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THE HEART OF MEDICAL EDUCATION

PITUITARY HIGHLIGHTS: ACROMEGALY & BEYOND

FROM ECE & ENDO 2023

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DEVELOPED BY PITUITARY CONNECT

This programme is developed by PITUITARY CONNECT, an international group of experts in the field of pituitary diseases.



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Expert Disclaimers:

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EDUCATIONAL OBJECTIVES

To educate learners on the **key clinical data in functioning pituitary adenomas, including acromegaly, from endocrinology congresses in the first half of 2023:**

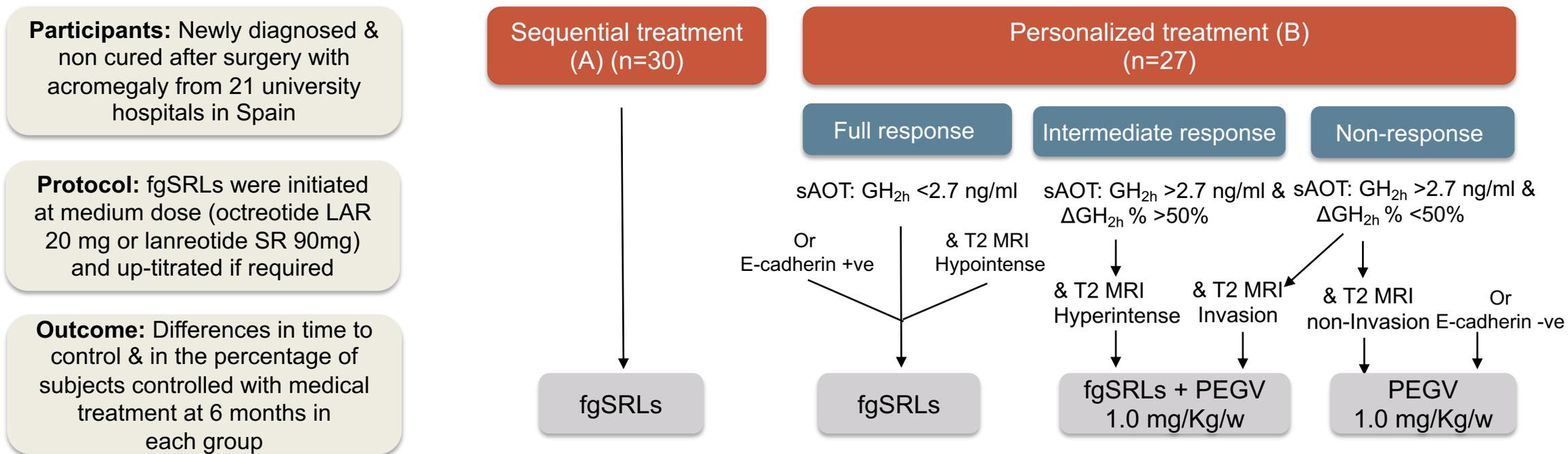
- Improve **overall awareness and understanding** of the latest acromegaly data
- Recognise key data for **current and potential future treatment options and strategies for acromegaly care**

PRECISION MEDICINE IN ACROMEGALY: RESULTS OF THE ACROFAST STUDY

Puig-Domingo M, et al. ECE 2023. Abstract EP730

ACROFAST: BACKGROUND AND STUDY DESIGN

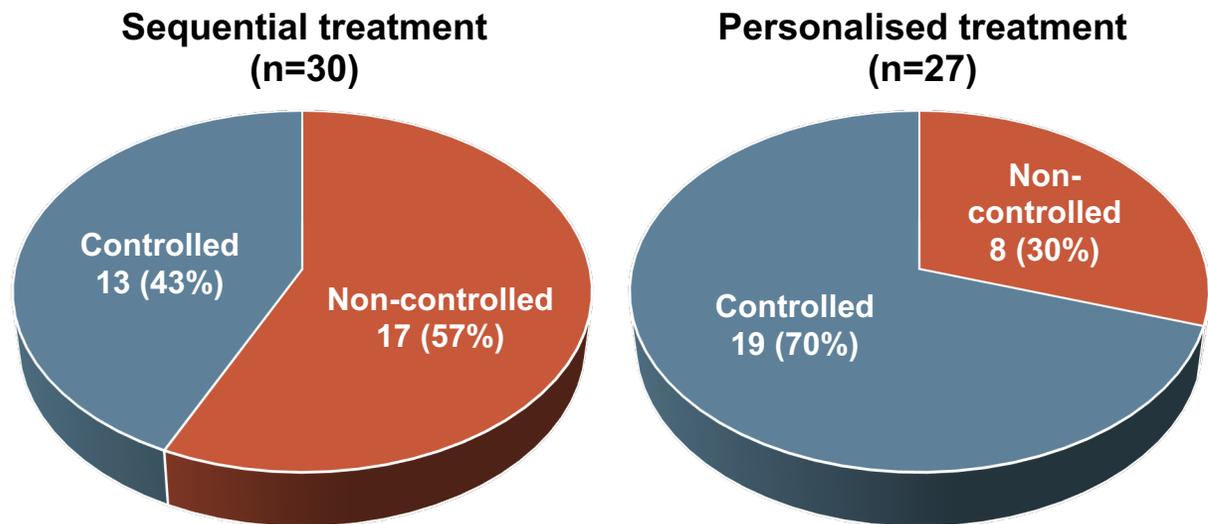
- Some biomarkers have been reported to predict first generation somatostatin receptor ligand (fgSRL) response including T2 MRI intensity, GH at 2 hours ($\text{GH}_{2\text{h}}$) and GH acute decrease ($\Delta\text{GH}_{2\text{h}} \%$) after short acute octreotide test (sAOT) and molecules such as SST2 and E-cadherin)
- The prospective ACROFAST trial evaluated the assignment of treatment according to fgSRLs response biomarkers compared to a control group in which fgSRLs or PEGV, or their combination were considered



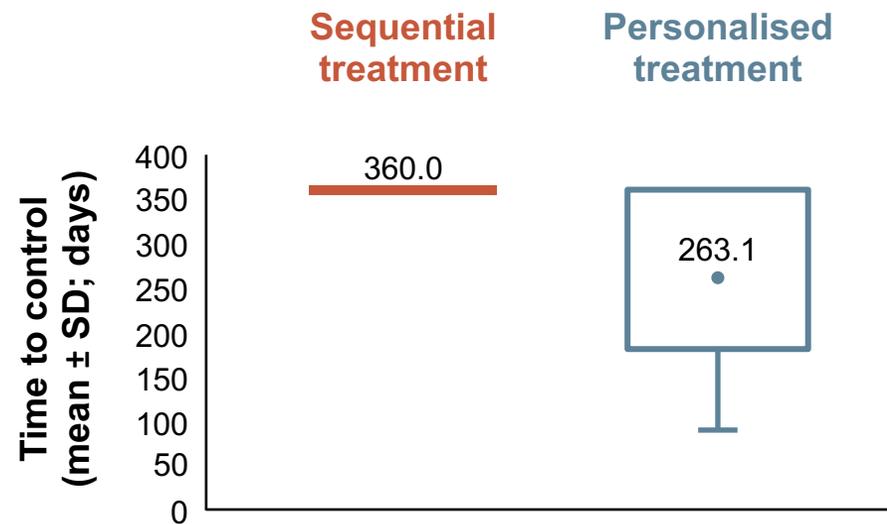
GH, growth hormone; LAR, long-acting release; MRI, magnetic resonance imaging; PEGV, pegvisomant; SR, sustained release; SRLs, somatostatin receptor ligands; SST2, somatostatin receptor type

ACROFAST: RESULTS

DIFFERENCES IN BIOCHEMICAL CONTROL AT 6 MONTHS OF MEDICAL TREATMENT
($p=0.03$; FISHER'S EXACT TEST)



DIFFERENCES IN TIME TO CONTROL AMONG NON-RESPONDERS
($p=0.04$; MANN-WHITNEY U TEST)



ACROFAST: SUMMARY

- Significantly higher proportion of patients in the personalized treatment group not only achieved hormonal control, but also achieved it in a significantly shorter period of time compared to the sequential group

Clinical Perspective

Personalised treatment guided by biomarkers, imaging and patient characteristics, should be the "standard of practice" and used in all patients with acromegaly to improve outcomes

[18F]FET PET-MRI: A NOVEL AND IMPROVED TECHNIQUE FOR DETECTION OF SMALL FUNCTIONAL PITUITARY ADENOMAS

Pruis I, et al. ECE 2023. Abstract OC3.3

[18F]FET PET-MRI: BACKGROUND AND STUDY DESIGN

Background

- Surgical planning for small functional pituitary adenomas is often complicated due to inconclusive diagnostic MRI in up to 40% of patients, therefore hampering cure rates
- This study investigated [18F]FET-PET MRI as a novel method for the detection of small functional pituitary adenoma

Protocol & Outcomes:

- Patients with CD (n=22) or acromegaly (n=6) with a suspected primary or recurrent small functional pituitary adenoma underwent [18F]FET PET-MRI
- Focal uptake of [18F]FET was evaluated by a single nuclear radiologist and MRI was separately evaluated by a single neuroradiologist
- Outcomes were compared with clinical follow-up and sensitivity and positive predictive values were calculated

[18F]FET PET-MRI: RESULTS

CUSHING'S DISEASE (N=22)

17 patients with primary diagnosis had also undergone IPSS

22 patients had positive [18F]FET PET findings, identifying pituitary adenomas as small as 3mm in size on accompanying MRI

14 patients underwent transsphenoidal surgery after [18F]FET PET (others waiting or refused)

11 of these 14 patients are in biochemical remission: estimated sensitivity of 100% and PPV between 78-100% to detect CD

ACROMEGALY (N=6)

3 patients had primary diagnosis

4 patients had positive [18F]FET PET findings

1 patient underwent transsphenoidal surgery after [18F]FET PET (others waiting or refused)

This patient is biochemically in remission

[18F] FET PET, 18F-fluoro-ethyl-tyrosine positron emission tomography; CD, Cushing's disease; IPSS, inferior petrosal sinus sampling; MRI, magnetic resonance imaging; PPV, positive predictive values

[18F]FET PET-MRI: SUMMARY

- [18F]FET PET-MRI shows high accuracy for localising small functional pituitary adenoma in patients with CD and acromegaly
- The diagnostic yield of this hybrid imaging technique exceeds that of MRI alone and IPSS

Clinical Perspective

With increased availability, [18F]FET PET-MRI could be used in clinical practice for localisation of small pituitary adenomas and thus increased yield of surgery or repeat surgery

TREATMENT PATTERNS IN ACROMEGALY: ANALYSIS OF REAL-WORLD US INSURANCE CLAIMS FROM THE MARKETSCAN[®] DATABASE

Fleseriu M, et al. ENDO 2023. Abstract THU-061

TREATMENT PATTERNS IN ACROMEGALY: BACKGROUND AND STUDY DESIGN

Background

- Medical treatments for acromegaly include fgSRLs (LAN, OCT, and oral octreotide) sgmSRLs (pasireotide), dopamine agonists (cabergoline), and GHRAs (pegvisomant)
- This study aims to describe real-world treatment patterns of individuals receiving medications for acromegaly in the United States

Methods

Key eligibility Criteria:

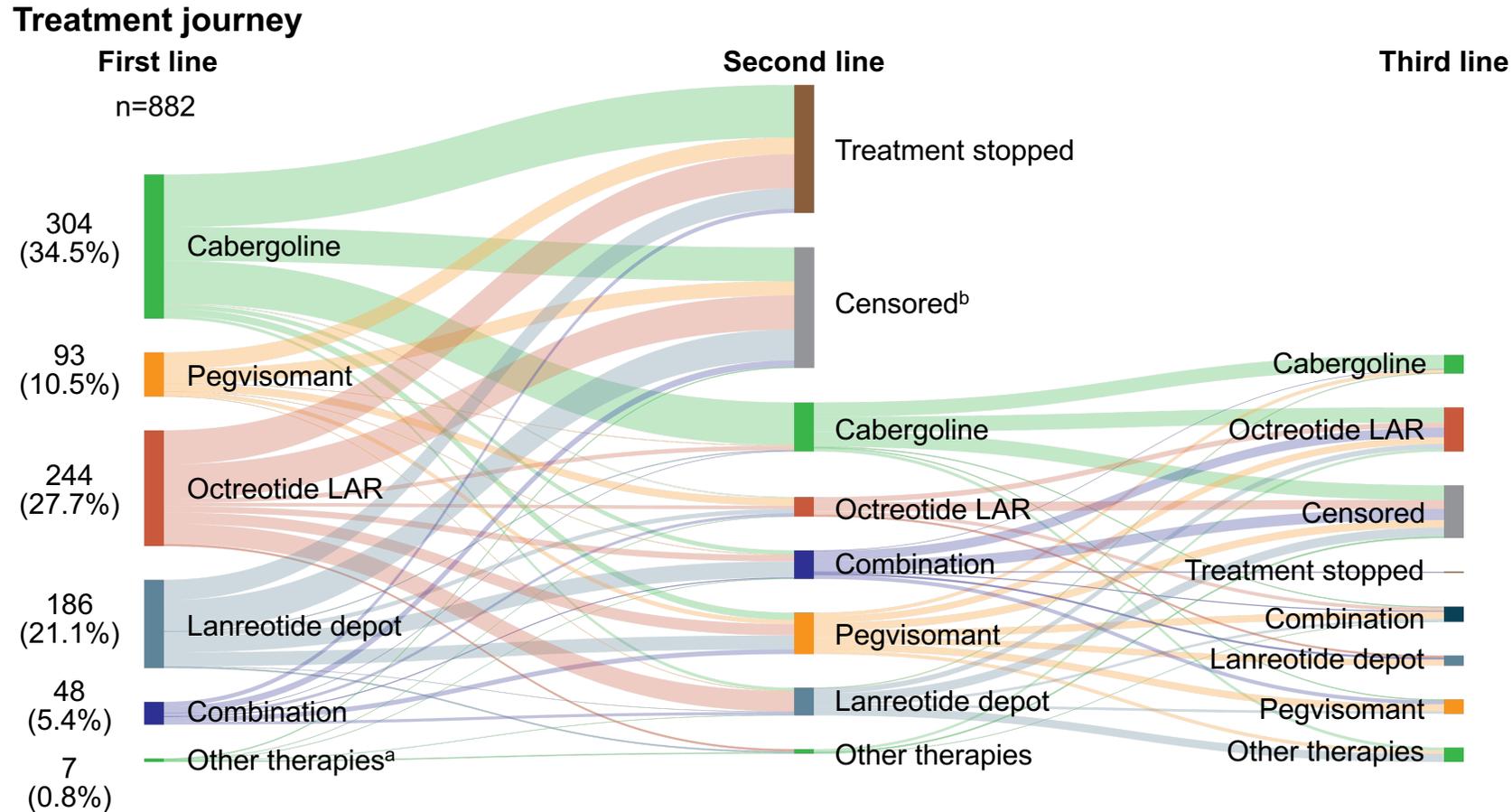
- Received monotherapy or combination therapy (≥ 2 treatments overlapping for > 3 m) for ≥ 90 days without treatment gaps
- ≥ 2 condition claims associated w/ acromegaly diagnosis
- Had data ≥ 3 m before and ≥ 6 m after diagnosis/first treatment claim (whichever earlier)
- ≥ 18 years old at diagnosis

Outcomes:

- Treatment frequency by LOT & changes between LOTs
- Treatment adherence and persistence for LOT 1
- Treatment up-/down-titration and extended dosing interval use, evaluated for OCT and LAN

fg/sgmSRLs, first-generation/second-generation multiligand somatostatin receptor ligand; GHRA, growth hormone receptor antagonist; LAN, lanreotide depot; LOT, line of treatment; m, months; OCT, octreotide long-acting release

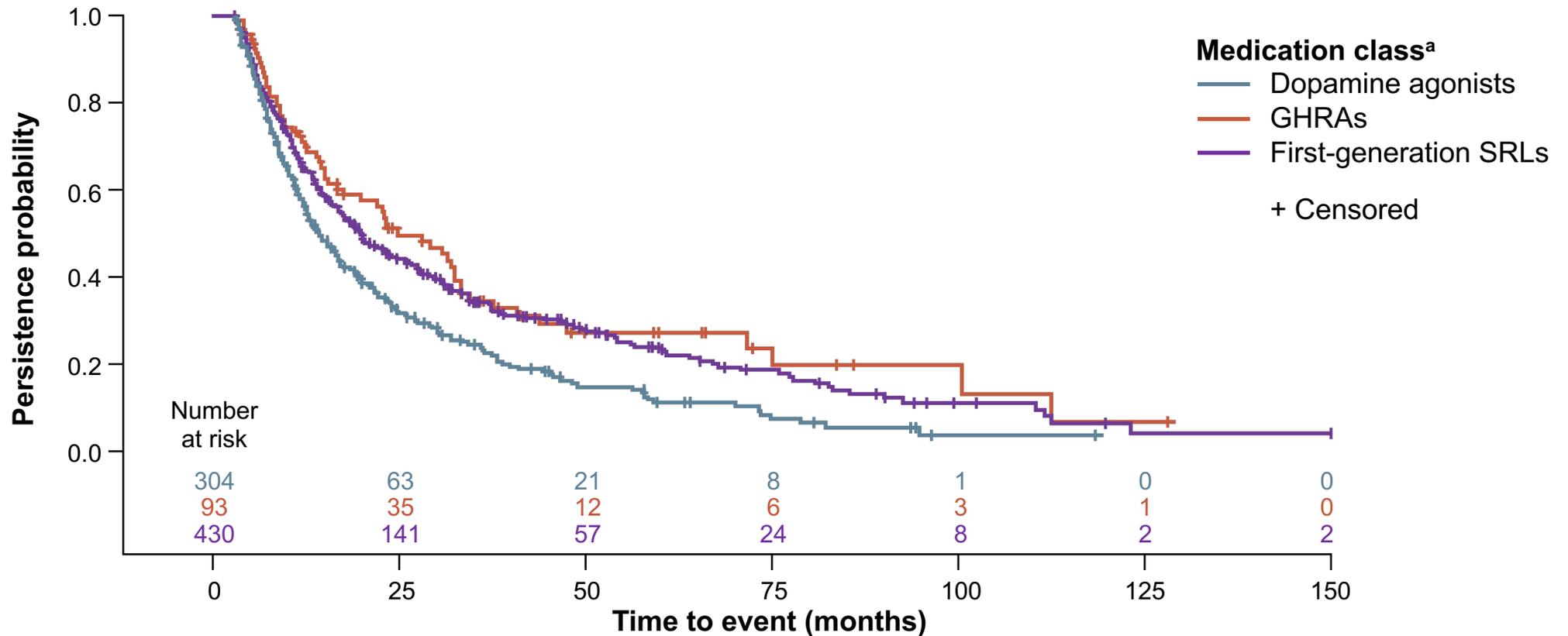
TREATMENT PATTERNS IN ACROMEGALY: CHANGES IN LOT FOR MONOTHERAPIES & COMBINATION THERAPIES



^a Includes other monotherapies, such as pasireotide and oral octreotide

^b Loss to follow-up or data cut-off on July 31, 2022, whichever occurred first
 LAR, long-acting release; LOT, line of therapy

TREATMENT PATTERNS IN ACROMEGALY: TREATMENT PERSISTENCE FOR MONOTHERAPIES IN LOT 1



^a Oral octreotide (n=5) and pasireotide (n=18) were not included due to small sample size

GHRA, growth hormone receptor antagonist; LOT, line of treatment; SRL, somatostatin receptor ligand

Fleseriu M, et al. ENDO 2023. Abstract THU-061 (poster presentation)

TREATMENT PATTERNS IN ACROMEGALY: TREATMENT TITRATION FOR FIRST-GENERATION SRL MONOTHERAPIES

Change type	Treatment line	Variable	LAN	OCT
Up-titration	LOT 1	Individuals with ≥1 dose up-titration, n (%)	107 (57.5)	105 (43.0)
	LOT 2		35 (58.3)	19 (30.7)
	LOT 3		17 (56.7)	7 (22.6)
Down-titration	LOT 1	Individuals with ≥1 dose down-titration, n (%)	72 (38.7)	62 (25.4)
	LOT 2		26 (43.3)	15 (24.2)
	LOT 3		13 (43.3)	3 (9.7)

^a Recommended starting dose for LAN is 90 mg every 4 weeks for 3 months; recommended starting dose for OCT is 20 mg every 4 weeks for 3 months

^b Percentages sum to over 100% as individuals may have received more than one dose within the same LOT

TREATMENT PATTERNS IN ACROMEGALY: SUMMARY

- Cabergoline was the most frequent of all LOT 1 medications (34.5%) despite having the shortest adherence and persistence
- OCT (27.7%) and LAN (21.1%), which had longer adherence and persistence, were also commonly used in LOT 1
- EDIs, which can achieve biochemical control and safety comparable with standard monthly administration while decreasing the clinical and economic burden on individuals were seldom used

Clinical Perspective

Real world data from administrative claims highlights that not all patients are treated per guideline recommendations; however, lack of biochemical data could limit some of the conclusions

LONG-TERM DEPOT SPECIFIC CHANGES IN ADIPOSE TISSUE AFTER TREATMENT OF ACROMEGALY

Falch CM, et al. ENDO 2023. Abstract THU-067

LONG-TERM DEPOT-SPECIFIC CHANGES IN AT AFTER TREATMENT OF ACROMEGALY: BACKGROUND AND STUDY DESIGN

Background

- Patients with active acromegaly present a decreased adipose tissue mass. Short-term studies show that AT increases following treatment; however, long term effects are unclear
- This study aims to characterize the depot specific changes of AT after treatment of acromegaly and identify contributing factors

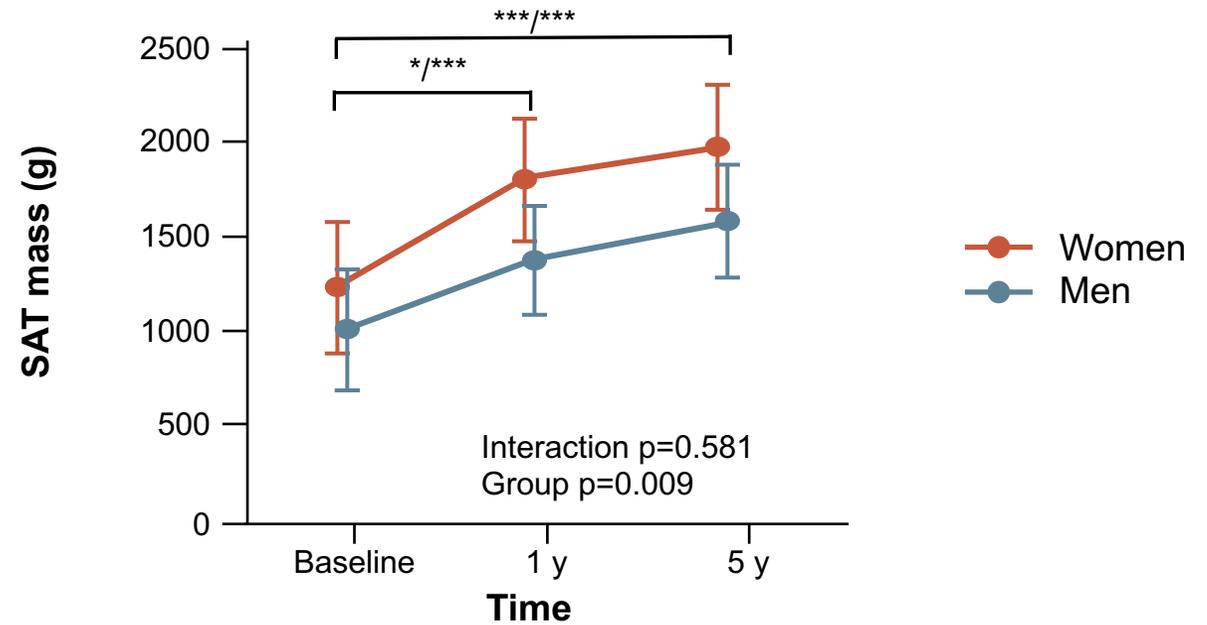
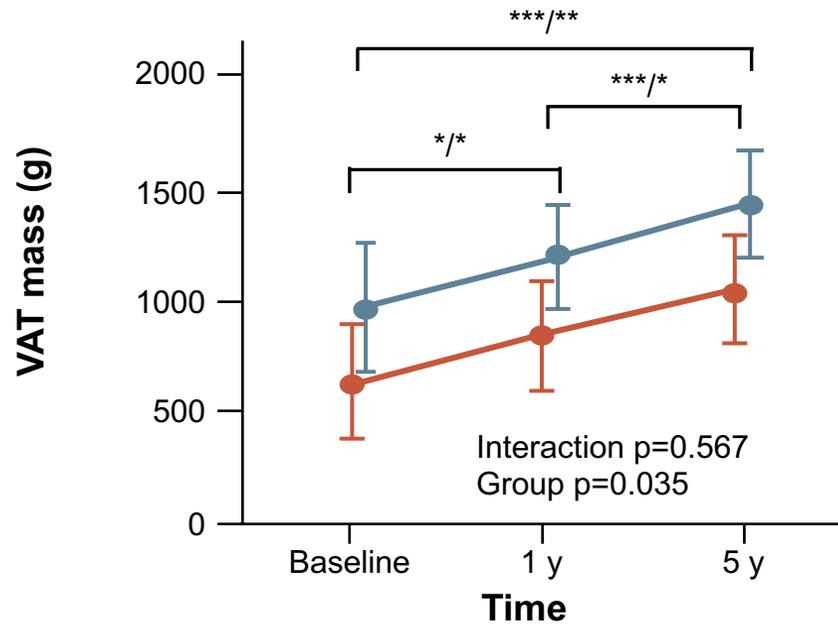
Methods

- Patients with acromegaly (n=62), VAT, SAT, TAT and A/G ratio were measured by DXA at diagnosis, and at a short- and long-term visit
- GH, IGF-1, glucose and HbA1c levels, gonadal status, and diabetes status were recorded
- Remission status was assessed at the long-term visit (IGF-1 $\leq 1.3 \times$ ULN)

A/G ratio, android gynoid ratio; AT, adipose tissue; DXA, dual energy X-ray absorptiometry; GH, growth hormone; HbA1c, haemoglobin A1c; IGF-1, insulin-like growth factor 1; SAT, subcutaneous adipose tissue; TAT, total adipose tissue; ULN, upper limit of normal; VAT, visceral adipose tissue

Falch CM, et al. ENDO 2023. Abstract THU-067 (poster presentation)

LONG-TERM DEPOT-SPECIFIC CHANGES IN AT AFTER TREATMENT OF ACROMEGALY: SEX DIFFERENCES IN FAT DEPOT CHANGES



- VAT and A/G ratio increased at both time points, whereas SAT and TAT mainly increased at short-term, plateauing afterwards
- VAT and A/G ratio were higher in men, and the A/G ratio increased more compared to women
- The increase in VAT, but not SAT, TAT or A/G ratio, was more pronounced in patients with diabetes mellitus

A/G ratio, android gynoid ratio; AT, adipose tissue; SAT, subcutaneous adipose tissue; TAT, total adipose tissue; VAT, visceral adipose tissue; y, years

* $p < 0.05$, ** $p < 0.02$, *** $p < 0.001$

Falch CM, et al. ENDO 2023. Abstract THU-067 (poster presentation)

LONG-TERM DEPOT-SPECIFIC CHANGES IN AT AFTER TREATMENT OF ACROMEGALY: KEY FINDINGS

- Glucose and HbA1c decreased at short-term and remained stable at long-term, with no obvious sex differences
- BMI remained stable
- The gonadal status had no effect on the increase in AT in women
- The increase in AT strongly correlated with the decrease in GH at long-term
- The decrease in glucose correlated with the decrease in HbA1c and IGF-1 at long-term
- Long-term remission had no effect on changes in AT mass during follow-up

LONG-TERM DEPOT-SPECIFIC CHANGES IN AT AFTER TREATMENT OF ACROMEGALY: SUMMARY

- Treatment of acromegaly leads to an increase in AT mass in a depot- and sex-specific manner both at short- and long-term follow-up
- Glucose metabolism improves rapidly after disease control and persists, whereas patients with diabetes mellitus have a higher VAT increase that may worsen their long-term metabolic outcome

Clinical Perspective

Increased awareness of long-term changes in adipose tissues following treatment of acromegaly is needed; increased adiposity, especially in patients with diabetes mellitus, needs to be recognized



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