Crinetics Pharmaceuticals

ACROMEGALY KOL EVENT

November 20, 2020

Safe Harbor Statement

This presentation contains forward-looking statements. All statements other than statements of historical facts contained in this presentation are forward-looking statements, including statements regarding: the potential benefits of paltusotine for acromegaly patients; the planned improvement of the paltusotine formulation and the timing thereof; the potential to initiate a Phase 3 program of paltusotine in acromegaly with our to-be-marketed formulation based on the Edge and Evolve results and the timing thereof; our plans to meet with the FDA and the timing of such meeting; the planned expansion of the paltusotine development program to include the treatment of carcinoid syndrome in patients with NETs and the expected timing thereof, including the initiation of a Phase 2 trial in these patients; the potential to initiate a Phase 1 trial of our lead ACTH antagonist and the timing thereof; and the potential to initiate a Phase 1 trial of CRN04777 and the timing thereof. In some cases, you can identify forward-looking statements by terms such as “may,” “believe,” “anticipate,” “could,” “should,” “estimate,” “expect,” “intend,” “plan,” “project,” “will,” “forecast” and similar terms. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, without limitation: topline data that we report is based on a preliminary analysis of key efficacy and safety data, and such data may change following a more comprehensive review of the data related to the clinical trials and such topline data may not accurately reflect the complete results of a clinical trial, and the FDA and other regulatory authorities may not agree with our interpretation of such results; advancement of paltusotine into a Phase 3 program and our lead ACTH antagonist and CRN04777 into Phase 1 trials are dependent on and subject to the receipt of further feedback from the FDA; we may not be able to obtain, maintain and enforce our patents and other intellectual property rights, and it may be prohibitively difficult or costly to protect such rights; the COVID-19 pandemic may disrupt our business and that of the third parties on which we depend, including delaying or otherwise disrupting our clinical trials and preclinical studies, manufacturing and supply chain, or impairing employee productivity; our dependence on third parties in connection with product manufacturing, research and preclinical and clinical testing; the success of our clinical trials and nonclinical studies for paltusotine and our other product candidates; regulatory developments in the United States and foreign countries; unexpected adverse side effects or inadequate efficacy of our product candidates that may limit their development, regulatory approval and/or commercialization; we may use our capital resources sooner than we expect; and other risks described under the heading “Risk Factors” in documents we file from time to time with the Securities and Exchange Commission. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. All forward-looking statements are qualified in their entirety by this cautionary statement, which is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and, except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions, and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

Company Overview

Highlights

- Nasdaq listed: CRNX
- Headquarters: San Diego, CA
- Employees: 80
- Shares: 32.9 million*
- Cash & Investments: $187 million*

Our Strategy: Discover, develop and commercialize new drugs for multiple rare endocrine diseases and endocrine-related tumors with:

- High unmet medical need
- Established biology
- Biomarker endpoints
- POC in Phase 1
- Small registration trials

*As of September 30, 2020

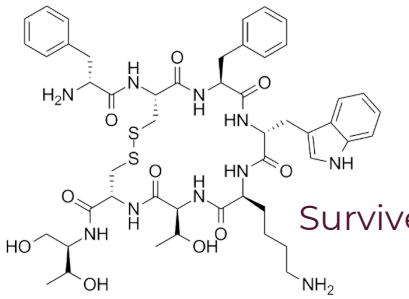
Pipeline: Rare Disease Franchise in Endocrinology

PROGRAM	DISCOVERY	PRECLIN	PHASE 1	PHASE 2	PHASE 3	ANTICIPATED NEXT MILESTONE
Paltusotine Acromegaly						End-of-Phase 2 meeting with FDA 1Q2021 Initiate Phase 3 acromegaly 1H 2021
Neuroendocrine Tumors (NETs)						Initiate Phase 2 in 2021
Oral ACTH Antagonist Cushing's Disease, Congenital Adrenal Hyperplasia (CAH)						Initiate Phase 1 late 2020/early 2021
CRN04777 Congenital Hyperinsulinism (CHI)						Initiate Phase 1 early 2021

All product candidates discovered and developed internally. Global rights retained and no licensing obligations.

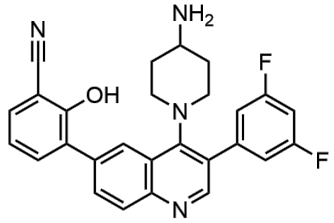
Paltusotine is Orally Bioavailable Just Like Other Traditional Oral Small Molecule Drugs

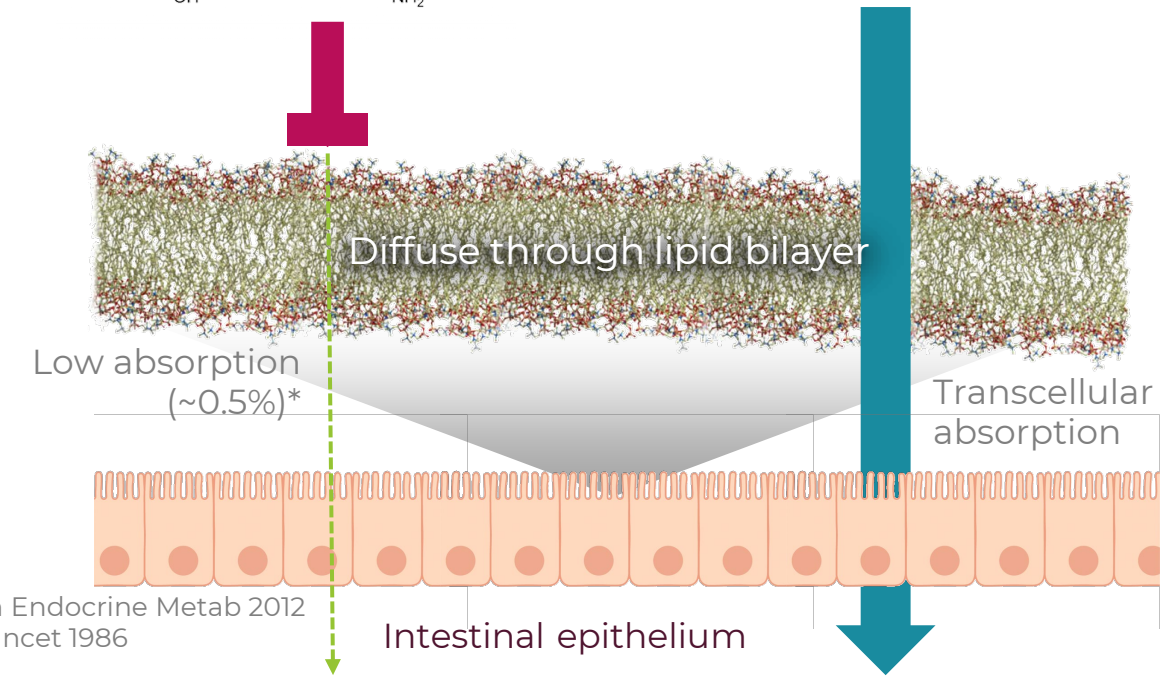
Peptide: Octreotide

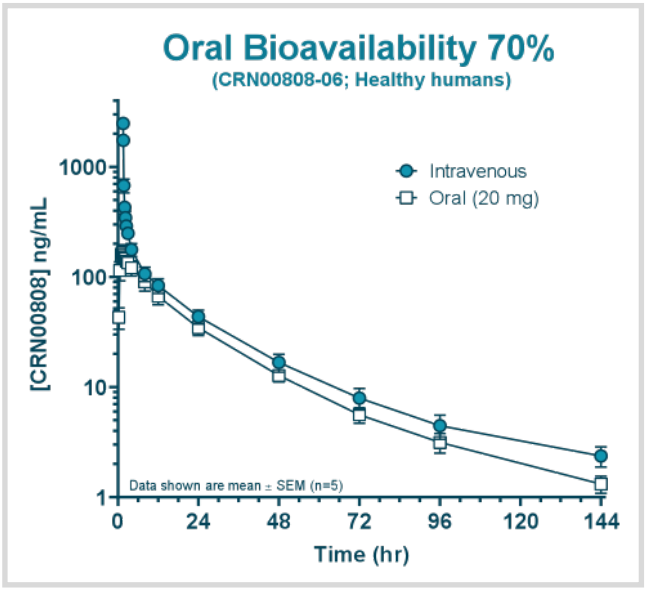


Survive proteolysis

Nonpeptide: paltusotine







	Paltusotine (CRN00808)
Oral Bioavailability	70%
Observed Half Life	42-50 hr.

*Tuvia S *et al* J Clin Endocrine Metab 2012
Williams G *et al* Lancet 1986

Paltusotine Target Profile

First-in-class oral nonpeptide SST2 agonist specifically designed for the treatment of acromegaly and NETs

ATTRIBUTE	POTENTIAL BENEFIT
Nonpeptide structure (small molecule)	Low COGS Ambient temperature supply chain
High SST2 potency/selectivity	Potent GH/IGF-1 suppression Low dose No increases in hyperglycemia
High oral bioavailability	Oral administration at home No injection pain or inconvenient office visits Low dose
Long half-life (42-50 hrs.)	Once daily administration Consistent exposure throughout month Forgiveness of missed dose
No drug-drug interactions	Easier prescribing for patients on other drugs No excipients that alter absorption of other drugs

Introduction to Today's Speakers

Peter Trainer, MD, FRCPE

Newly appointed Vice President of Clinical Endocrinology at Crinetics

Former Associate Medical Director and Clinical Lead for endocrinology for The Christie NHS Foundation Trust (The Christie)

Honorary Professor of Endocrinology at the University of Manchester in Manchester

Clinical Director of Manchester Academic Health Science Centre

Mônica Gadelha, MD, PhD

Lead investigator in the ACROBAT studies

President-elect of the Pituitary Society

Professor of Endocrinology at the Medical School of the Universidade Federal do Rio de Janeiro (UFRJ) and directs the Neuroendocrine Research Center at Hospital Universitário Clementino Fraga Filho of the UFRJ

INTRODUCTION TO ACROMEGALY

Dr. Peter Trainer, VP of Clinical Endocrinology at Crinetics

Acromegaly

David & Goliath

acros	- extremity
megale	- great

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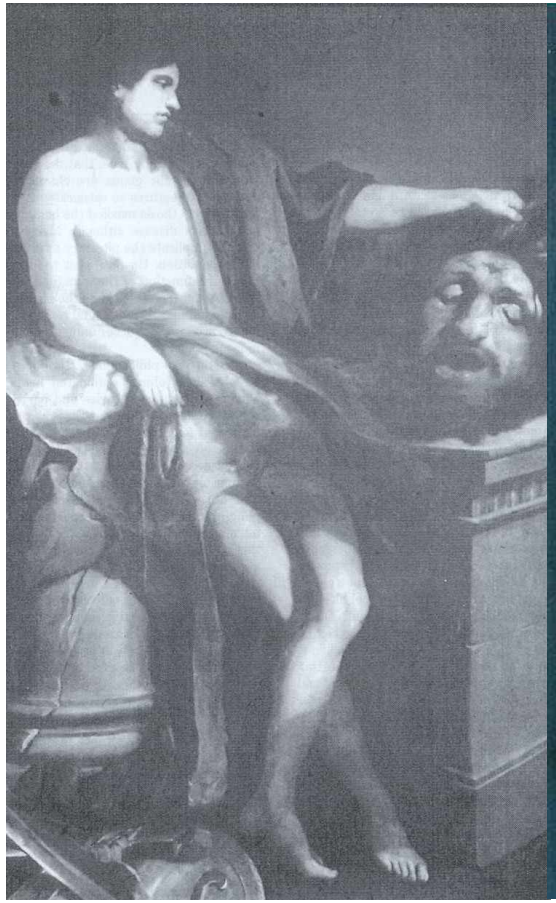
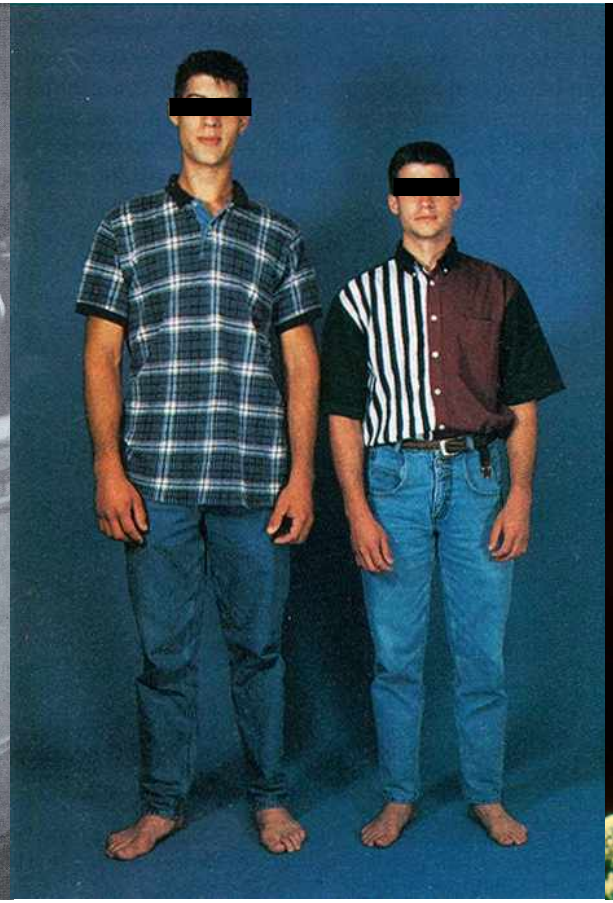
Science Centre

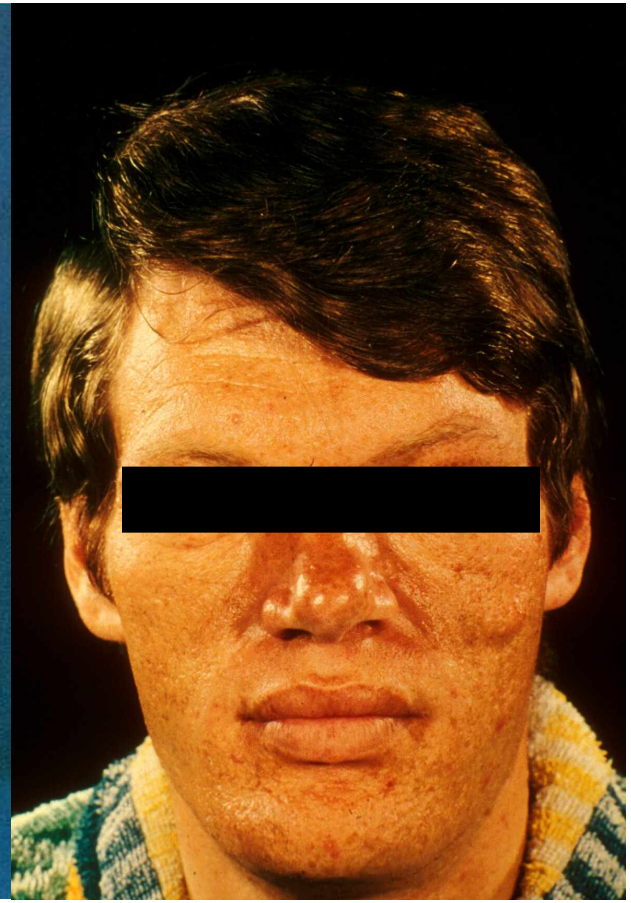
Acromegaly



David & Goliath



Identical Twins



More typical presentation

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Gagel NEJM 1999 340 524

Delayed diagnosis is a challenge

- Incidence 3-4 per million
- Prevalence 60-70 per million
- Gender ratio 1:1
- Commonest age at diagnosis: 40s

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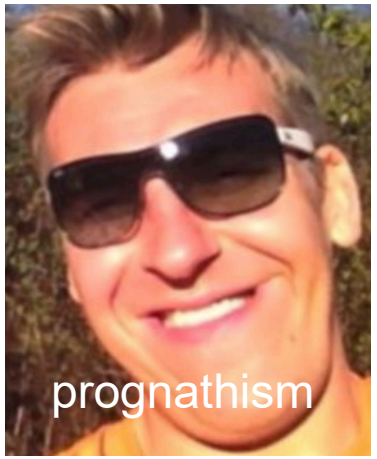
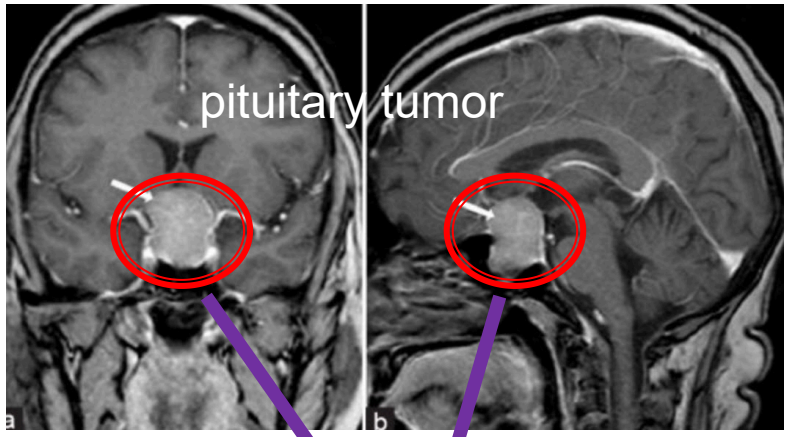
Phenotype of acromegaly



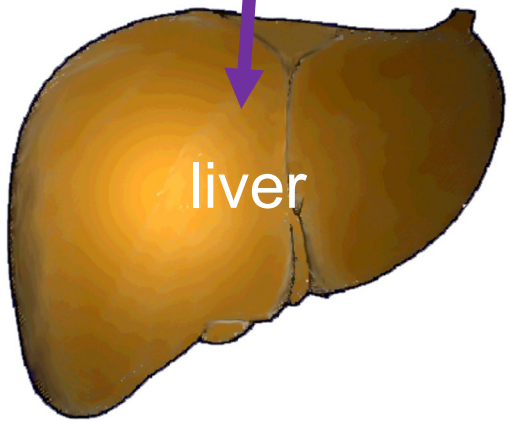


IGF-I

GH

IGF-I

IGF-I



IGF-I

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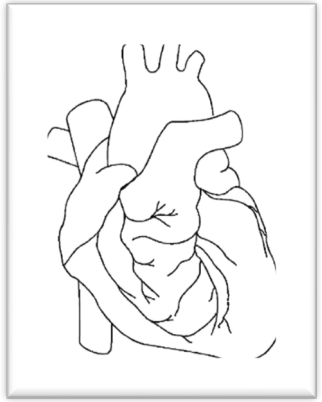
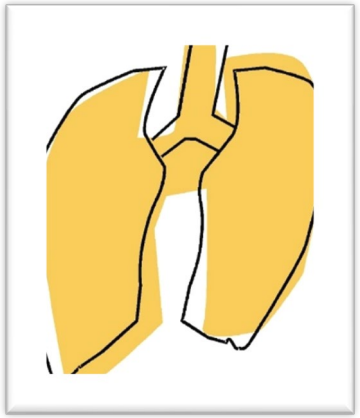
Complications of acromegaly



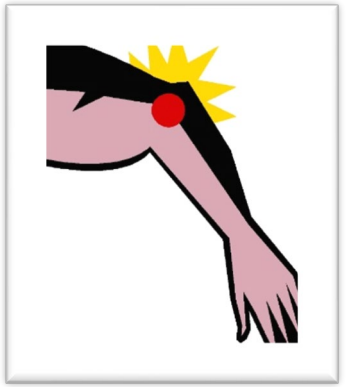
hypertension
and heart disease

cerebrovascular events
and headache

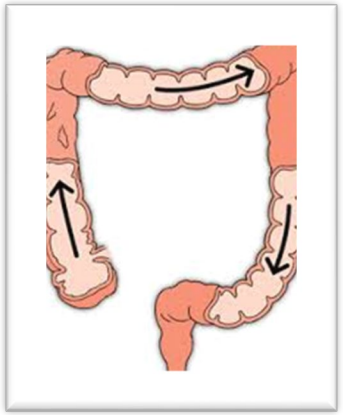
Acromegaly
co-morbidities



sleep apnea

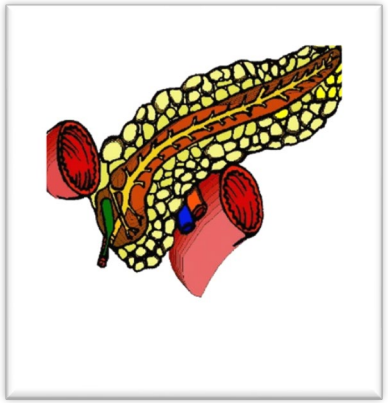


arthritis



colon

bone



insulin-resistant diabetes

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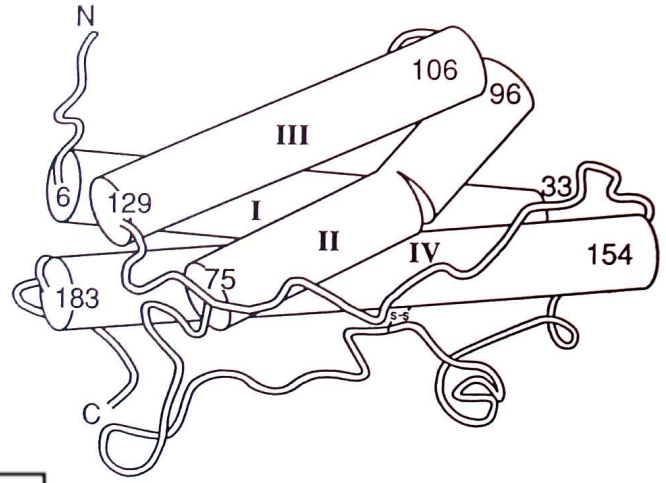
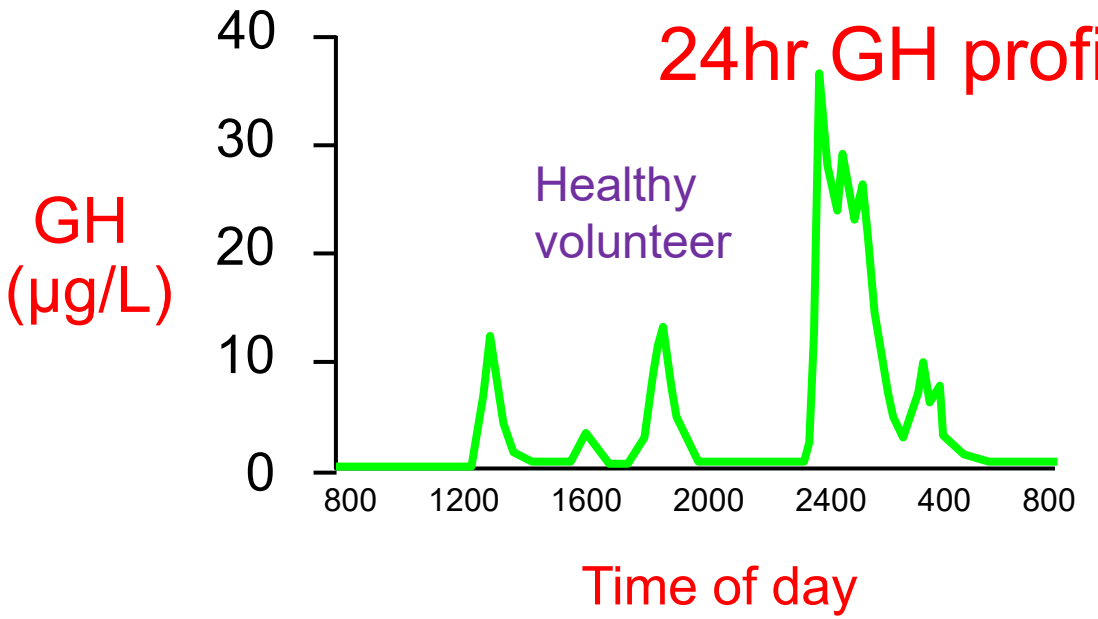
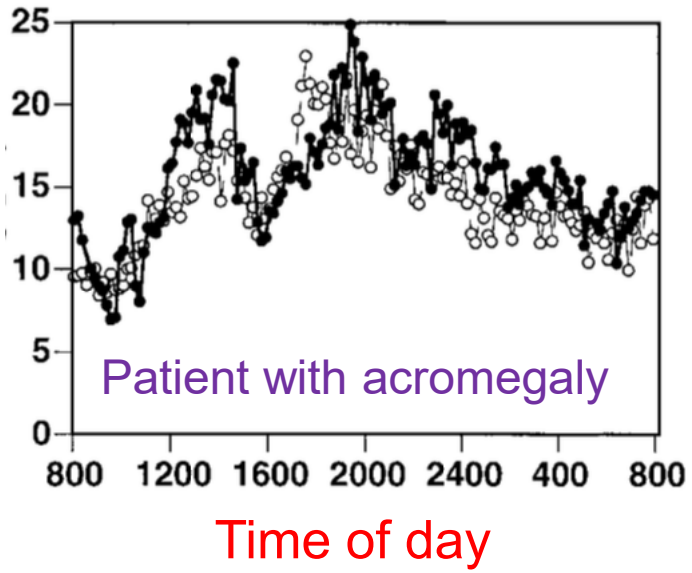
Growth Hormone

191 amino acid peptide, 22 kD
secretion greatest during puberty, declines with age



24hr GH profiles





GH measurement:
- random of little value
- in diagnosis trough rather than peak or mean useful

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Insulin Growth Factor-I (IGF-I)

70 amino acid single chain protein, MW 7.6 kD

regulated by GH

autocrine, paracrine, endocrine secretion

circulating IGF-I 70% hepatic in origin

provides a measure of integrated GH secretion

single sample suffices – no circadian rhythm

age-related decline

Diagnosis of acromegaly

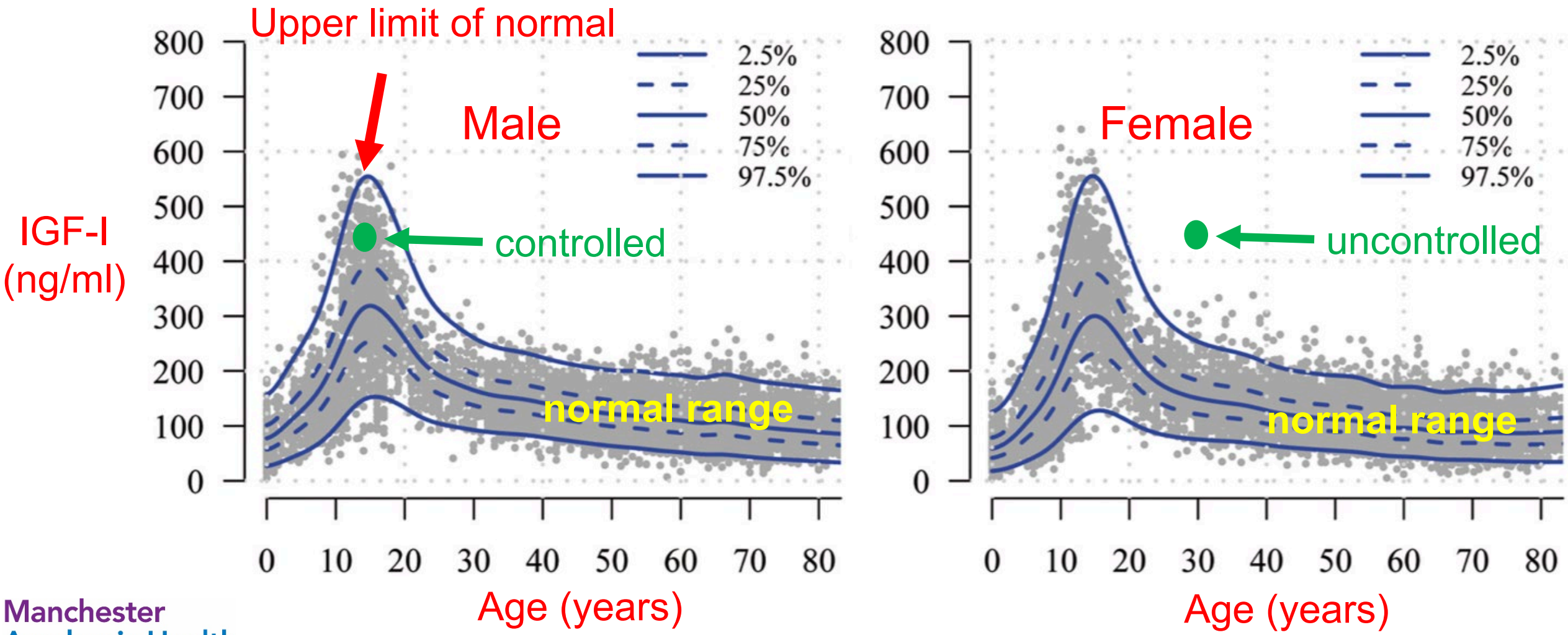
The challenge is for the diagnosis to be considered:
biochemical confirmation is usually straight forward

Biochemical confirmation of diagnosis
GH:
failure to suppress during an oral glucose tolerance test

Elevated IGF-I:
defined in terms of upper limit of normal (ULN) rather than mass units (ng/ml)

Serum IGF-I levels decline with age

normative data for IDS iSYS assay (based on 15014 subjects)



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Bidlingmaier JCEM 2014 99 1712

Serum IGF-I levels decline with age

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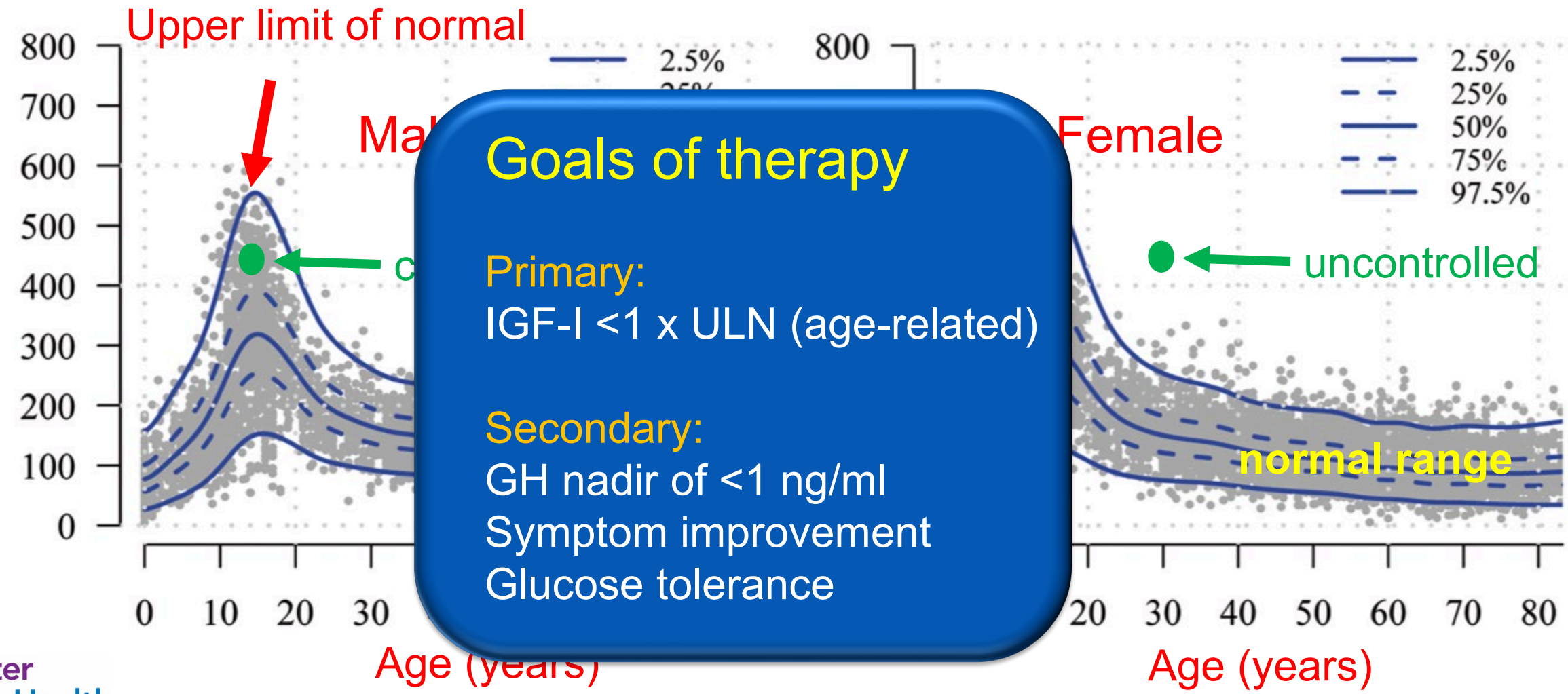

Goals of therapy

Primary:
IGF-I <1 x ULN (age-related)

Secondary:
GH nadir of <1 ng/ml
Symptom improvement
Glucose tolerance

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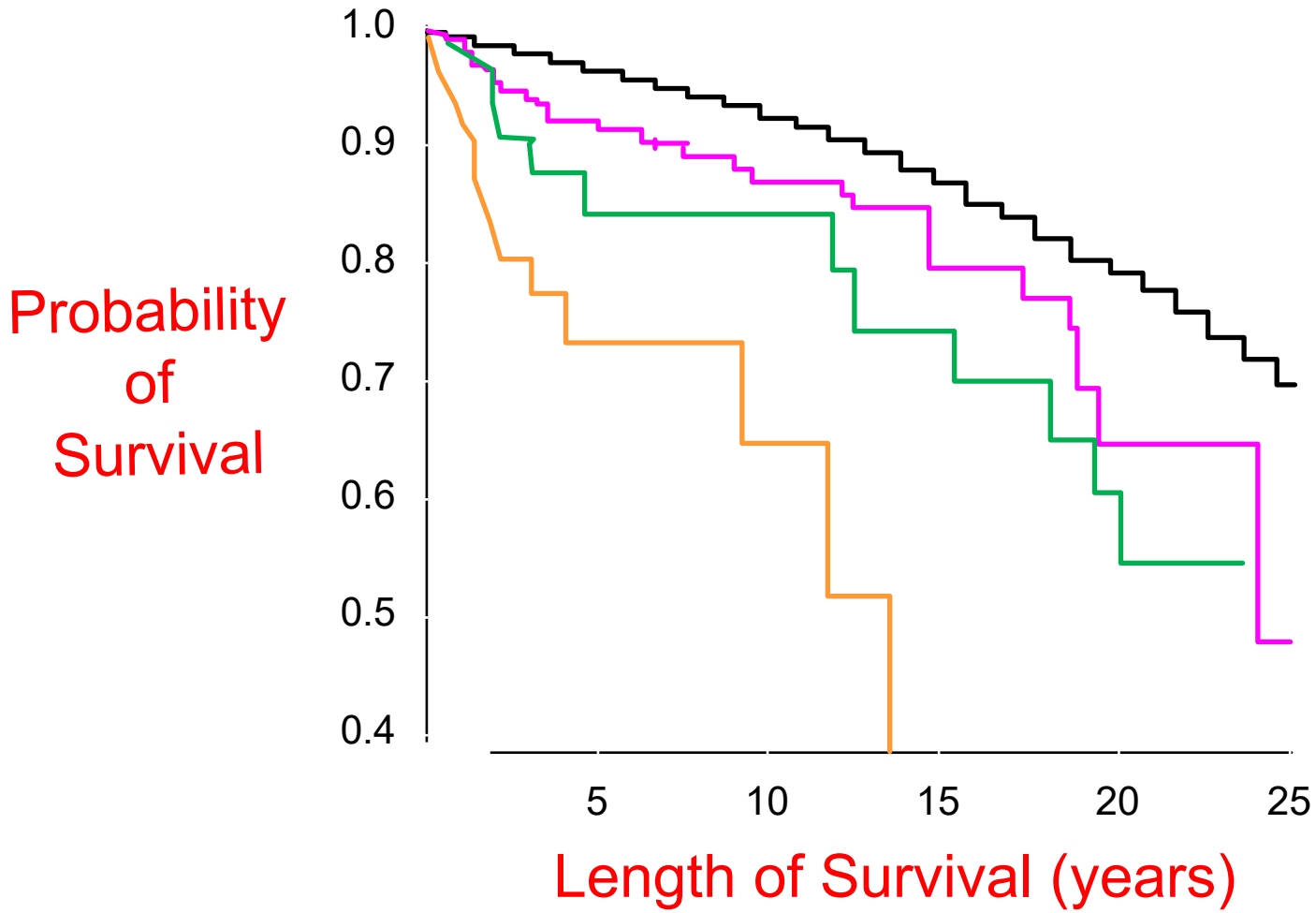
Bidlingmaier JCEM 2014 99 1712

The Impact of Acromegaly on Survival



General population

All acromegaly

Acromegaly & diabetes

Acromegaly & cardiac disease

Life expectancy
⇓ 10 years

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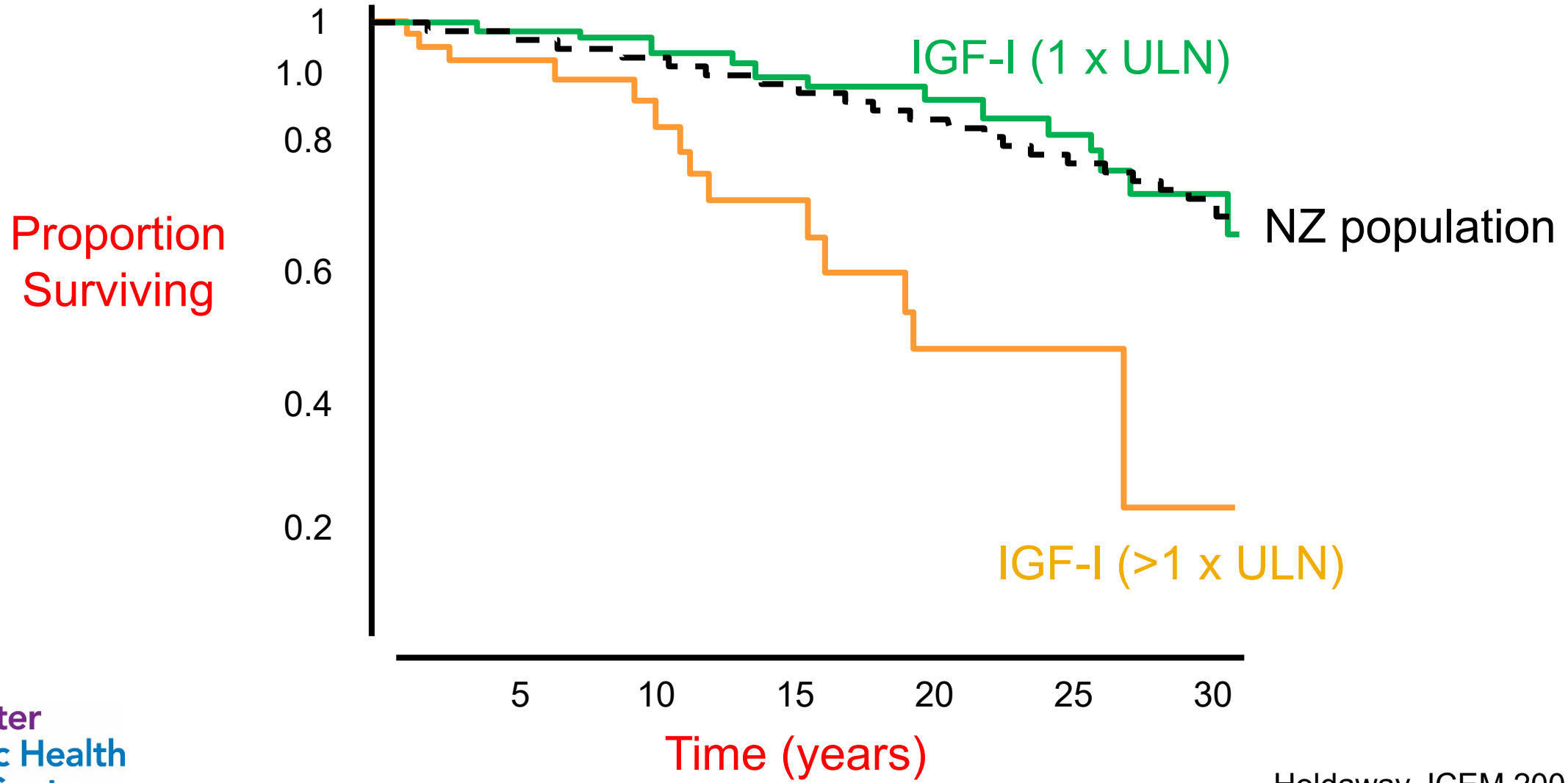
Adapted from Rajasoorya Clin End 1994 41 95

Relationship between probability of survival and IGF-I



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Holdaway JCEM 2004 89 667

The challenges of reliance on IGF-I measurement

Differences between assay technologies

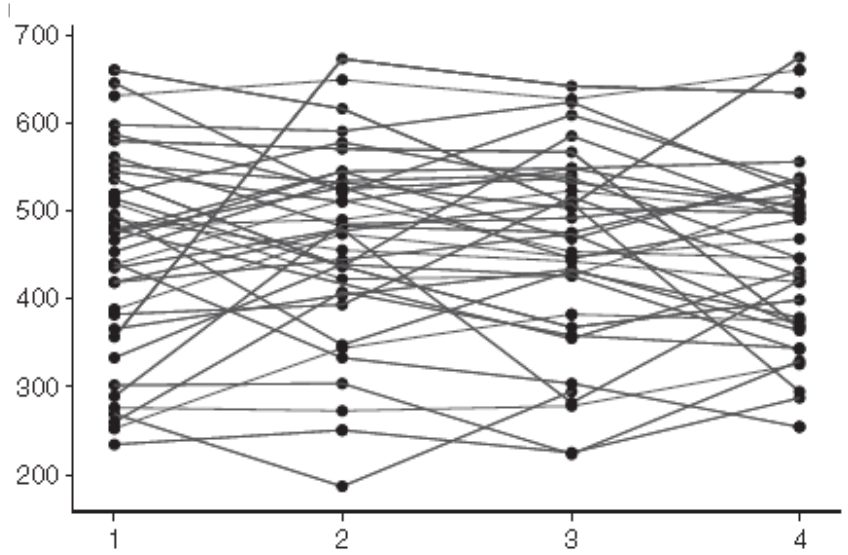
Variable quality of reference ranges

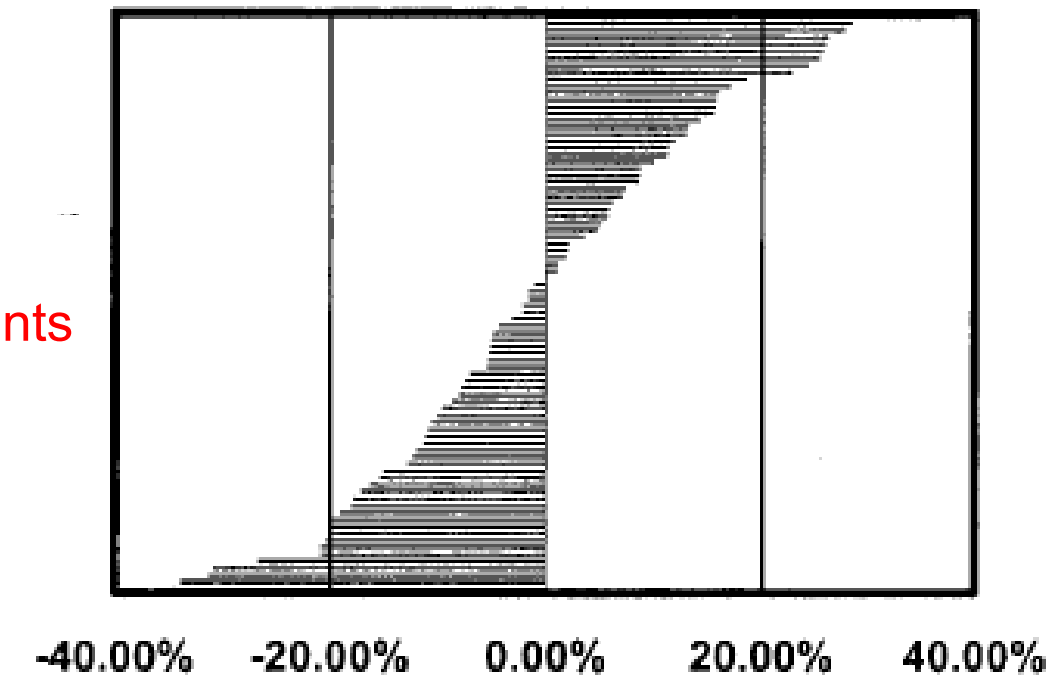
IGF-I levels can be variable within a single patient

A single elevated IGF-I (>1 x ULN) is not indicative of loss of disease control

Variability and reliability of single IGF-I measurements

Serial measurement in athletes





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Milani JCEM 2004 89 2271
Erotokritou-Mulligan CE 2010 72 520

Treatment of Acromegaly

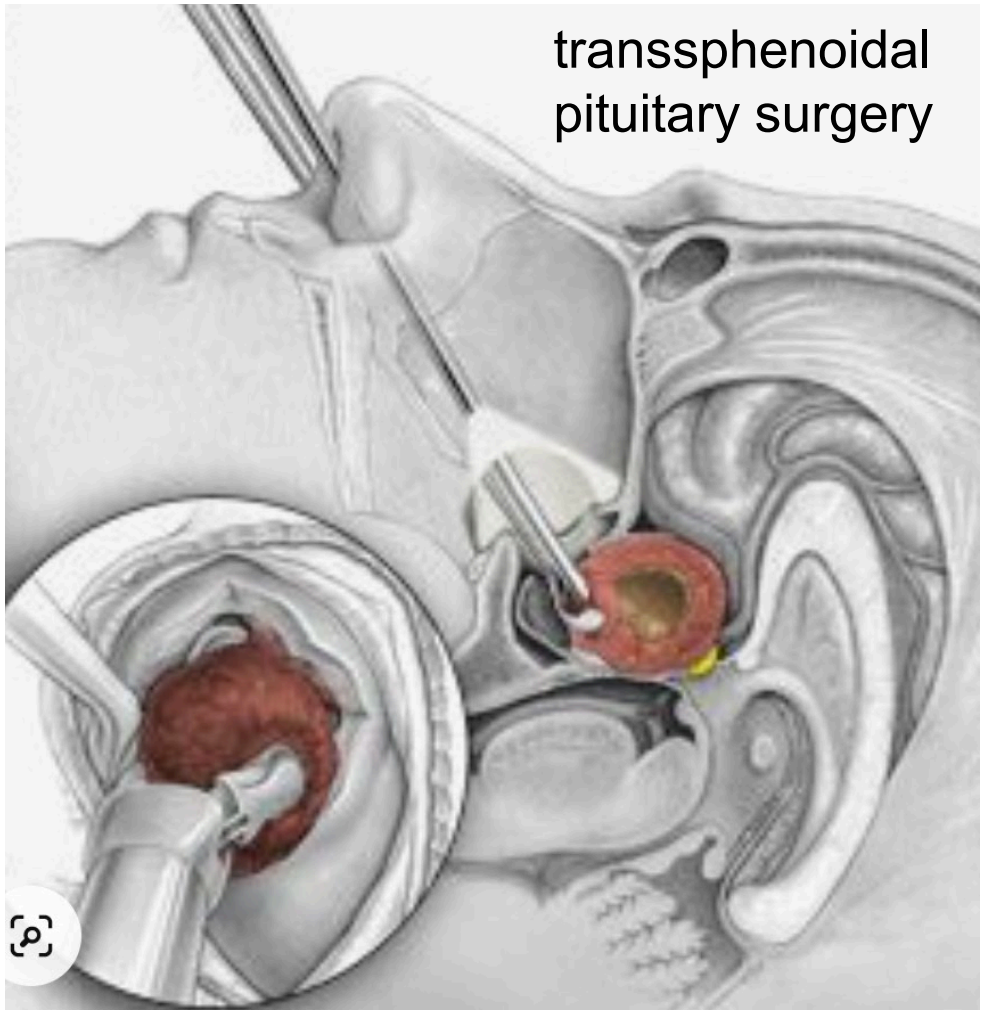
Modes of therapy

Surgery transsphenoidal hypophysectomy
remission rates
microadenomas 30-90%
macroadenomas <50%

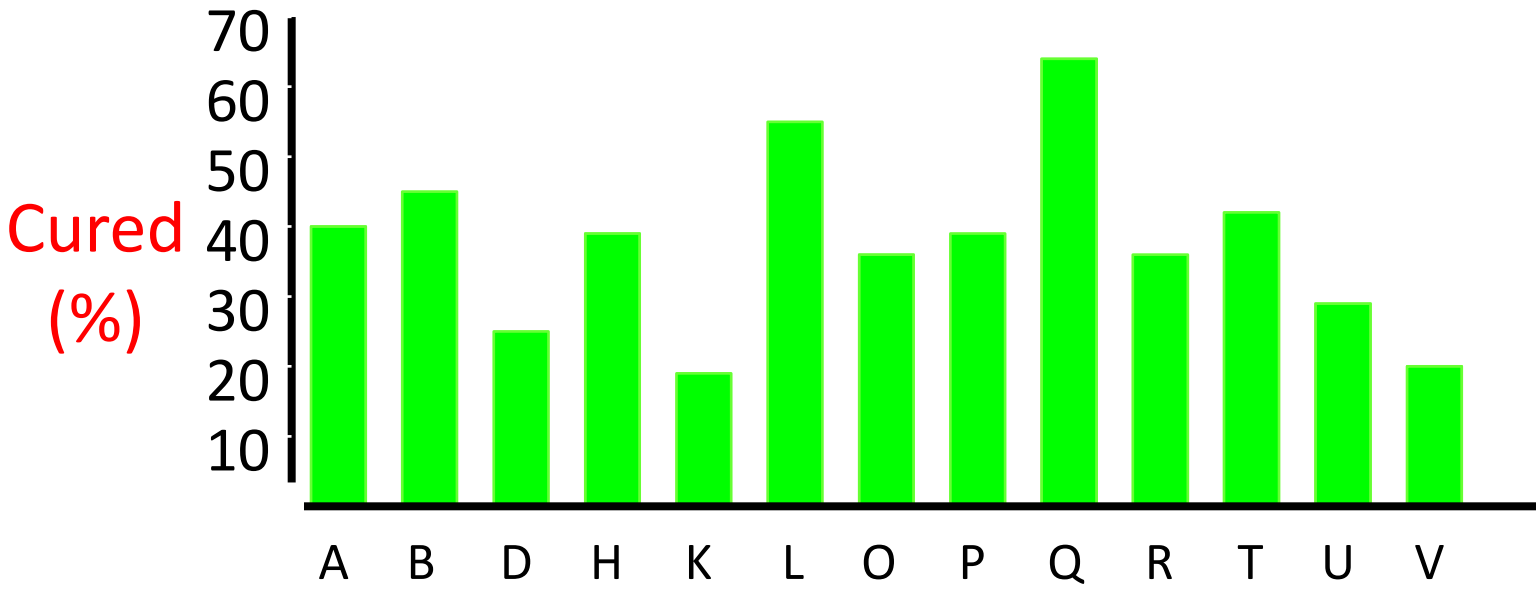
Radiotherapy

Medical dopamine agonists
somatostatin analogues, also referred to as somatostatin receptor ligands (SRLs)
GH Receptor antagonist

Cure rate in different UK surgical centres



UK National Acromegaly Register



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Bates CE 2008 68 136

Pituitary Radiotherapy

Controls tumor growth

Lowers GH secretion

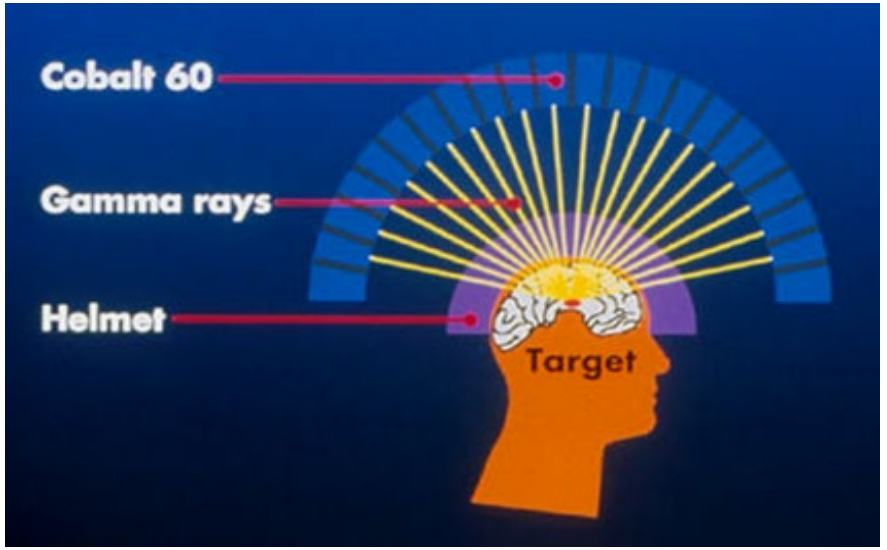
proton beam

single fraction (radiosurgery)

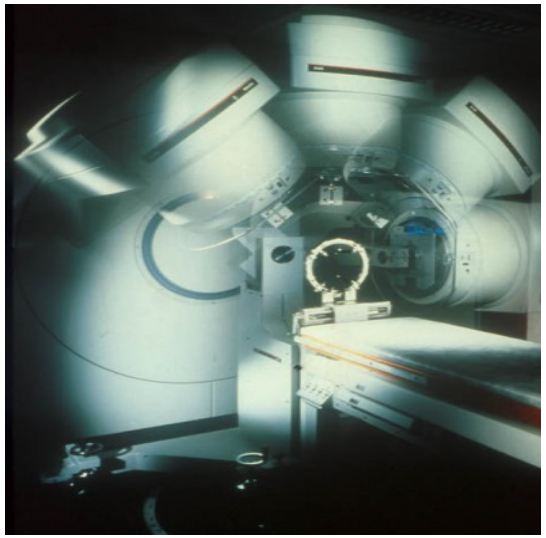
e.g. Gamma Knife

multifractional

e.g. LINAC, proton beam



Gamma Knife®



LINAC

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Pituitary Radiotherapy

Controls tumor growth

Lowers GH secretion

very effective at controlling tumor growth

takes several years to ‘normalize’ GH secretion

……. longer to control IGF-I

Medical therapy required until GH/IGF-I controlled

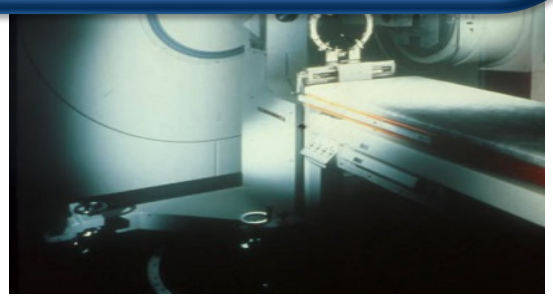
single fraction (radiosurgery)

e.g. Gamma Knife

multifractional

e.g. LINAC, proton beam

Gamma Knife®



LINAC

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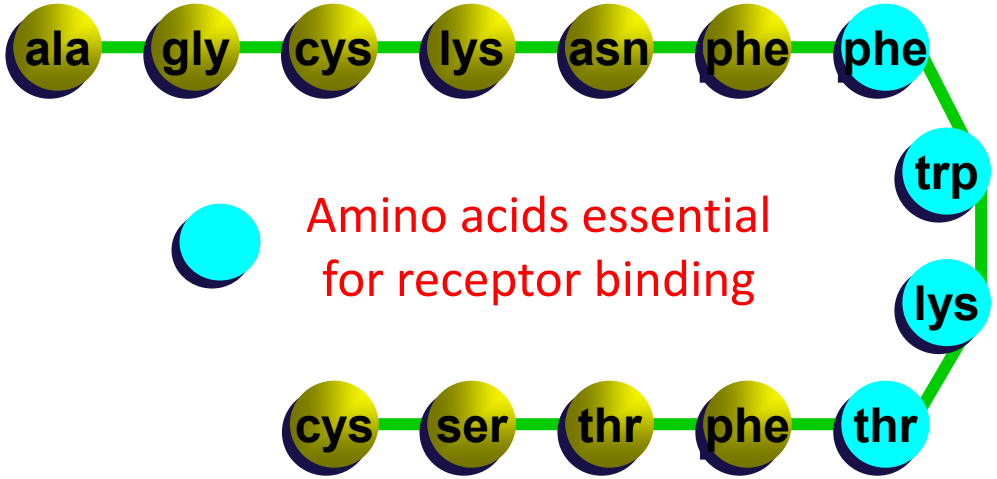
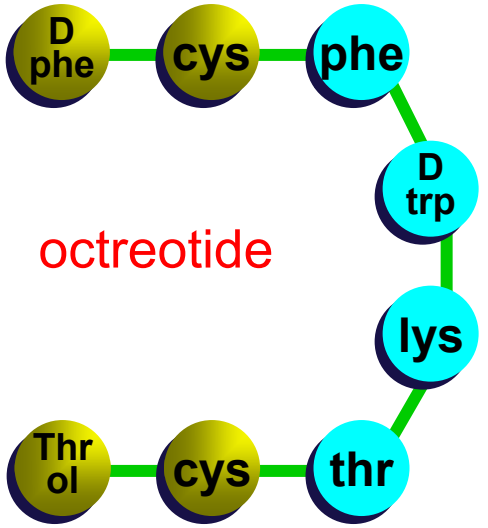
Somatostatin Receptor Ligands



Amino acids essential for receptor binding

Human somatostatin



octreotide

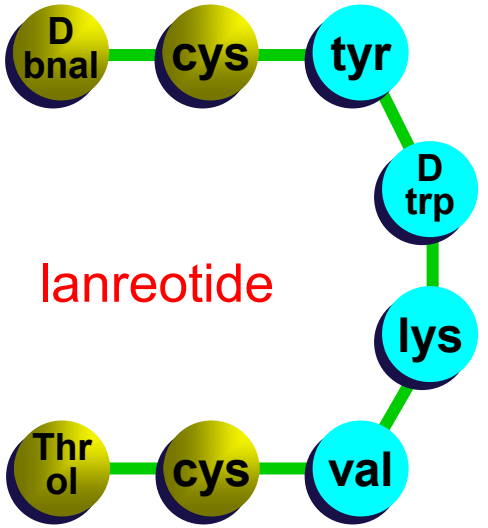
five somatostatin receptor sub-types (SST)

octreotide & lanreotide – predominately bind SST2

'Gold Standard' for medical therapy

first choice therapy for patients not by 'cured' surgery

once monthly parenteral preparations



lanreotide

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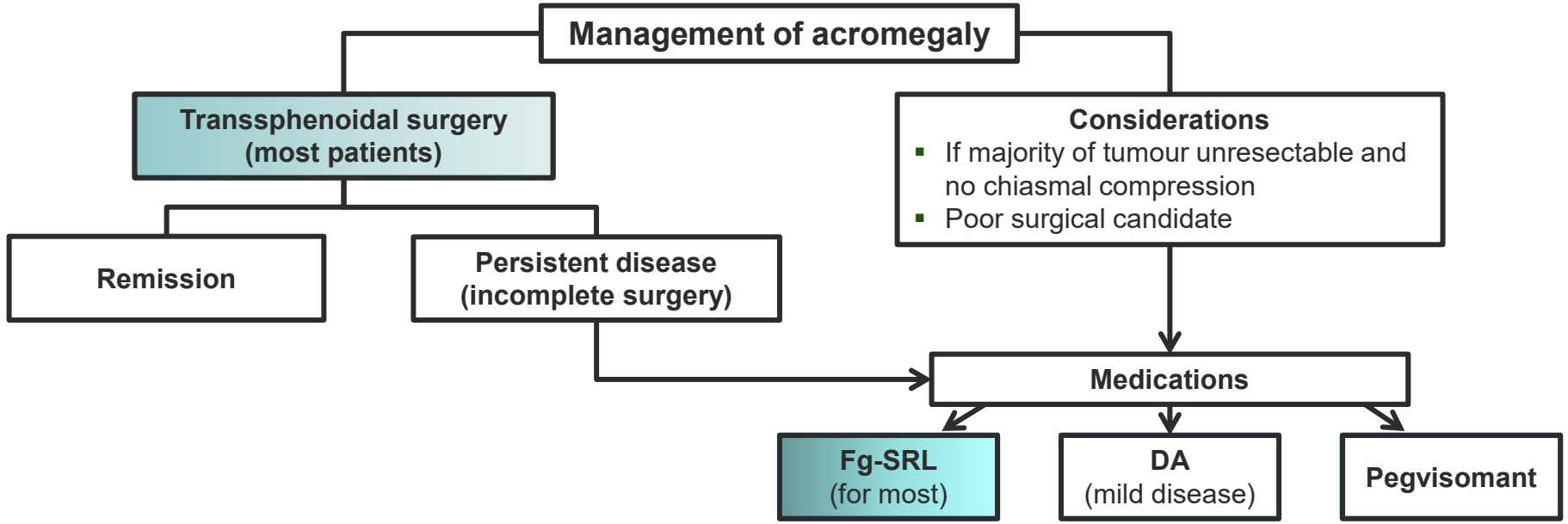
Experience with Paltusotine in the Acrobat Phase 2 Studies

Mônica Gadelha, MD, PhD
Academia Nacional de Medicina
Faculdade de Medicina da Universidade Federal do Rio de Janeiro
Instituto Estadual do Cérebro Paulo Niemeyer

Disclosure of Conflicts of Interest

- ✓ Speaker: Novartis; Ipsen; Pfizer
- ✓ Principal Investigator clinical trials: Crinetics, Novartis, Recordati
- ✓ Advisory board member: Novartis, Crinetics, Ipsen, Recordati

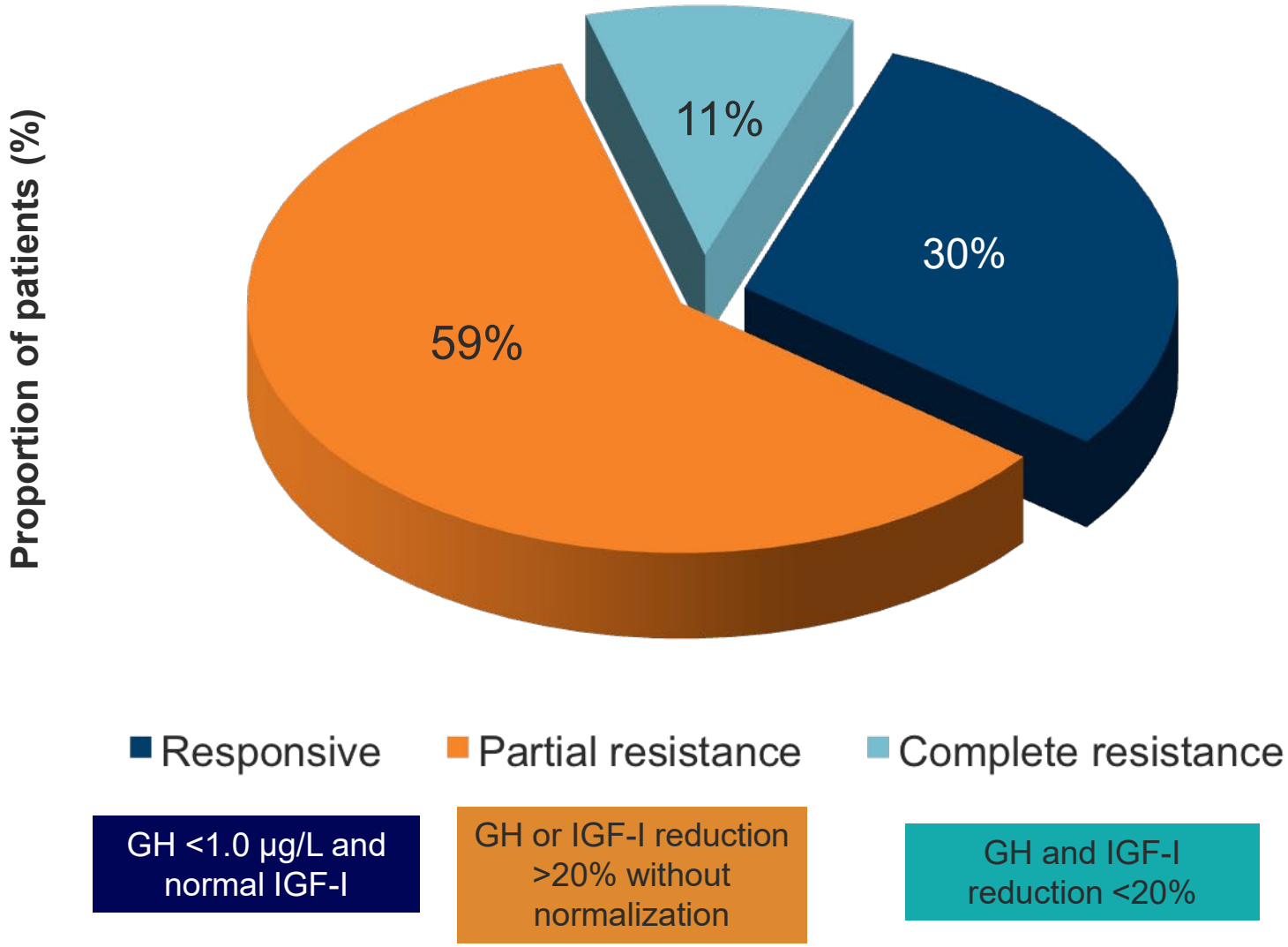
Recommendations of the last Endocrine Society guideline



Abbreviations:
- Fg-SRL: first generation somatostatin receptor ligand (octreotide, lanreotide)
- DA: dopamine agonist

Katznelson L *et al. J Clin Endocrinol Metab* 2014
Gadelha M *et al.* Endocr Rev 2019
Giustina A *et al.* J Clin Endocrinol Metab 2020

Results of treatment with first-generation injectable SRL in our center (n=198)



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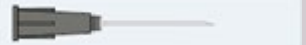
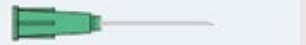
Octreotide LAR injection

	Outer Diameter (mm)	Gauge Needle	Gauge x length (mm)
	0.70	22	0.7 X 30
	0.80	21	0.8 X 30
	1.1	19	1.1 X 38

- Monthly deep intramuscular injection
- Upper outer quadrant of the buttocks
- Trained health professional

Lanreotide autogel injection

	Outer Diameter (mm)	Gauge Needle	Gauge x length (mm)
	0.45	26	0.45 X 13
	1.2	18	1.2 X 20

- Deep subcutaneous injection
- Upper outer quadrant of the buttocks
- Trained health professional

Geer *et al. BMC Endocrine Disorders* (2020) 20:117
https://doi.org/10.1186/s12902-020-00595-4

BMC Endocrine Disorders

RESEARCH ARTICLE Open Access

Patient reported outcome data from acromegaly patients treated with injectable somatostatin receptor ligands (SRLs) in routine clinical practice

Eliza B. Geer[1], Jill Sisco[2], Daphne T. Adelman[3], William H. Ludlam[4], Asi Haviv[4], Shuqian Liu[5], Susan D. Mathias[6*], Dana Gelbaum[4] and Lizheng Shi[5]

Table 3 Frequency and Severity of Injection Site Reactions, All Patients

Injection Site Reaction	Experienced % Yes (N[a])	Mild % (n[b])	Moderate % (n[b])	Severe % (n[b])
Pain at injection site **during** injection	83% (87)	56% (49)	31% (27)	13% (11)
Pain at injection site **several hours** after injection	68% (71)	60% (43)	32% (23)	7% (5)
Pain at injection site **several days** after injection	49% (51)	65% (33)	28% (14)	8% (4)
Bruising at the injection site(s)	45% (47)	70% (33)	30% (14)	0% (0)
Swelling at the injection site(s)	47% (49)	65% (32)	33% (16)	2% (1)
Nodules (knots and bumps under the skin) at the injection site(s)	63% (66)	47% (31)	42% (28)	11% (7)
Scar tissue/hardness of the skin at the injection site(s)	42% (44)	41% (18)	46% (20)	14% (6)

[a]Of total sample
[b]Of those who reported experiencing the injection site reaction

Geer et al., *BMC Endocrine Disorders* 2020

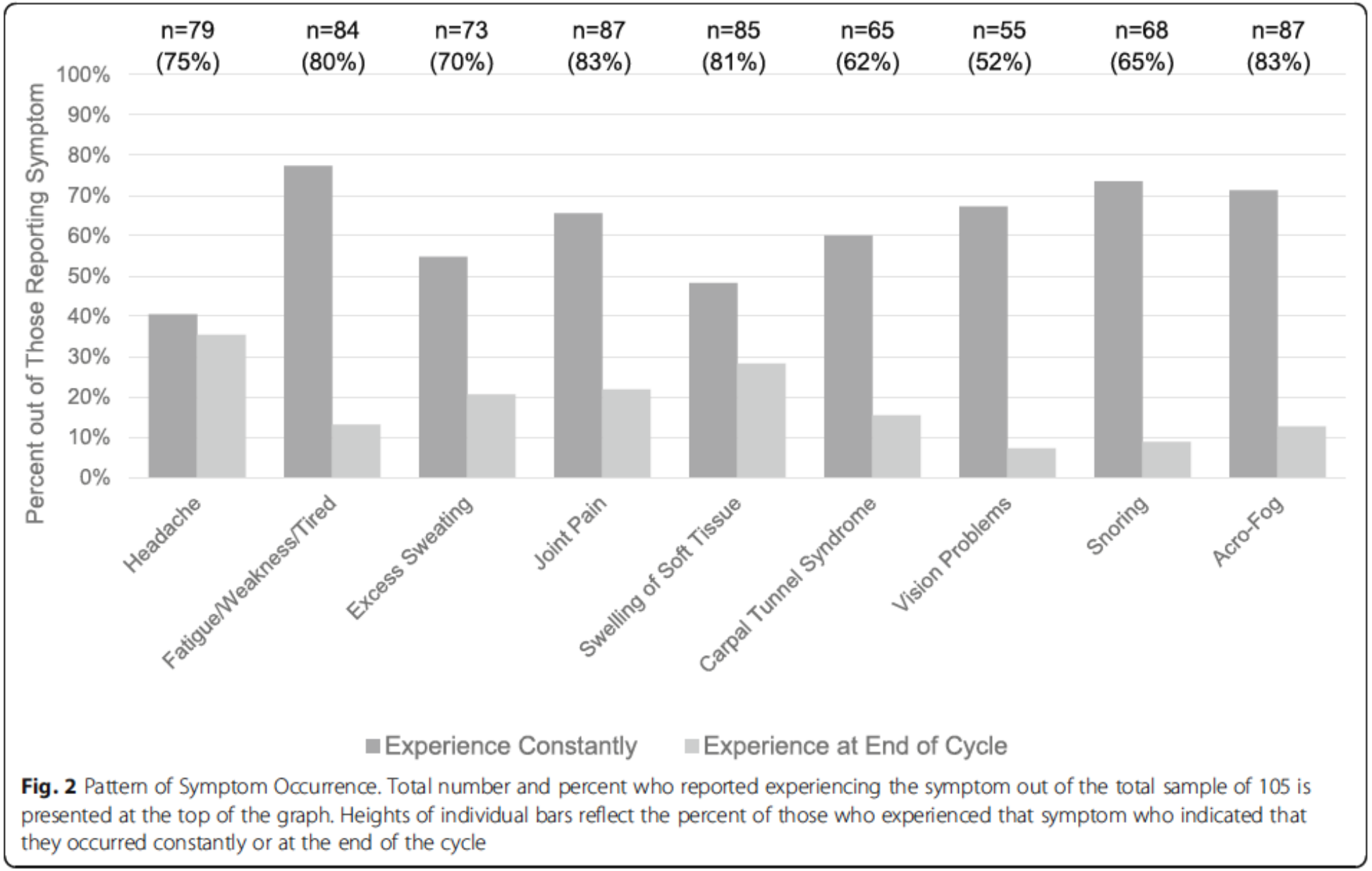
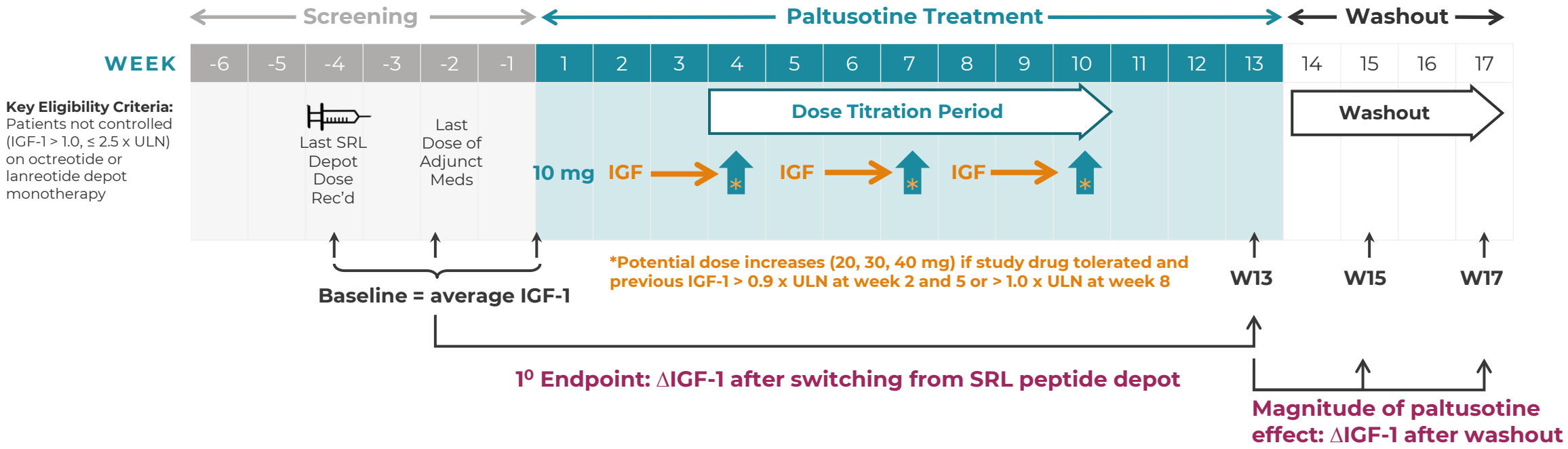


Fig. 2 Pattern of Symptom Occurrence. Total number and percent who reported experiencing the symptom out of the total sample of 105 is presented at the top of the graph. Heights of individual bars reflect the percent of those who experienced that symptom who indicated that they occurred constantly or at the end of the cycle

Geer et al., *BMC Endocrine Disorders* 2020

ACROBAT Edge Study Design

A global clinical trial conducted at 45 clinical sites in 13 countries



Primary Endpoint: Change in IGF-1 at Week 13 vs. baseline (average of three IGF-1 screening values)
Primary Hypothesis was: No change in the median IGF-1 at Week 13 versus baseline
Primary Analysis Population: Group 1 patients (those previously on octreotide or lanreotide depot monotherapy)
Open Label Extension (-05 Advance Study): Available to patients who complete Edge and Evolve

ACROBAT Edge Patient Groups

Group	Pre-Trial Therapy	Baseline IGF-1 (x ULN)	Total Enrolled
1	SRL monotherapy (octreotide or lanreotide)	> 1.0 ≤ 2.5	25
2	SRL + cabergoline	> 1.0 ≤ 2.5	10
3	SRL + cabergoline	≤ 1.0	5
4	Pasireotide	≤ 1.0	4
5	SRL + Pegvisomant	≤ 1.0	3

Prespecified Primary Analysis Population

Exploratory Populations

Prespecified Primary Analysis Population (Group 1)[1]

- Patients treated with SRL (octreotide or lanreotide) with elevated IGF-1 at baseline—representing the majority of patients in clinical practice
- The primary hypothesis was that the group would show no change in the median IGF-1 at Week 13 versus baseline

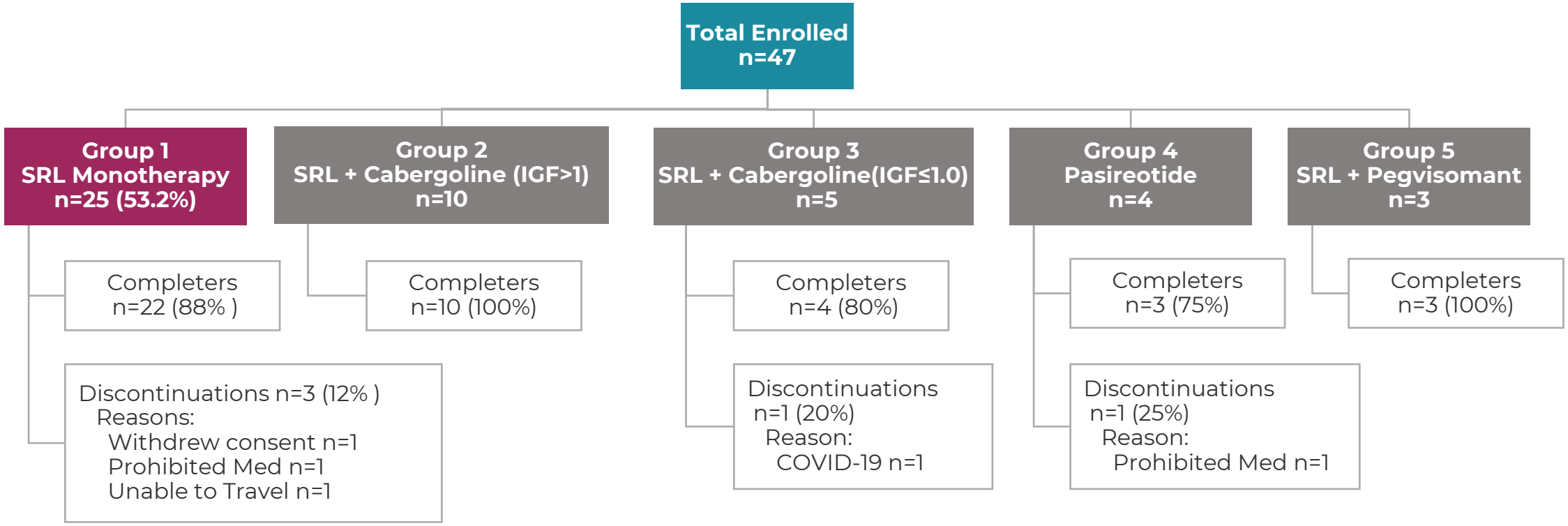
Exploratory populations (Groups 2-5)

The study also evaluated whether paltusotine can contribute to the care of patients treated with more intensive treatment regimens

[1]Prespecified in Edge Statistical Analysis Plan

ACROBAT Edge Patient Disposition

89% of patients completed the study

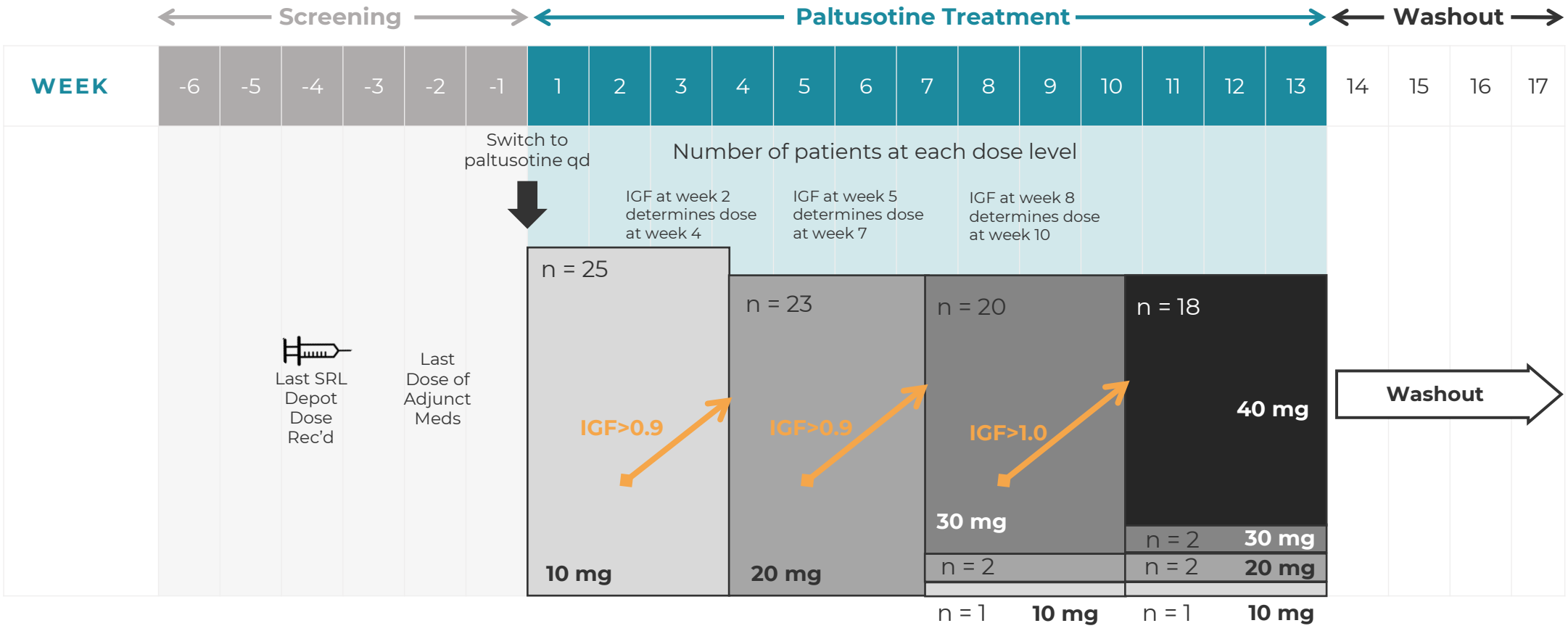


ACROBAT Edge Patient Characteristics

	Group 1 (N=25)	Group 2 (N=10)	Group 3 (N=5)	Group 4 (N=4)	Group 5 (N=3)	Total (N=47)
Demographics						
Median Age, years (Min, Max)	52 (31, 71)	53 (31, 70)	51 (43, 69)	56 (46, 67)	38 (35, 66)	51 (31, 71)
Median Weight, kg (Min, Max)	91 (61, 155)	85 (56, 136)	87 (57, 91)	107 (73, 120)	78 (59, 82)	87 (56, 155)
Sex						
Female	11 (44%)	7 (70%)	3 (60%)	3 (75%)	3 (100%)	27 (57%)
Male	14 (56%)	3 (30%)	2 (40%)	1 (25%)	0	20 (43%)
Prior Therapies						
Lanreotide depot Dose, mg/mo.	n=12	n=3	n=2	NA	n=2	n=19
# patients on 60/90/120 mg/mo.	1 / 4 / 7	0 / 0 / 3	0 / 0 / 2	--	1 / 1 / 0	2 / 5 / 12
Octreotide LAR Dose, mg/mo.	n=13	n=7	n=3	NA	n=1	n=24
# patients on 10/20/30/40 mg/mo.	1 / 0 / 9 / 3	0 / 0 / 7 / 0	0 / 1 / 1 / 1	--	0 / 0 / 0 / 1	1 / 1 / 17 / 5
Pasireotide dose, mg/mo.	NA	NA	NA	n=4	NA	n=4
# patients on 40/60 mg/mo.	--	--	--	2 / 2	--	2 / 2
Cabergoline dose, mg/week	NA	n=10	n=5	NA	NA	n=15
Median (Min, Max)	--	2.3 (0.5, 3.5)	1.5 (0.5, 2.0)	--	--	2 (0.5, 3.5)
Pegvisomant dose, mg/week	NA	NA	NA	NA	n=3	n=3
Median (Min, Max)	--	--	--	--	60 (20, 70)	60 (20, 70)

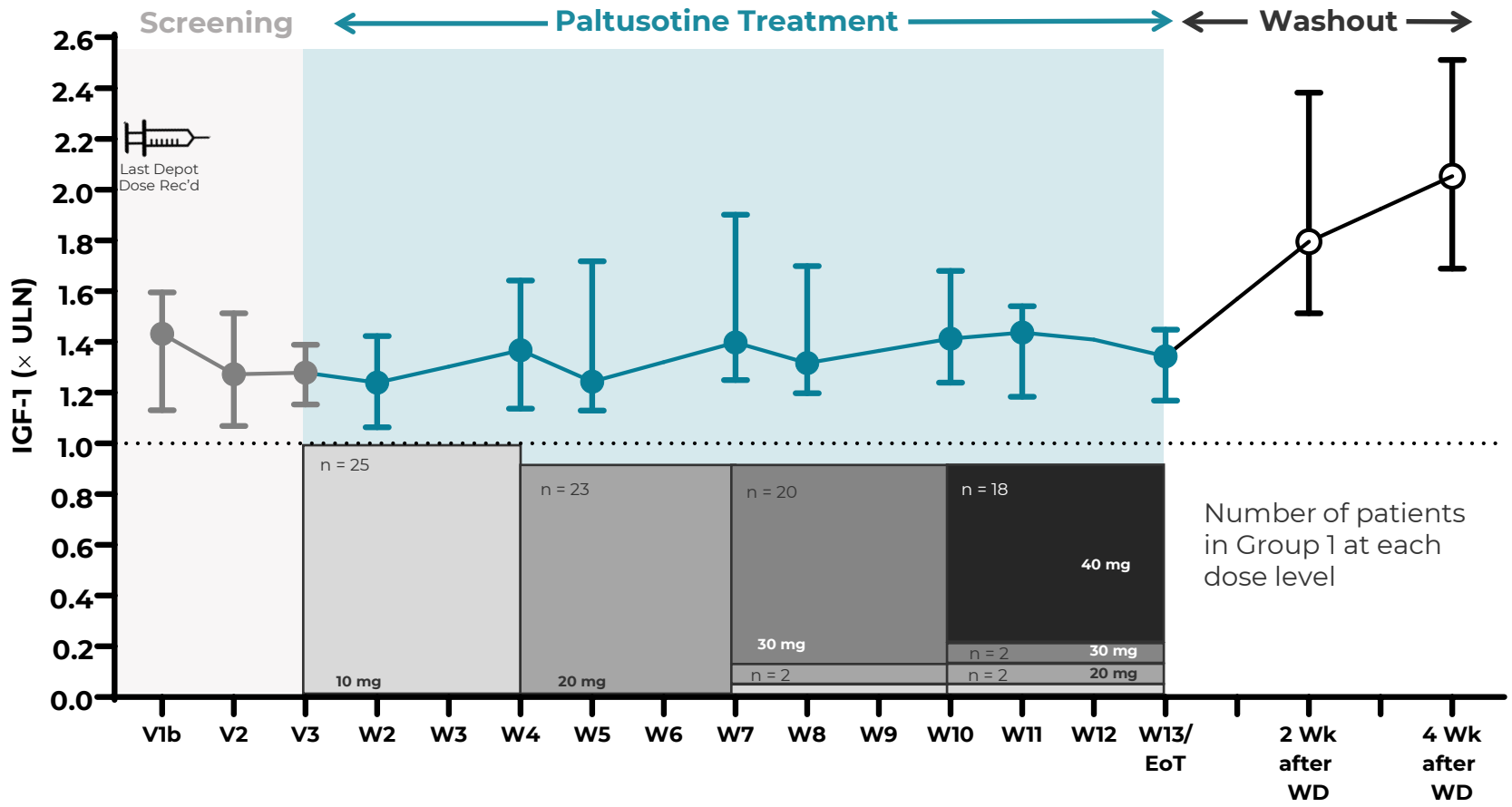
ACROBAT Edge Dose Titration

Most Group 1 patients up-titrated to the highest dose (40 mg)



Dose escalation determined by central reader based on tolerability and IGF-1 (Site staff, patient, sponsor blinded to dose)

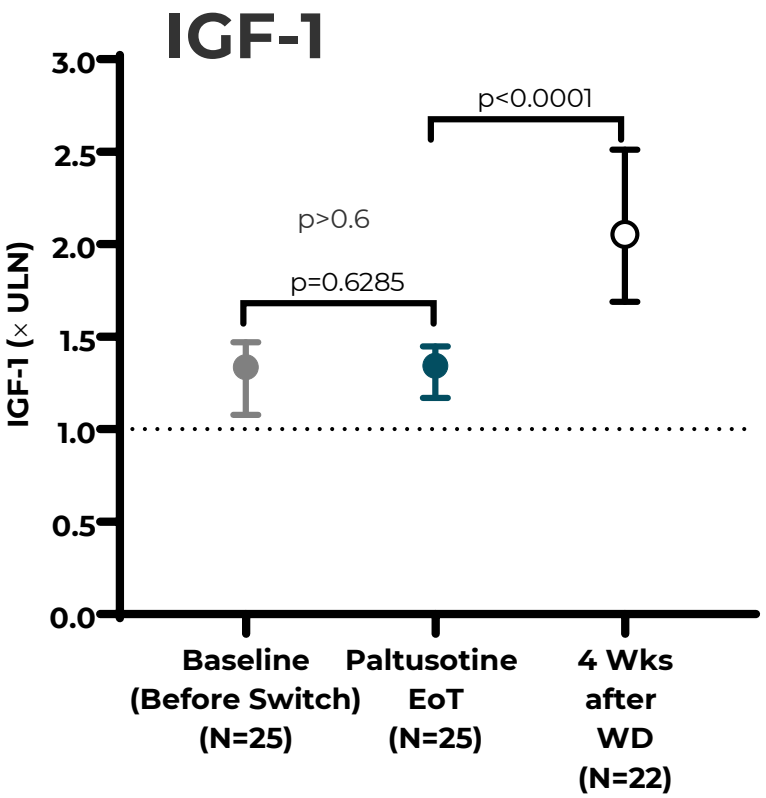
IGF-1 Levels Were Maintained After Switching to Paltusotine from Injected SRL Depots

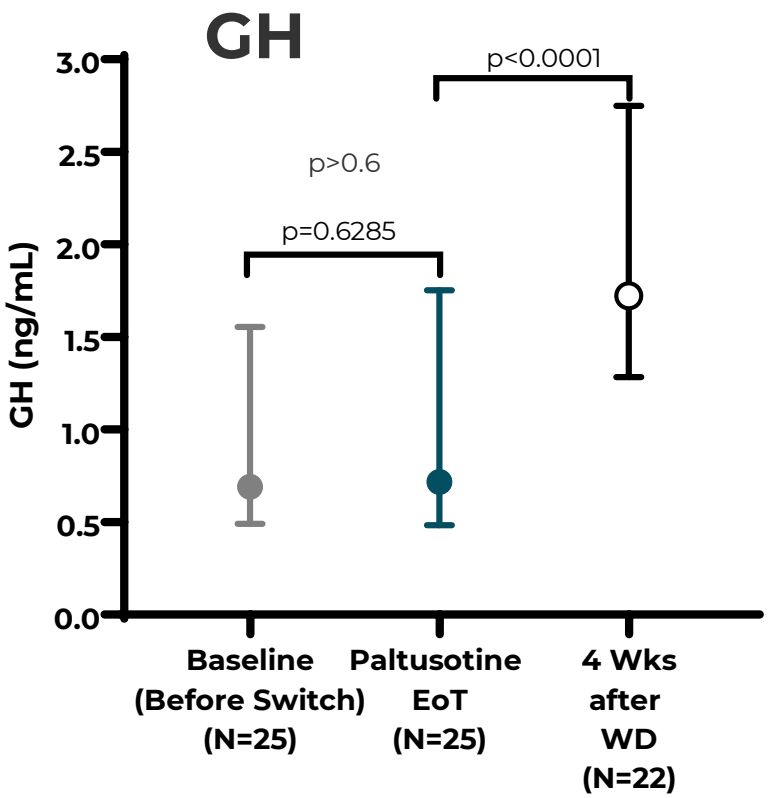


Potential dose increases (20, 30, 40 mg) if study drug tolerated and previous IGF-1 > 0.9 x ULN at week 2 and 5 or > 1.0 x ULN at week 8
Data presented are median (Interquartile Range [IQR]: 25th percentile, 75th percentile) from Group 1 patients in Acrobat Edge; Screening Period could range from 4-6 weeks.
WD = Withdrawal, where 2 Wks. after WD is defined as Week 15 or result within 7-21 days after last dose and 4 Wks. after WD is defined as Week 17 or result at least 22 days after last dose.

Paltusotine Maintained IGF-1 and GH Levels After Switching From Injected SRL Peptide Depots

IGF-1 and GH levels after 13 weeks of paltusotine treatment did not significantly change from baseline in patients previously treated with injected SRL depots (Group 1). Rise in IGF-1 and GH after withdrawal, which characterized the magnitude of therapeutic activity for oral paltusotine.

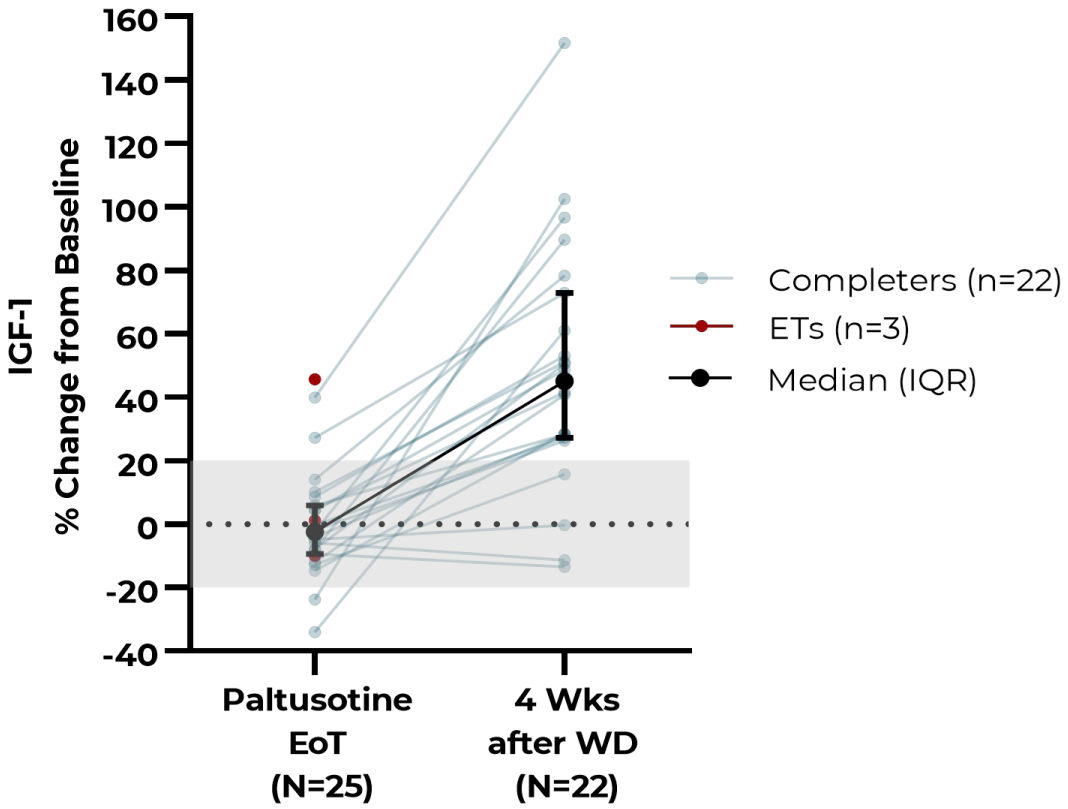




Data presented are median (Interquartile Range [IQR]: 25th percentile, 75th percentile) EoT = End of Treatment defined as Week 13 (Visit 14) or last on treatment value carried forward (LOCF). Wks. after WD is defined as Week 17 or result at least 22 days after last dose.
Note: p-values are based on non-parametric Wilcoxon Sign Rank test of whether the median change is different from zero.

Switching to Once Daily Oral Paltusotine Maintained IGF-1 Levels in 87% of Group 1 Patients

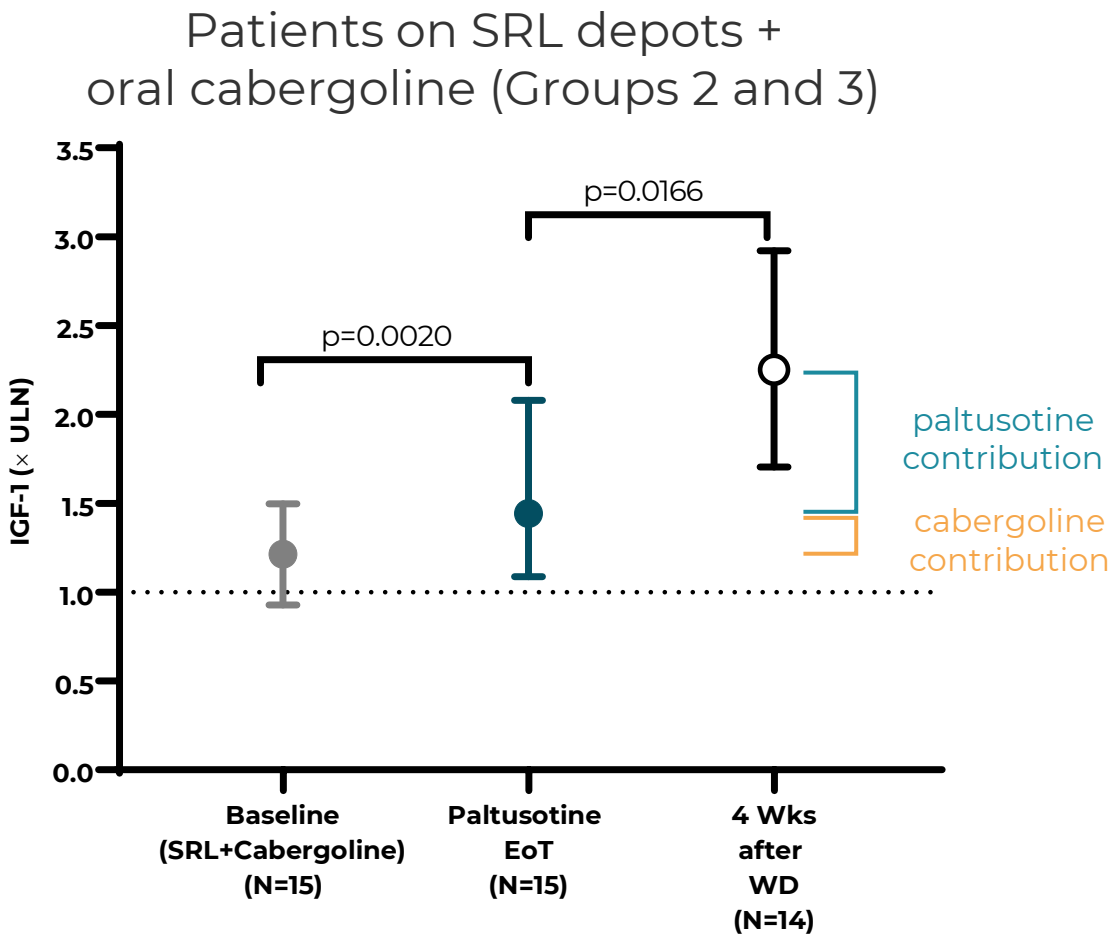
Individual patient percent change in IGF-1 at end of treatment vs. baseline and change at 4 weeks after withdrawal of paltusotine



- 20/23[1] patients (87%) who completed the dosing period achieved IGF-1 levels at EoT that were within 20% of baseline or lower
- 18/22[2] (82%) patients who completed the study showed a meaningful (>20%) rise from baseline in IGF-1 four weeks after withdrawal of paltusotine

[1]Two patients discontinued prior to the completion of the dosing period
[2]One patient discontinued during the washout period

Paltusotine Suppressed IGF-1 in Patients Previously Receiving Combination Therapy with Cabergoline

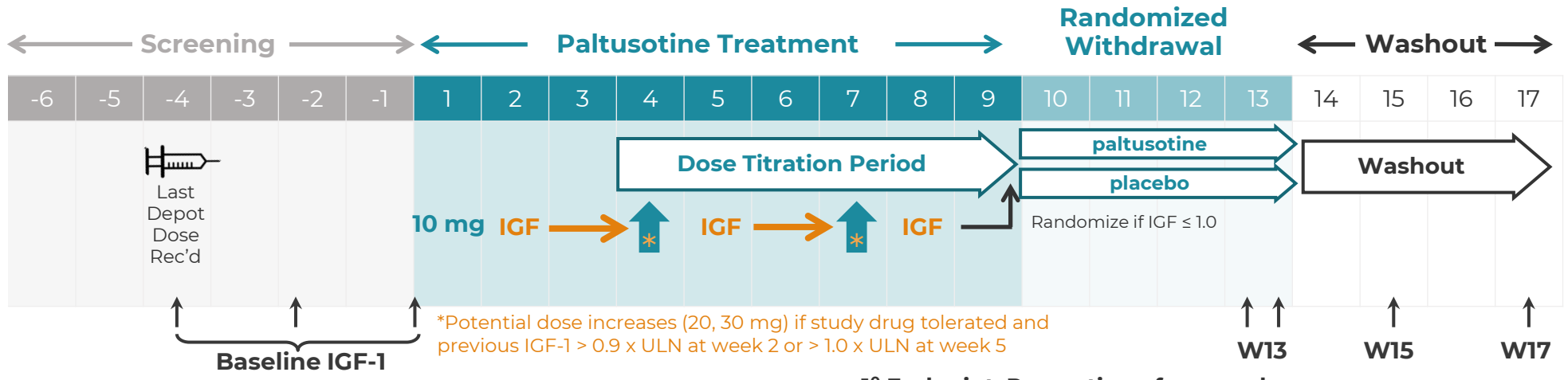


- Paltusotine contributed to IGF-1 lowering in patients previously treated with injected SRL peptide depots + oral cabergoline combination therapy
- Variable IGF-1 results were observed in Group 4 (n=4) and Group 5 (n=3)
- Patients represented by Groups 2-5 will not be included in Phase 3 program

Data presented are median (Interquartile Range [IQR]: 25th percentile, 75th percentile). EoT = End of Treatment defined as Week 13 (Visit 14) or last on treatment value carried forward (LOCF). WD = Withdrawal, where 2 Wks after WD is defined as Week 15 or result within 7-21 days after last dose and 4 Wks after WD is defined as Week 17 or result at least 22 days after last dose. Note: p-values are based on non-parametric Wilcoxon Signed Rank test of whether the median change is different from zero.

ACROBAT Evolve Trial Design

Randomized, double-blind global clinical trial conducted at 44 clinical sites in 13 countries



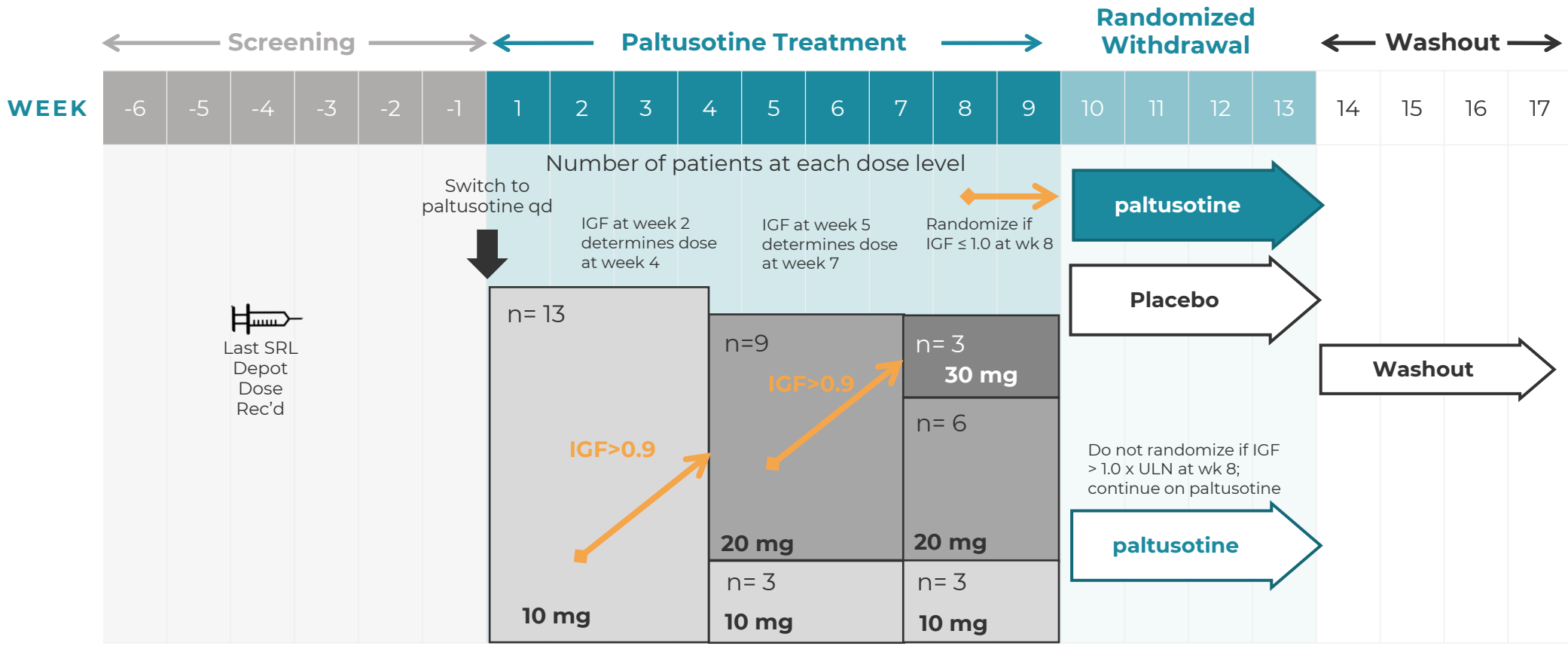
1⁰ Endpoint: Proportion of responders (IGF ≤ 1.0x ULN) vs placebo at week 13

Evolve Enrollment discontinued April 2020

- Edge enrollment was complete at the time, and interim results were positive
- Discontinuing Evolve enabled data to be available for end of Phase 2 regulatory interactions on Edge timeline
- 13 previously enrolled patients were allowed to complete participation in the study
- Reduced sample size did not allow for meaningful statistical comparisons between groups in the randomized withdrawal period
- Exposure response data were analyzed in conjunction with Edge group 1 patients
- **Open Label Extension (-05 Advance Study):** Available to patients who complete Edge and Evolve

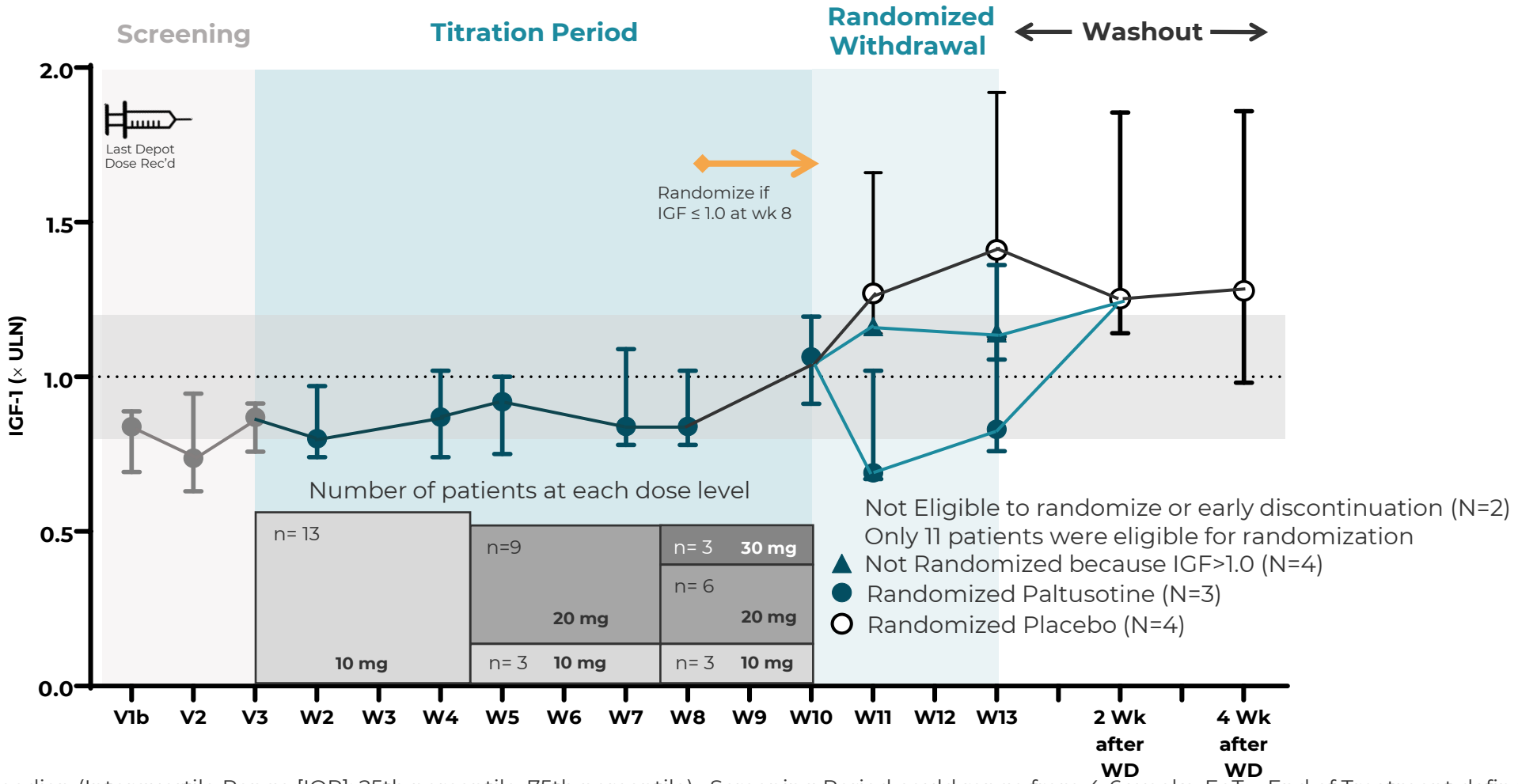
ACROBAT Evolve Dose Titration

Most patients did not reach the highest dose (30 mg)



Dose escalation determined by central reader based on tolerability and IGF-1 (site staff, patient, and sponsor blinded to dose)

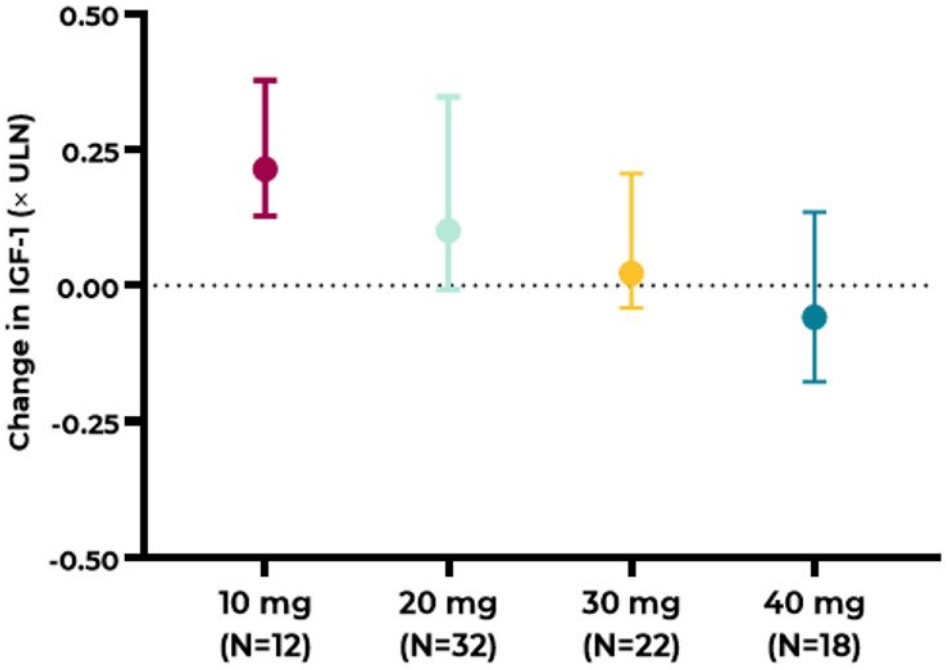
Evolve Patients Contribute to Dose Response Data, but Most Did Not Titrate to More Effective Dose Levels



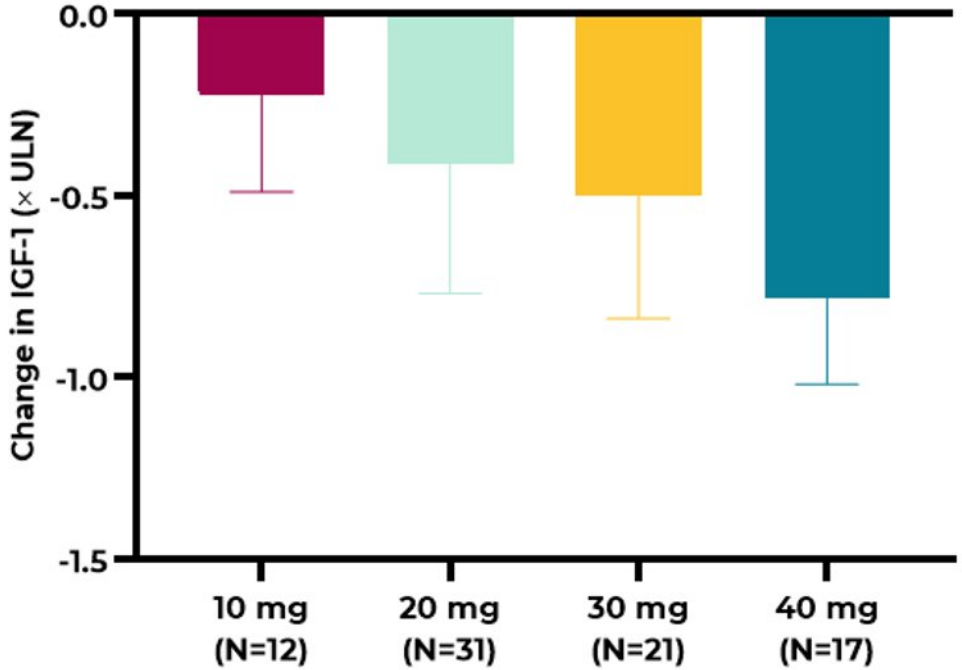
Data presented are median (Interquartile Range [IQR]: 25th percentile, 75th percentile). Screening Period could range from 4-6 weeks. EoT = End of Treatment defined as Week 13 (Visit 14) or last on treatment value carried forward (LOCF). WD = Withdrawal, where 2 Wks after WD is defined as Week 15 or result within 7-21 days after last dose and 4 Wks after WD is defined as Week 17 or result at least 22 days after last dose.

Post-Hoc Analysis of Edge (Group 1) and Evolve Provide Evidence of a Dose Response

Results from Switching to Paltusotine: Change in IGF-1 from Baseline to Steady State at Indicated Dose



Magnitude of Paltusotine Activity: Change in IGF-1 from Steady State to 4 Weeks After Withdrawal



Steady state IGF-1 at the indicated dose: Patients were on the indicated dose for at least 12 days. Data prior to Week 7 were excluded because of insufficient washout of depot injection during this window. Data are shown from Week 7, Week 10, and Week 13.
Data presented are median +/- IQR. EoT = End of Treatment defined as Week 13 (Visit 14) or last on treatment value carried forward (LOCF).
WD = Withdrawal, where 2 Wks after WD is defined as Week 15 or result within 7-21 days after last dose and 4 Wks after WD is defined as Week 17 or result at least 22 days after last dose. One subject is missing 4 Weeks after withdrawal observation.
Octreotide and lanreotide concentrations were measured 17 weeks after depot dose (W13 of the treatment period). Octreotide was completely washed out. Lanreotide concentrations were >75% reduced from baseline.

Paltusotine was Generally Well Tolerated Across Clinical Trials

Treatment Emergent Adverse Events ≥ 5%*	Edge/Evolve Patients (N=60) n (%)	Healthy volunteers (N=128^) n (%)
Common Acromegaly Symptoms		
Headache	19 (32%)	23 (18%)
Arthralgia	15 (25%)	0
Fatigue	13 (22%)	6 (5%)
Peripheral swelling	11 (18%)	0
Paraesthesia	10 (17%)	1 (1%)
Hyperhidrosis	10 (17%)	0
Sleep apnoea syndrome	4 (7%)	0
Common SRL Side Effects		
Diarrhoea	5 (8%)	27 (21%)
Abd pain/Abd pain upper	5 (8%)/2(3%)	25 (20%)/6(5%)
Abdominal discomfort	4 (7%)	12 (9%)
Abdominal distension	3 (5%)	7 (6%)
Other		
Catheter site pain	0	9 (7%)
Nausea	0	9 (7%)
Back pain	5 (8%)	2 (2%)
Dyspepsia	3 (5%)	0
Urinary tract infection	3 (5%)	0

Acrobat Edge and Evolve

- No study discontinuations due to adverse events
- No patients required rescue treatments with standard acromegaly medications during treatment
- No safety signals seen with vital signs
- No safety signals seen in clinical laboratories, including no amylase/lipase elevations > 3x ULN, HbA1c, LFTs, ECGs
- No treatment related SAEs; 2 non-treatment related SAEs:
  1. Nephrolithiasis: lithotripsy for pre-existing kidney stone
  2. Headache: admission for diagnostic evaluation

*TEAEs include any AE that newly appears, increases in frequency, or worsens in severity following initiation of study drug through 28 days after last dose.
^ Treated with 1 or more doses of CRN00808.HCl as of 31 August 2020

Our Center Experience: Open Label Extension Study (Advance)

All 13 patients included in Evolve and Edge were transferred to open label extension study (Advance)

No patient experienced clinical worsening of acromegaly at the end of studies Evolve and Edge

When questioned, all patients stated that they preferred paltusotine to injectable somatostatin receptor ligands

For the vast majority of patients, fasting was not a problem

Our center experience…
Patients were asked about the preference between the use of oral sst2 agonist (Paltusotine) versus injectable somatostatin

All patients preferred the oral medication

"The needles made me feel bad."

"As agulhas me faziam sentir mal"
Female, 66 years old

"I feel more comfortable taking the medicine every day as a tablet, than the monthly injection."

"Sinto-me mais confortável tomando o medicamento todos os dias em comprimido, do que uma vez por mês a injeção" Male, 50 years old

"I feel better with the oral."

"Me sinto mais disposto com a medicação oral"
Male, 63 years old

"Much more convenient."

"Muito mais cômodo"
Female, 55 years old

NeuroEndo, UFRJ, 2020

Conclusions

- Fg-SRLs are the first-line medical treatment for the vast majority of patients with acromegaly.
- The patients report significant burden of this treatment including incomplete control of their symptoms (even those with IGF-I < 1x ULN) and injection site reactions.
- There is an unmet need for new fg-SRLs formulations for patients with acromegaly.
- Paltusotine is a once-daily oral medication.
- The ACROBAT Edge trial showed that paltusotine may be an effective option for patients with acromegaly that respond to injectable fg-SRLs.
- Side effects and compliance issues related to injectable fg-SRLs may be avoided with paltusotine treatment.

Thank you

mgadelha@hucff.ufrj.br

PALTUSOTINE NEXT STEPS AND Q&A

Scott Struthers, PhD, Founder and CEO

Paltusotine Development Program 2021 Plans

- End-of-phase 2 meeting with FDA in 1Q 2021
- Planned initiation of Phase 3 acromegaly program in 1H 2021 with to-be-marketed formulation
- Planned initiation of NETs trial in carcinoid syndrome in 2021

Q&A

Crinetics Pharmaceuticals

THANK YOU