Cell-lineage specific differences in presentation and outcomes of non-functioning pituitary adenomas – a multicentre study in patients seen at Endo-ERN reference centres

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Study Planned

Administrative details

EU PAS number

EUPAS1000000489

Study ID

1000000489

DARWIN EU® study

No

Study countries

- [ ] Belgium
- [ ] Denmark

- [ ] European Union
- [ ] Finland
- [ ] France
- [ ] Germany
- [ ] Greece
- [ ] Italy
- [ ] Netherlands
- [ ] Romania
- [ ] Spain
- [ ] Sweden

Study description

In 2017, the evaluation of cell lineage-specific transcription factors (TFs) by immunohistochemistry (IHC) has

Study protocol been added to the World Health Organization (WHO) histopathological classification of pituitary neuroendocrine tumours (ENDO4) and this was maintained in the most recent WHO histopathological classification of 2022 (ENDO5). After the introduction of cell lineage-specific TFs into the histopathological classification, pituitary adenomas (PAs) that were negative for all anterior pituitary hormones could be classified into one of the three cell lineages based on positivity of cell lineage-specific TFs. As a results, non-functioning (NF) gonadotroph adenomas now include SF1+/H- NFPAs besides the previously identified LH+/FSH+ NFPAs, non-functioning corticotroph adenomas are expanded with TPIT+/H+ adenomas, and adenomas differentiating into the PIT1 cell lineage include PIT1+/H- adenomas. The radiological presentation and clinical prognosis of these newly defined histopathological subtypes have not been studied widely. A recent systematic review and meta-analysis (van der Hoeven et al. (2025)) concluded that there are indeed differences in radiological presentation at time of surgery, where cavernous sinus invasion was more prevalent in TPIT+ NFPAs and NCAs

compared with SF1+ NFPAs and in NCAs compared with PIT1 NFPAs. The authors of this review also concluded that data on differences in recurrence rates and the use of postoperative radiotherapy is lacking. The primary aim is to evaluate the associations between TF expression identified by IHC (exposure) and the radiological presentation, recurrence rates and therapeutic prognosis (outcome) in patients with non-functioning pituitary adenomas treated at an Endo-ERN Reference Centre.

Study status

Planned

Research institutions and networks

Institutions

Amsterdam UMC

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Institution | Educational Institution | Hospital/Clinic/Other health care facility

Networks

European Reference Network on Rare Endocrine Conditions (Endo-ERN)

Contact details

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Study timelines

Date when funding contract was signed

Planned: 01/10/2023

Study start date

Planned: 14/10/2024

Date of final study report

Planned: 01/03/2027

Sources of funding

- EU institutional research programme

Study protocol

Cell-lineage_specific_differences_in_presentation_and_outcomes_of_non-functioning_pituitary_adenomas_version_1.1_2024_11_07.pdf (1.94 MB)

Regulatory

Was the study required by a regulatory body?

No

Is the study required by a Risk Management Plan (RMP)?

Not applicable

Methodological aspects

Study type

Study type list

Study topic:

Disease /health condition

Study type:

Non-interventional study

Study design:

For this study, data is collected both retrospectively and prospectively using the Core Registry and the Condition Specific Pituitary Tumour Module of the

European Registries for Rare Endocrine Conditions (EuRRECa; Workpackage 5 of Endo-ERN).

Main study objective:
The primary aim is to evaluate the associations between TF expression identified by IHC and the radiological presentation, recurrence rates and therapeutic prognosis in patients with non-functioning pituitary adenomas treated at an Endo-ERN Reference Centre who received surgery, and of whom pituitary tissue is available for analysis of cell lineage-specific TF expression patterns using immunohistochemistry.

Study Design

Non-interventional study design
Cohort

Population studied

Short description of the study population
Patients with non-functioning pituitary adenomas who are treated at an Endo-ERN Reference Center who received surgery and of whom pituitary tissue is available for the analysis of cell lineage-specific TF expression patterns (SF1+, TPIT+, PIT1+ or none) identified by immunohistochemistry.

Age groups

- **Paediatric Population (< 18 years)**
  - Neonate
    - Preterm newborn infants (0 – 27 days)
    - Term newborn infants (0 – 27 days)

    - Infants and toddlers (28 days – 23 months)
    - Children (2 to < 12 years)
    - Adolescents (12 to < 18 years)
- **Adult and elderly population (≥18 years)**
    - Adults (18 to < 65 years)
        - Adults (18 to < 46 years)
        - Adults (46 to < 65 years)
    - Elderly (≥ 65 years)
        - Adults (65 to < 75 years)
        - Adults (75 to < 85 years)
        - Adults (85 years and over)

Study design details

Outcomes

Primary outcomes are the associations between exposure to the TF expression patterns (SF1+, TPIT+, PIT1+ or none) and outcomes:

• KNOSP score 3-4 (9) at time of first surgery

• Recurrence

• The number of interventions per 100 PY (pituitary surgery, radiation, medical treatment)

• Time to radiation

• Time to second intervention

in patients with non-functioning pituitary adenomas treated with surgery and seen at Endo-ERN Reference centers

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Data analysis plan

Descriptive data (n/N (%), mean ± SD, median (IQR)) will be analyzed depending on data structure and normality by Chi-square test or Fisher’s exact

test, One way ANOVA (followed by post-hoc tests to identify differences between two specific groups), and Kruskal Wallis test (by post-hoc tests to identify differences between two specific groups).

Time-to-event data will be analyzed by Kaplan-Meier Survival Curves and Log-Rank tests, followed Simple Cox Regression analysis to assess the unadjusted HR per histopathological subtype in reference to SF1+ NFPAs.
The number of interventions will be standardized to the follow-up duration by dividing the number of interventions in a group by the sum of the individual follow-up times in years across all subjects in that group, multiplied by 100. Differences in the rate of interventions adjusted for the different follow-up times will be evaluated by calculating incidence rate ratios.

Data management

ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No