrocortisone Group" is non-inferior to "Hydrocortisone Group" if judged by the margin of 0.1.
§ Indicates that "No-Hydrocortisone Group" is inferior to "Hydrocortisone Group".
# The analysis was adjusted with Cochran-Mantel-Haenszel weighting for preoperative baseline cortisol level and body mass index.
eFigure 1. ROC Curve for Preoperative Cortisol in Predicting AI Before POD3 After Surgery

The cut-off value was estimated as 9.25, with a sensitivity of 0.786 and (1-specificity) of 0.553. AI, adrenal insufficiency; POD3, the 3rd postoperative day; ROC, receiver operator characteristic.
Figure 2. ROC Curve for Preoperative Cortisol in Predicting AI From POD3 to POM3

The cut-off value was estimated as 8.8, with a sensitivity of 0.796 and (1-specificity) of 0.333. AI, adrenal insufficiency; POD3, the 3rd postoperative day; POM3, the 3rd postoperative month; ROC, receiver operator characteristic.