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| --- | --- | --- | --- | --- | --- | --- |
|  | **Prolactinomas** | | | **NF-PitNETs** | | |
| ***AIP*mut**  n=17 | ***AIP*neg**  n=377 | ***p* value** | ***AIP*mut**  n=14 | ***AIP*neg**  n=172 | ***p* value** |
| **Cohort type based on family history of PitNETs**  Familial cohort  Sporadic cohort | 82.4%  17.6% | 48.5%  51.5% | **0.006** | 100%  0% | 68.6%  31.4% | **0.013** |
| **Gender**  Male  Female | 52.9%  47.1% | 33.2%  66.8% | 0.092 | 64.3%  35.7% | 57.0%  43.0% | 0.595 |
| **Age at disease onset ≤ 18 yr** | 45.5% | 40.6% | 0.747 | 50.0% | 12.4% | **0.003** |
| **Age at first symptoms (yr)** | 27.5 ± 17.9 | 24.1 ± 10.8 | 0.959 | 22.6 ± 7.7 | 36.6 ± 17.3 | **0.016** |
| **Age at diagnosis (yr)** | 30.7 ± 16.5 | 26.2 ± 11.2 | 0.619 | 29.2 ± 14.8 | 39.4 ± 17.3 | **0.038** |
| **Delay in diagnosis (yr)** | 4.5 ± 8.8 | 2.4 ± 4.6 | 0.665 | 1.1 ± 2.3 | 1.5 ± 3.3 | 0.761 |
| **Pituitary apoplexy** | 16.7% | 2.8% | **0.009** | 0 | 8.6% | 0.270 |
| **Hypopituitarism at diagnosis** | 62.5% | 59.0% | 0.846 | 9.1% | 41.5% | **0.041** |
| **Number of pituitary deficiencies at diagnosis** | 1.38 ± 1.51 | 0.93 ± 1.04 | 0.470 | 0.18 ± 0.60 | 1.00 ± 1.40 | **0.045** |
| **Macroadenoma** | 75.0% | 63.7% | 0.358 | 30.8% | 85.0% | **<0.001** |
| **Maximum tumor diameter (mm)** | 14.4 ± 16.1 | 20.6 ± 19.7 | 0.270 | 9.0 ± 9.8 | 22.8 ± 15.9 | **0.001** |
| **Suprasellar extension** | 42.9% | 34.9% | 0.665 | 27.3% | 56.2% | 0.071 |
| **Cavernous sinus invasion** | 16.7% | 22.7% | 0.728 | 18.2% | 22.4% | 0.753 |
| **Ki-67 > 3%** | 0 | 52.9% | 0.303 | 33.3% | 63.2% | 0.907 |
| **Number of treatments** | 1.12 ± 0.78 | 1.39 ± 0.90 | 0.212 | 0.46 ± 0.78 | 1.19 ± 1.01 | **0.005** |
| **Number of surgeries** | 0.35 ± 0.49 | 0.35 ± 0.68 | 0.609 | 0.31 ± 0.48 | 0.89 ± 0.66 | **0.001** |
| **Reoperation** | 0 | 18.6% | 0.246 | 0 | 13.9% | 0.423 |
| **Radiotherapy** | 5.9% | 7.2% | 0.838 | 7.7% | 20.8% | 0.257 |
| **Dopamine agonists** | 70.6% | 86.6% | 0.068 | 7.7% | 7.2% | 0.948 |
| **Multimodal treatment** | 28.6% | 22.8% | 0.618 | 50.0% | 28.9% | 0.365 |
| **≥ 3 treatments** | 7.1% | 8.0% | 0.907 | 0 | 13.3% | 0.435 |
| **Active disease at last follow-up** | 15.4% | 29.1% | 0.289 | 10.0% | 18.8% | 0.494 |
| **Hypopituitarism at last follow-up** | 25.0% | 23.0% | 0.897 | 10.0% | 45.7% | **0.040** |
| **Number of pituitary deficiencies at last follow-up** | 0.75 ± 1.49 | 0.58 ± 1.16 | 0.847 | 0.10 ± 0.31 | 1.16 ± 1.50 | 0.067 |
| **Follow-up duration (yr)** | 13.6 ± 12.5 | 9.3 ± 10.1 | 0.150 | 7.5 ± 7.1 | 8.1 ± 11.3 | 0.551 |

**Supplemental Table 1: Comparative analysis between *AIP*mut vs *AIP*neg prolactinomas and *AIP*mut vs *AIP*neg NF-PitNETs.** Categorical data are shown as %; continuous variables are shown as mean ± standard deviation. *AIP*mut, *AIP* mutation-positive; *AIP*neg, *AIP* mutation-negative; NF-PitNET, non-functioning pituitary neuroendocrine tumor; PitNET, pituitary neuroendocrine tumor; yr, years.