20 October 2014

Shareholder & Investor Presentations

As announced on the 9th October, Professor Peter Trainer, Chief Investigator of the Phase II clinical trial of ATL1103, will today present to shareholders and investors whilst in Melbourne. Following his presentation the CEO Mark Diamond will give an investor update (copy of these presentations follow this announcement). The Melbourne presentation is also being recorded and will be available for viewing by tomorrow at 12.00pm via a link on the ANP website homepage www.antisense.com.au or directly on the following link:

http://webcasting.brrmedia.com/broadcast/127892

Antisense Therapeutics Limited (ASX: ANP) is an Australian publicly listed biopharmaceutical drug discovery and development company. Its mission is to create, develop and commercialise second generation antisense pharmaceuticals for large unmet markets. ANP has 4 products in its development pipeline that it has in-licensed from Isis Pharmaceuticals Inc. (NASDAQ:ISIS), world leaders in antisense drug development and commercialisation - ATL1102 (injection) which has successfully completed a Phase II efficacy and safety trial, significantly reducing the number of brain lesions in patients with multiple sclerosis, ATL1103 a second-generation antisense drug designed to block GHr production and thereby lower blood IGF-I levels and is in clinical development as a potential treatment for growth and other GH-IGF-I disorders, ATL1102 (inhaled) which is at the pre-clinical research stage as a potential treatment for asthma and ATL1101 a second-generation antisense drug at the pre-clinical stage being investigated as a potential treatment for cancer.

Contact Information: Website: www.antisense.com.au
Managing Director: Mark Diamond +61 (3) 9827 8999

Modern Management of Acromegaly

MANCHESTER 1824

The University of Manchester

Peter J Trainer
Christie Hospital





Melbourne
20th October 2014

Manchester Academic Health Science Centre

Disclosures

Investigator:
Chiasma (Roche), Antisense Pharmaceuticals, Ipsen, Cortendo
& Novartis (UK CI for LCI699)

Advisory Group Member (unpaid):
Chiasma, Roche, Novartis, HRA Pharma
Antisense Pharmaceuticals

Chairman
Bioscientifica

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Diagnosis can take many years



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Metabolic Actions of GH

Proteins

- Increases protein synthesis, increases muscle mass

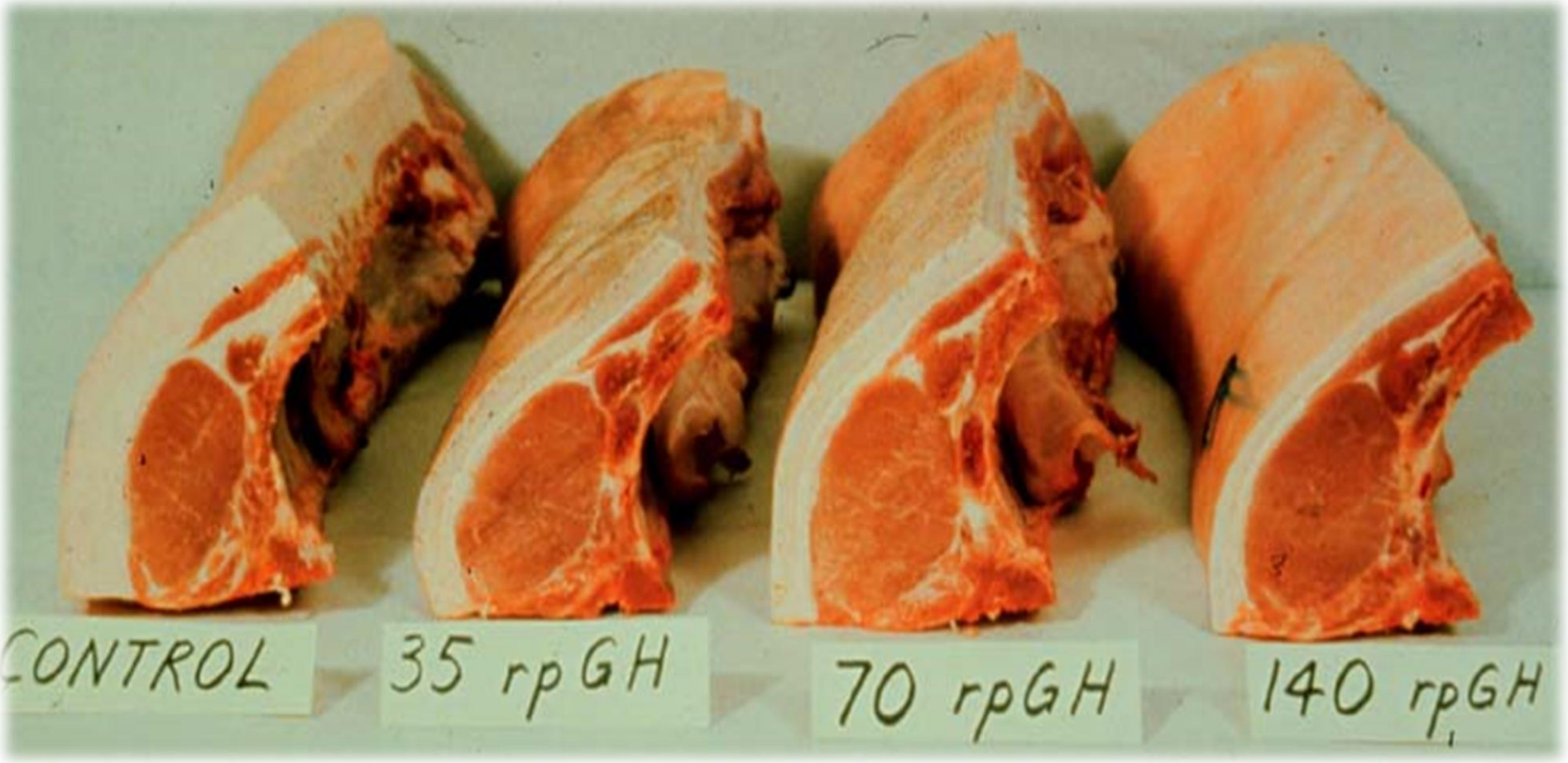
Lipids

- Stimulates lipolysis
- Inhibits lipogenesis
- Decreases adipose mass

Carbohydrates

- Increases hepatic gluconeogenesis
- Inhibits glucose uptake in muscle

What every athlete knows!!!



Dose dependent decrease in fat, and increase in muscle and bone!!!

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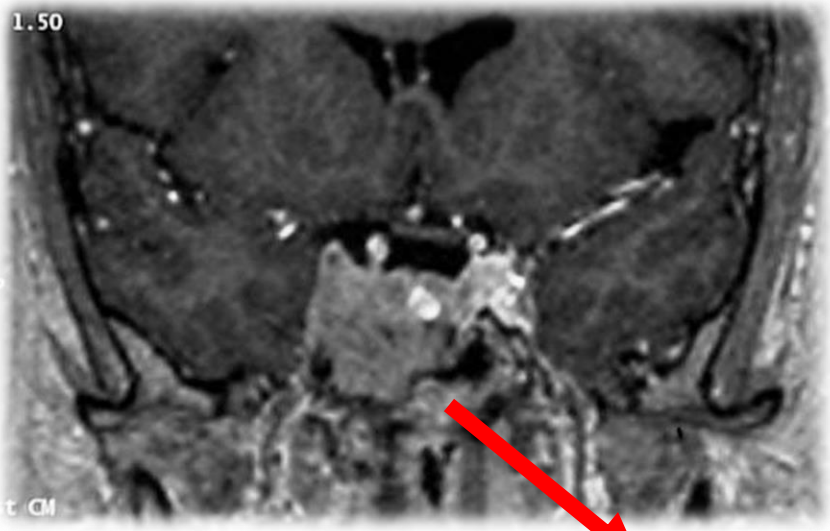
Pathogenesis of acromegaly

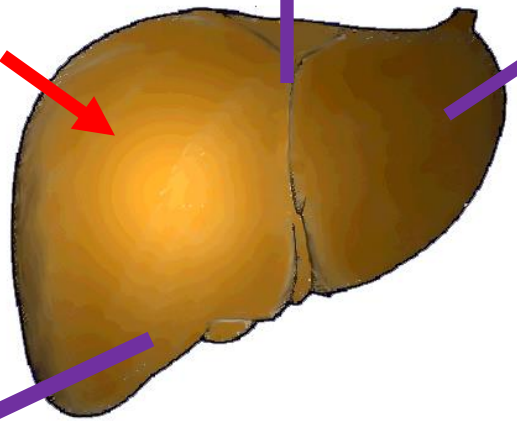




IGF-I

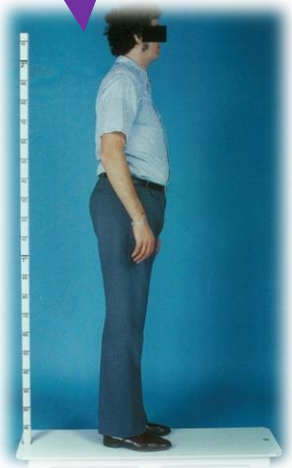
GH





IGF-I

IGF-I



IGF-I

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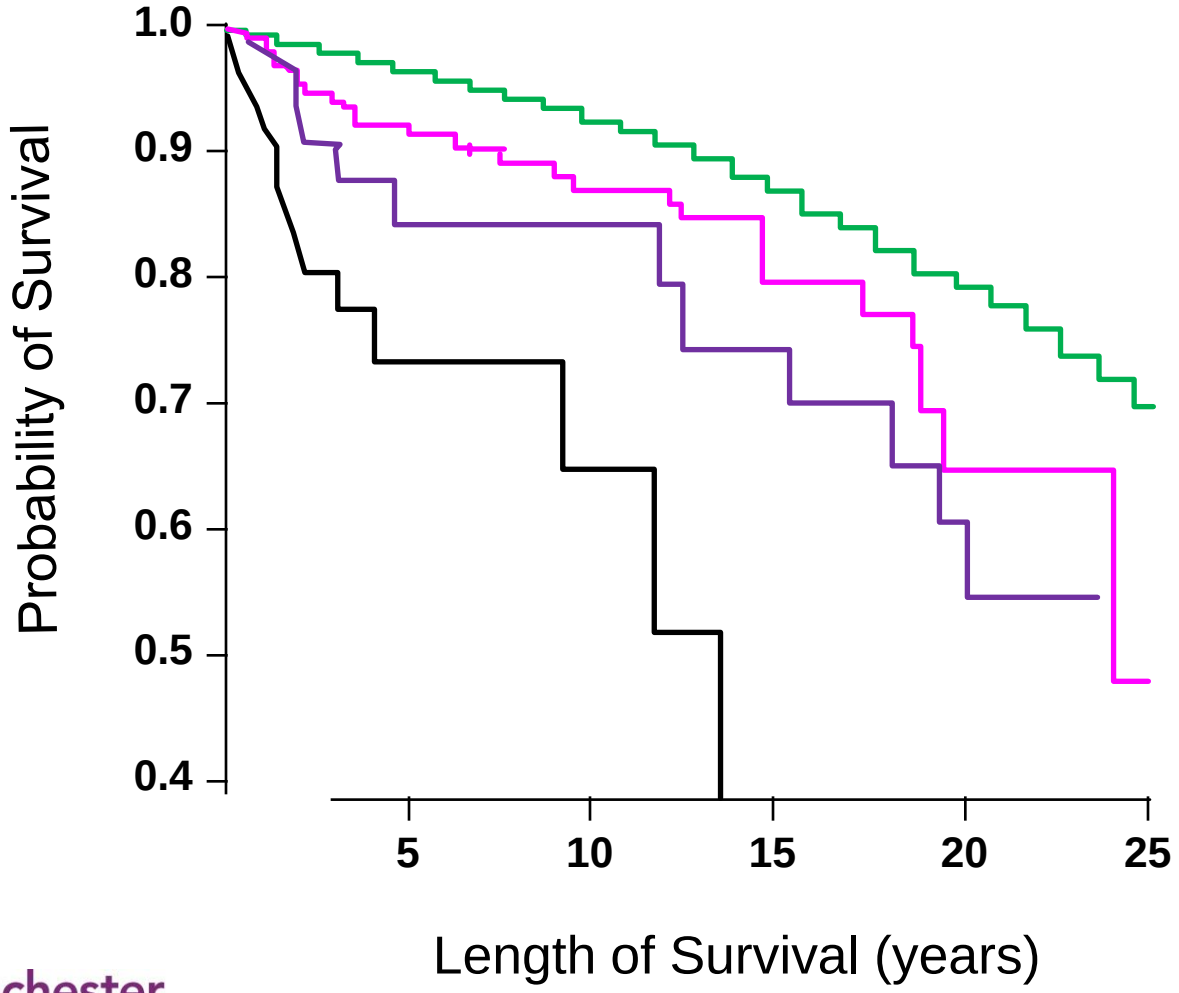
The Impact of Acromegaly on Survival



General population

All acromegaly

Acromegaly + diabetes

Acromegaly + cardiac disease

Life expectancy ⇓ 10 years

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Rajasoorya CE 1994 41 95

Acromegaly and Mortality

Retrospective study (n=79)

- Overall mortality ⇑ (mortality ratio 2.68)
- 57% deaths cardiovascular
- GH <5 mU/l post-treatment - mortality risk normal

Therefore reduction of GH <5 mU/l a clinical priority

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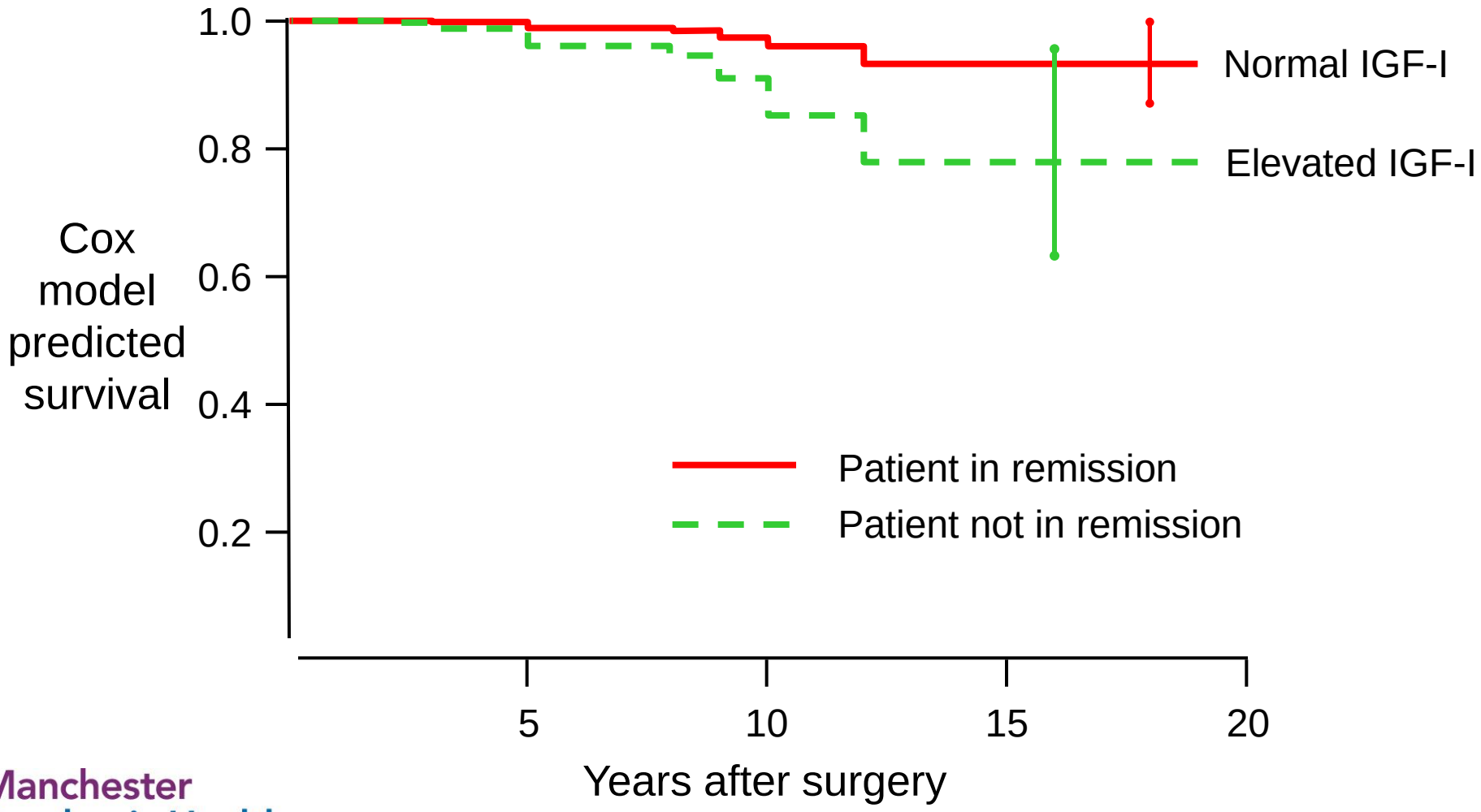
Bates QJM 1993 86 293

Long-term Mortality After Transsphenoidal Surgery



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Swearingen JCEM 1998 83 3419

Objectives of therapy in acromegaly

- restoration of basal GH and IGF-I to normal levels
- relief of symptoms
- reversal of visual and soft tissue changes
- prevention of further skeletal deformity
- normalization of pituitary function

Surgery as primary therapy for acromegaly



Microadenoma (<1 cm)
Surgical cure rate ~90%

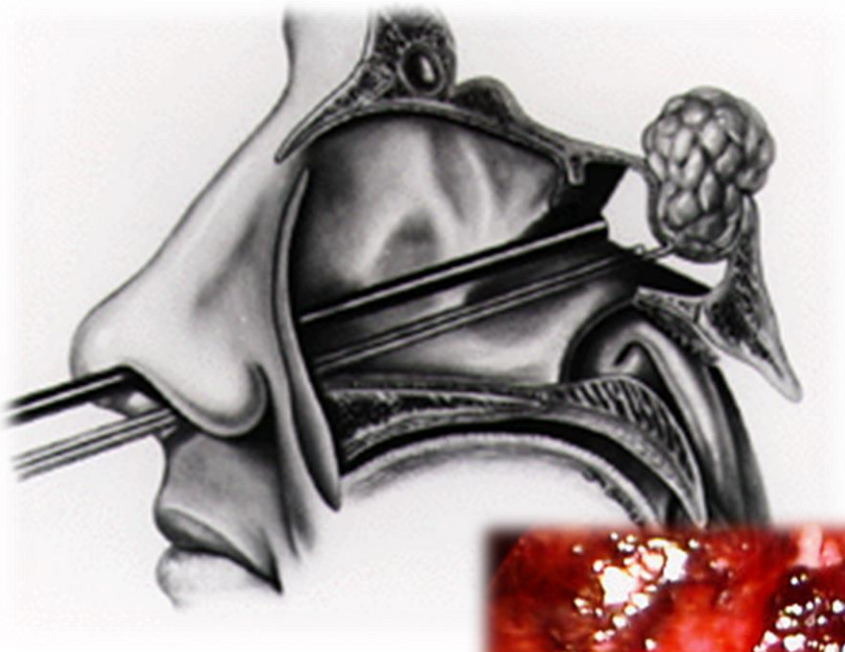


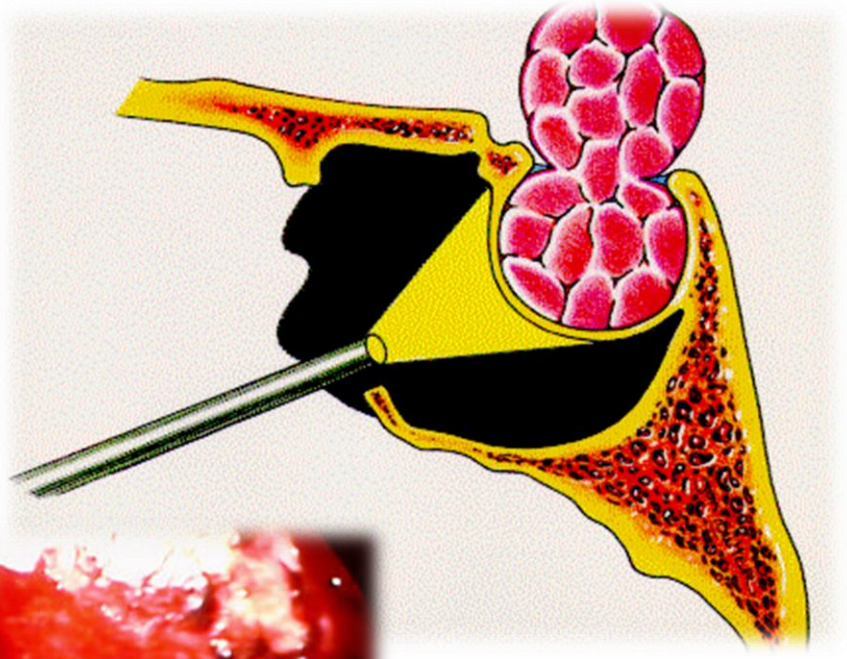
Macroadenoma (>1 cm)
Surgical cure rate <50%

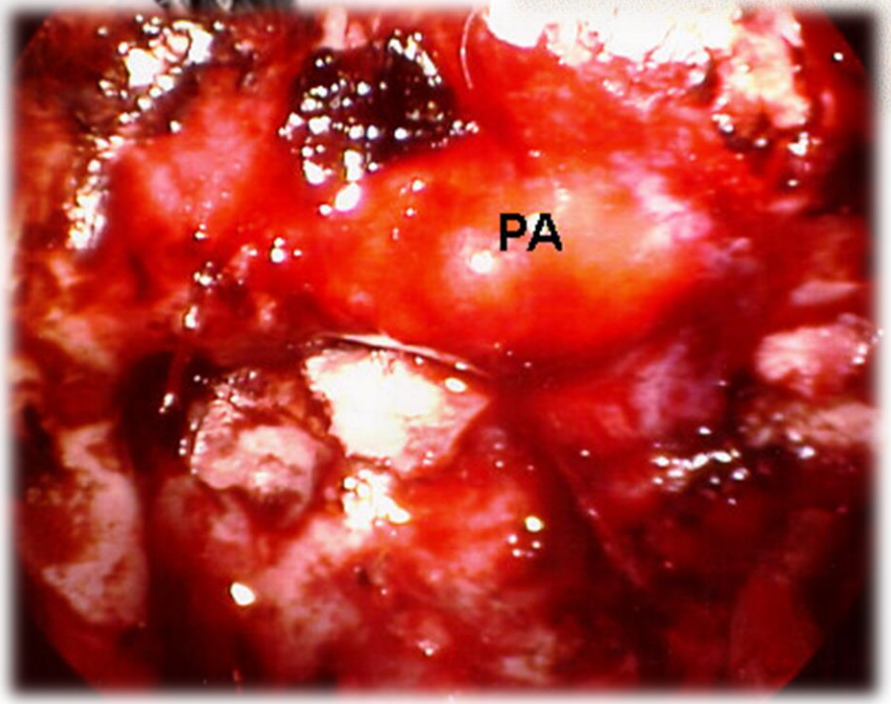
Two important determinants of success of surgery

- size of tumour
- the surgeon

Transsphenoidal Surgery







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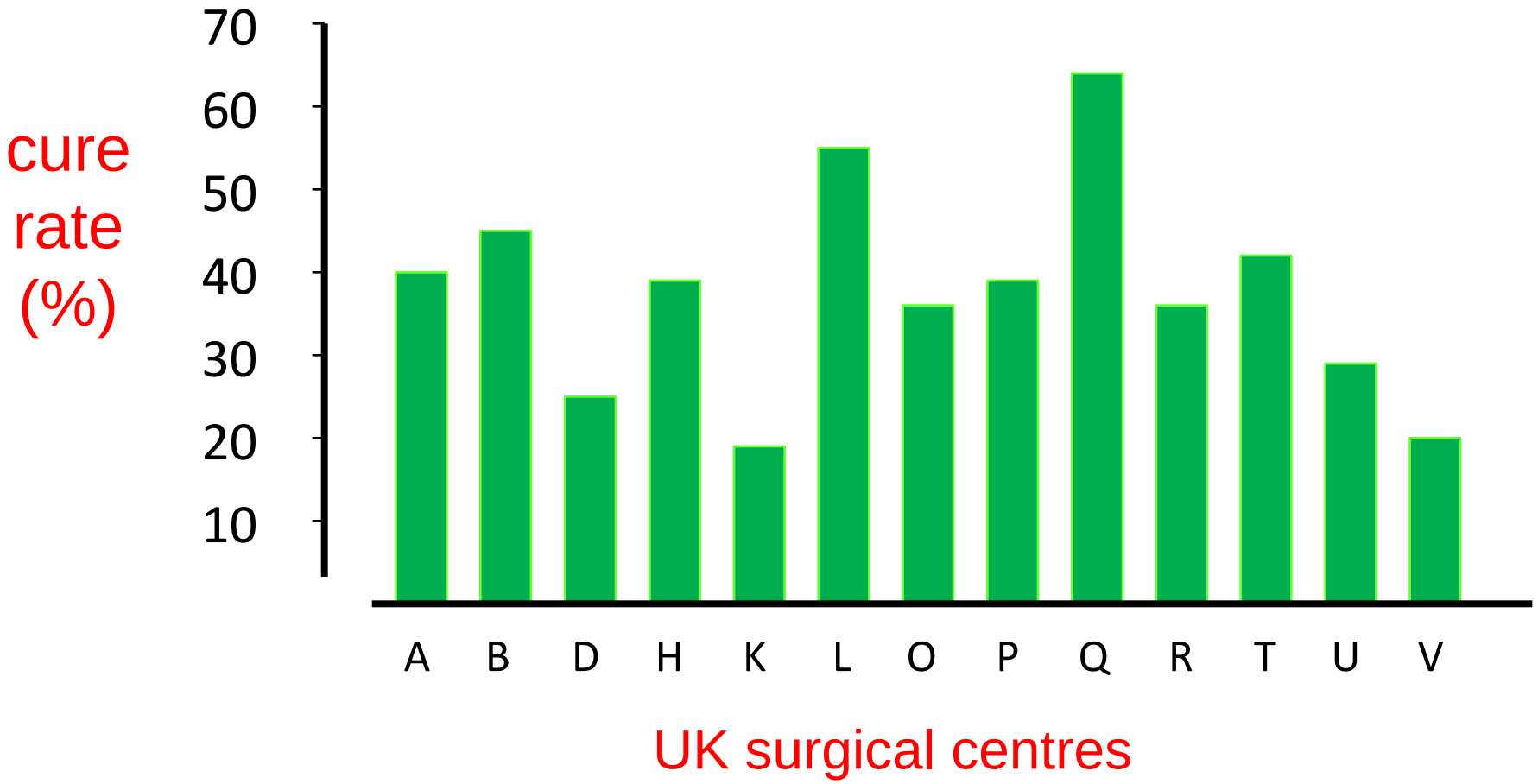
UK cure rate of patients in different surgical centres



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Bates CE 2008 68 136

Complications of pituitary surgery

Complication	# of operations <200	200-500	>500
Anaesthetic complications	3.5	1.9	0.9*
Carotid artery injury	1.4	0.6	0.4*
CNS injury	1.6	0.6	0.4*
			0.8*
			0.5*
			0.4*
Meningitis	1.9	0.8	0.5#
Nasal septum perforation	7.6	4.6	3.3*
Post-operative epistaxis	4.3	1.7	0.4*
Post-operative sinusitis	9.6	6.0	3.6*
Hypopituitarism	20.6	14.9	7.2*
DI	19.0	NA	7.6*
Death	1.2	0.6	0.2*

Transsphenoidal surgery requires dedicated surgeons

* P<0.001
#P<0.05

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Ciric Neurosurgery 1997 40 225

Radiotherapy

- 40 years experience
- mass of data

Conventional

multi-fractional





proton beam

Stereotactic

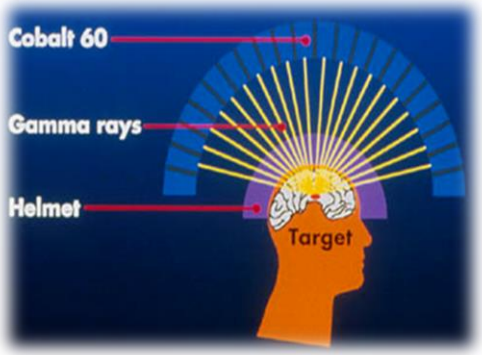
single fraction

less radiation to surrounding tissues

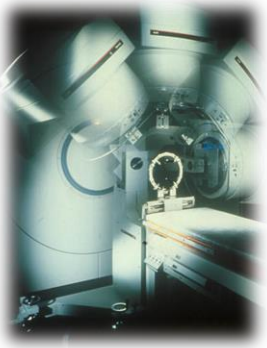
Gamma Knife®

LINAC

Proton beam



Gamma Knife



LINAC

- the future
- limited experience

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Dopamine Agonists

Goals

- Control GH
- Control IGF-I
- Improve well-being

Advantages

- No hypopituitarism
- Oral administration
- Rapid onset

Control (normal IGF-I)

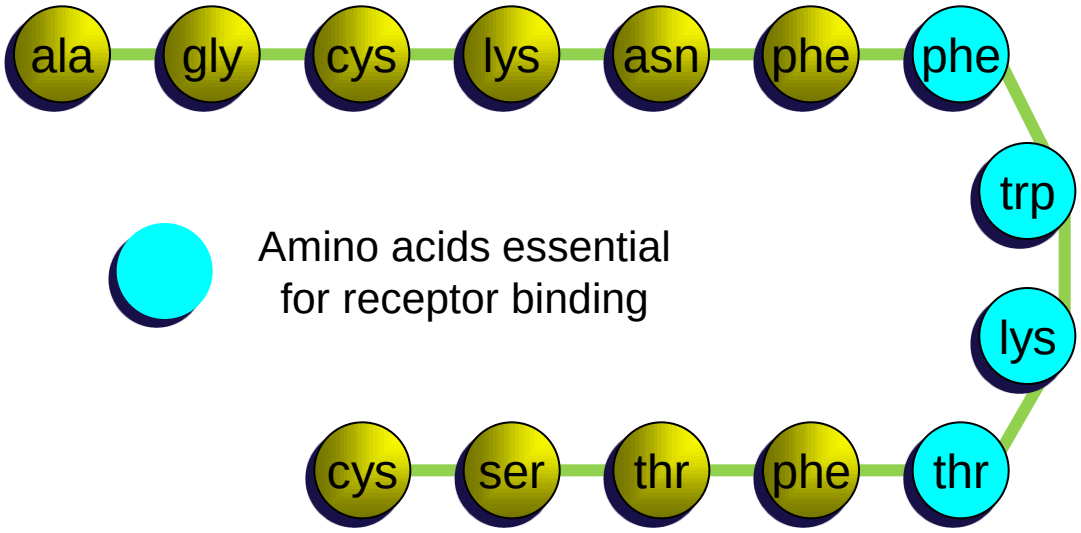
- bromocriptine 10%
- cabergoline 37%
  - more potent
  - fewer side effects
  - twice weekly

Disadvantages

- Relatively ineffective
- Side effects
- Concern over cardiac
  - valve fibrosis

Somatostatin Analogues

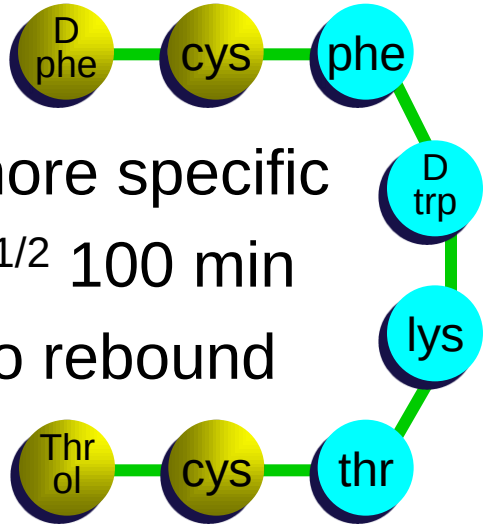
Human somatostatin



Amino acids essential for receptor binding

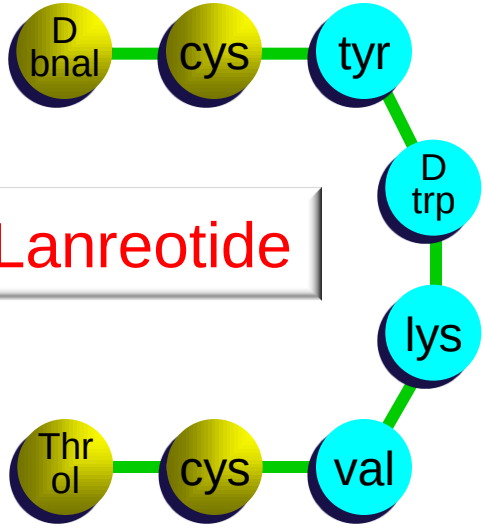
- inhibit multitude of hormones
- T $^{1/2}$ 3 minutes
- rebound
- binds all 5 receptor sub-types

Octreotide



- more specific
- T$^{1/2}$ 100 min
- no rebound

Lanreotide



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Pre-Treatment GH and Outcome in Acromegalics on Somatostatin Analogues

British Acromegaly Register

Pre-Treatment GH (mU/l)	Remission Rate % (GH <5 mU/l)
5-10	60
10-20	48
20-30	54
30-60	31
60-100	19
>100	14

Primary octreotide therapy study (POTS)

Pre-treatment GH (mU/l)	Remission rate
<25	100%
25 – 50	75%
>50	33%

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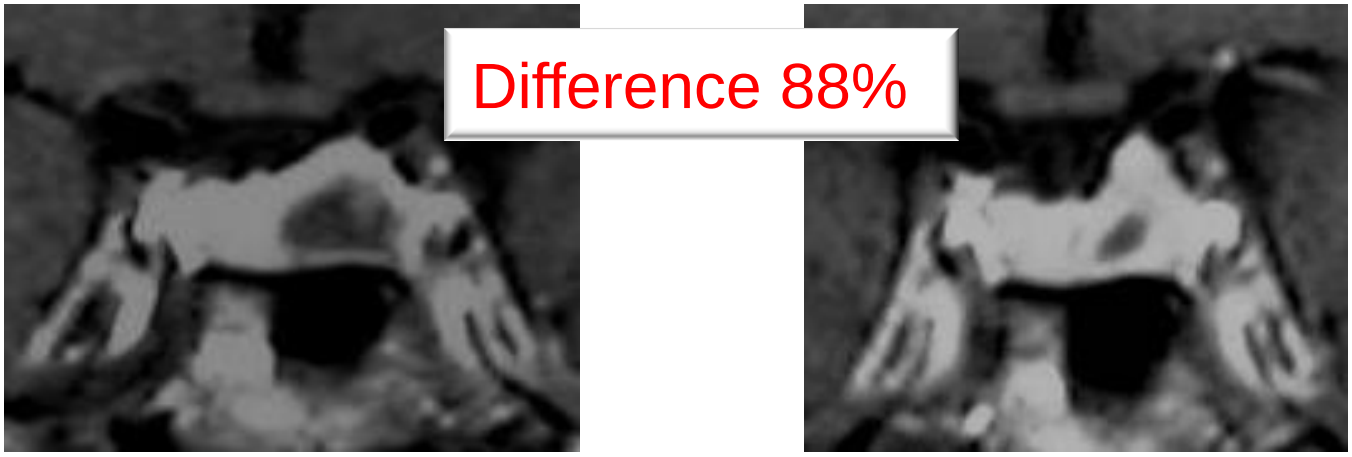
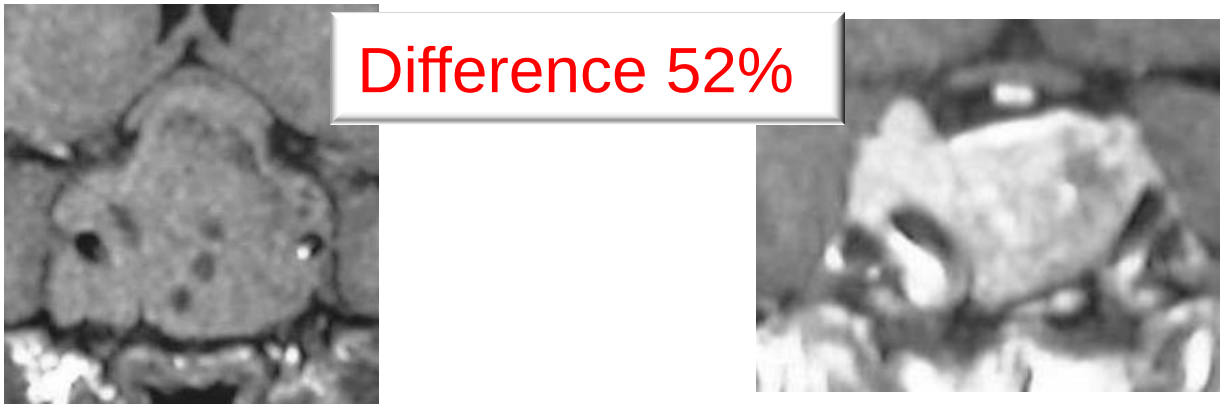
Tumour shrinkage with LAR as primary therapy



Baseline 552 mm3 24 weeks 63 mm3



Baseline 61733mm^3 24 weeks 29537 mm^3

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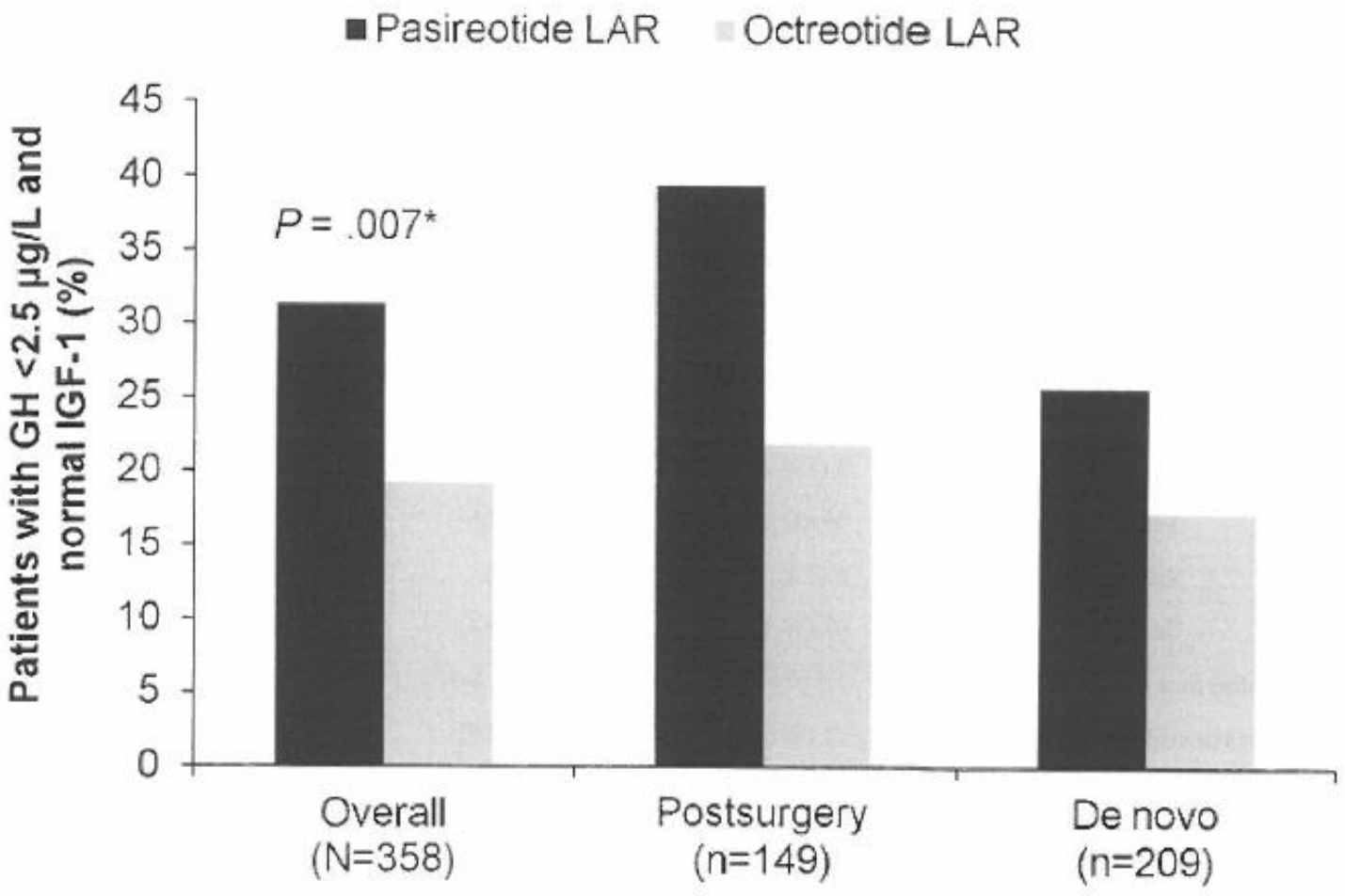
Bevan JCEM 2002 87 4554

Pasireotide v octreotide: head to head study



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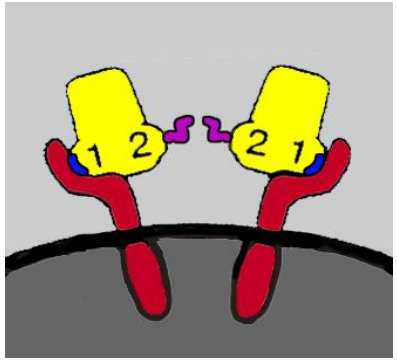
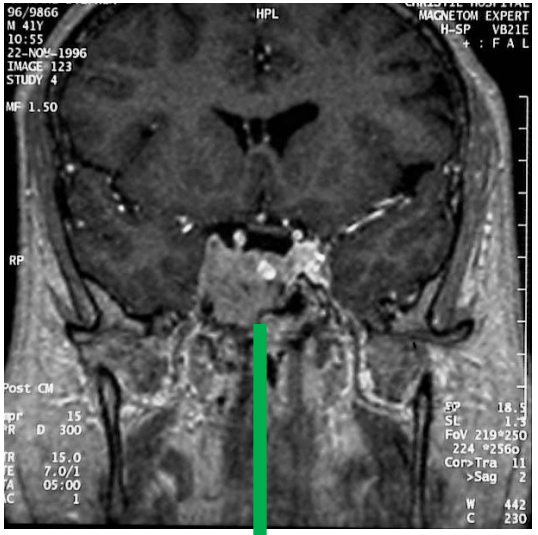
Colao JCEM 2014 99 791

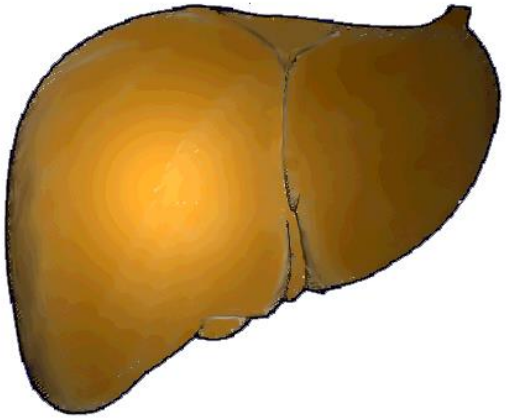


Pegvisomant



- 191 amino acid GH analogue
- 9 amino acid substitutions
- 4 - 5 PEG moieties
- molecular weight 42 - 46000 D
- half-life >70 hours
- subcutaneous administration

GH



serum GH cannot be used as a disease marker

Goal of therapy - to lower IGF-I into the age-related reference range

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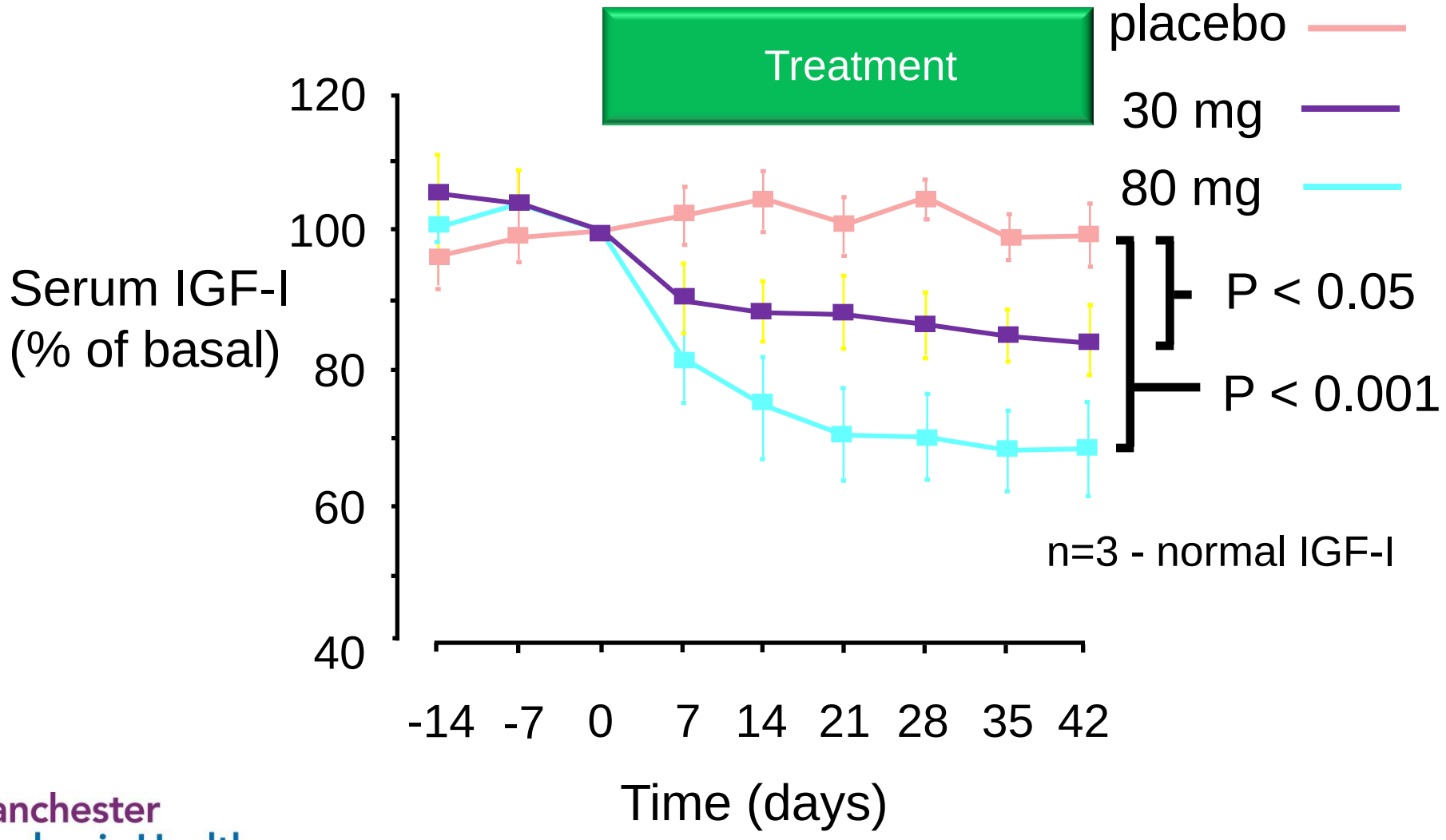
IGF-I as percent of basal in 46 patients with acromegaly on *weekly* pegvisomant



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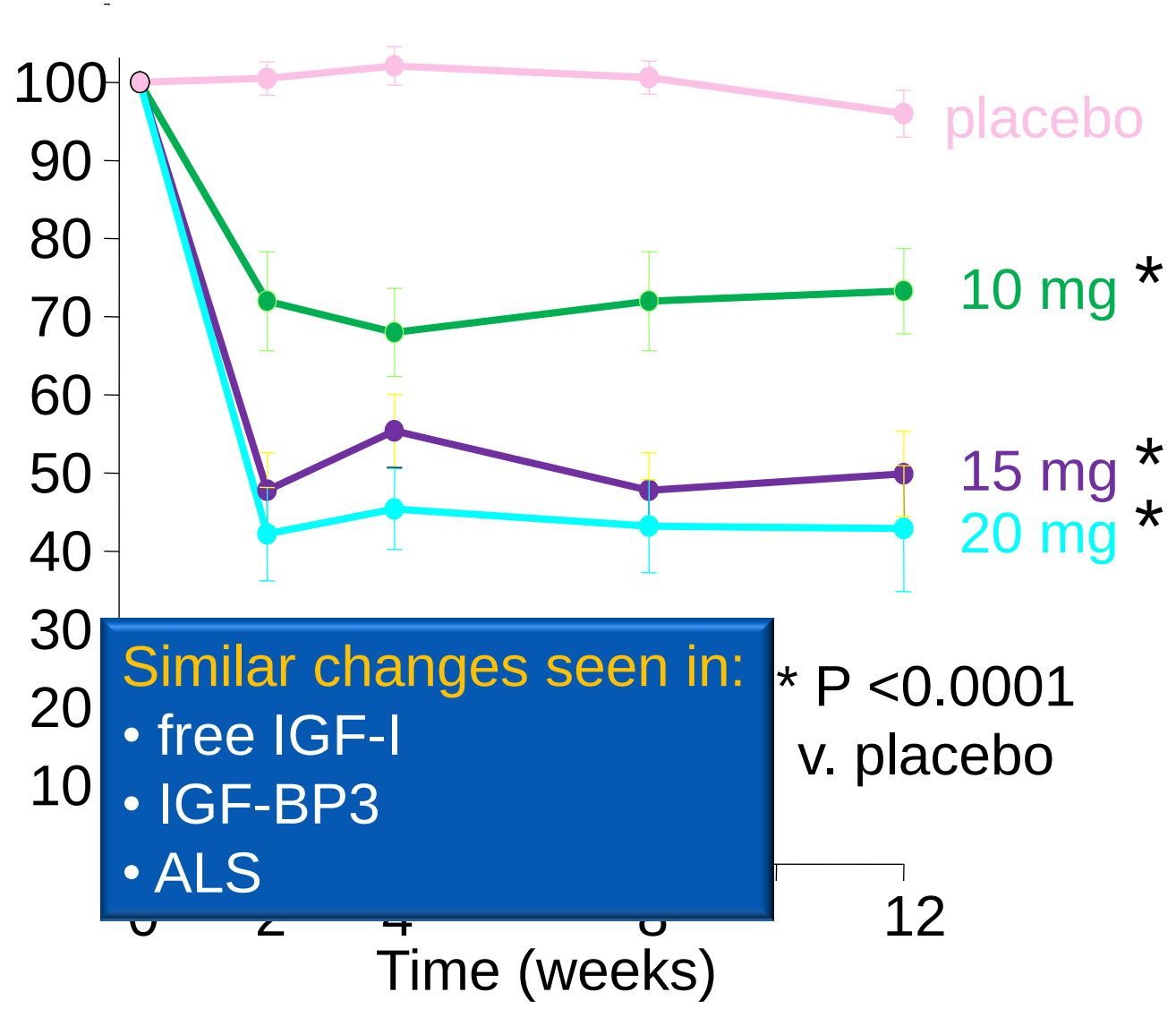
van der Lely, ENDO 1998 Abs OR4-1

IGF-I changes in 112 patients with acromegaly on daily pegvisomant



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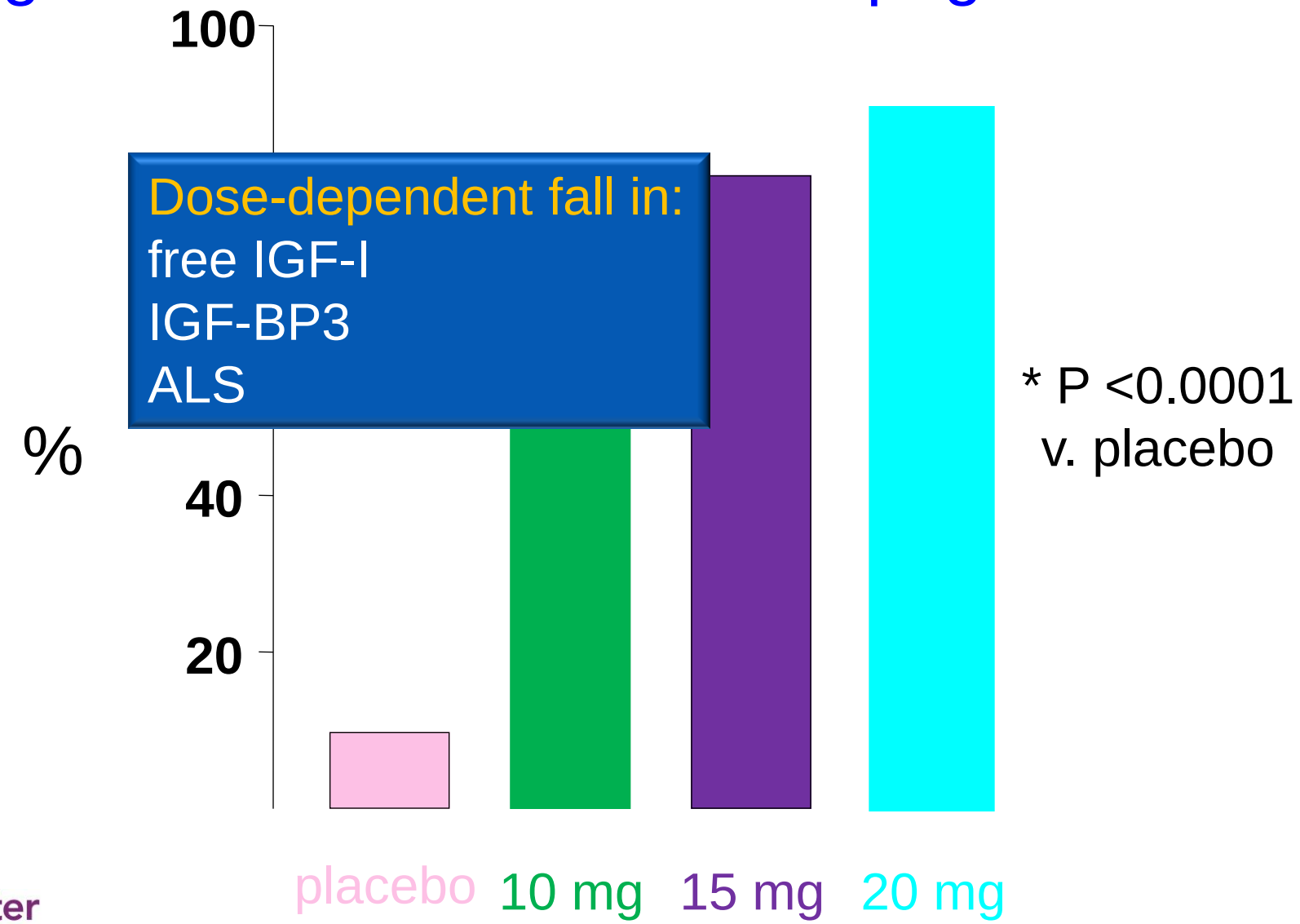
Trainer NEJM 2000 342 1171

Percentage achieving a normal age-related serum IGF-I with pegvisomant



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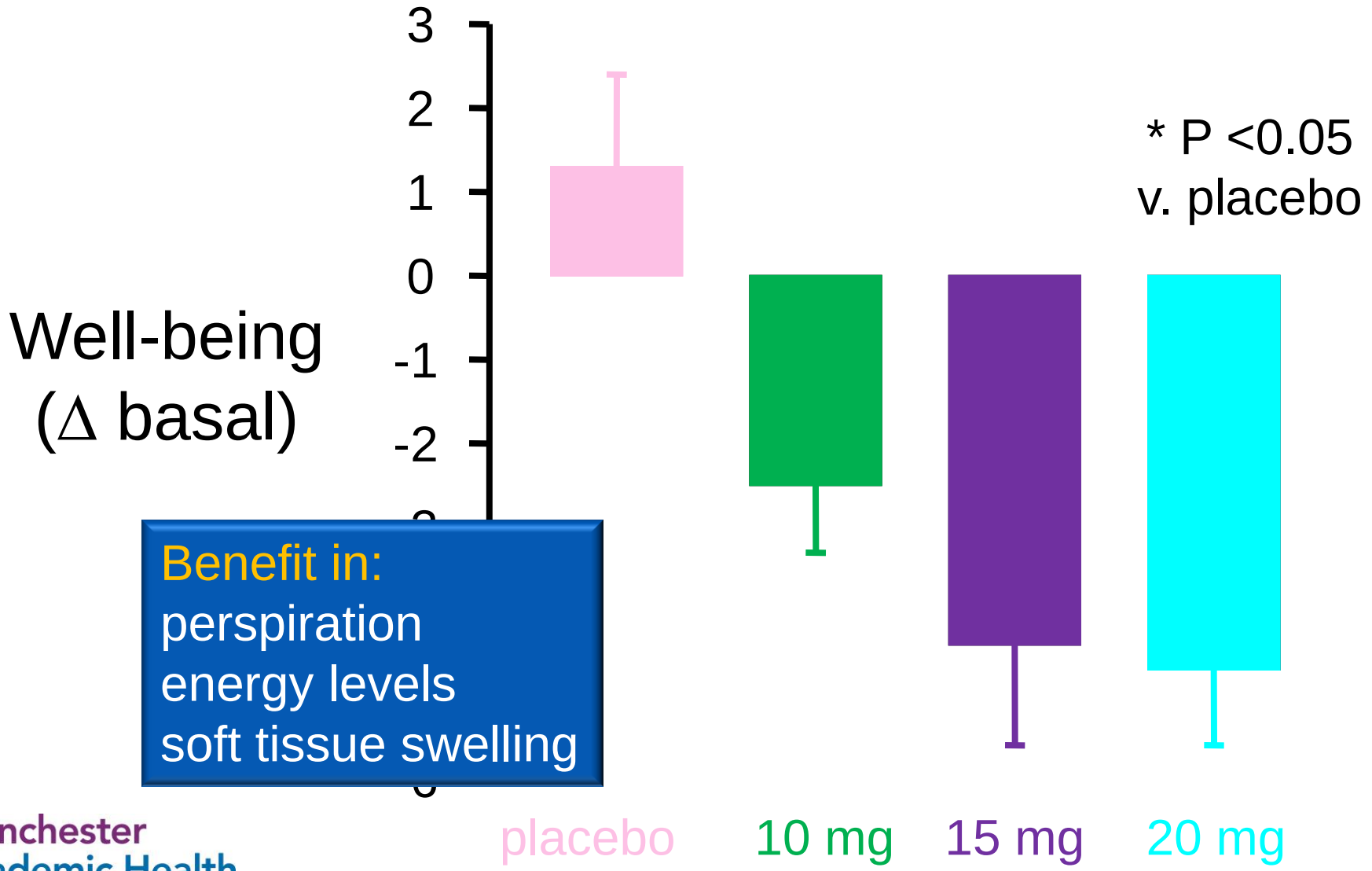
Trainer NEJM 2000 342 1171

Change in well-being after 12 weeks of daily pegvisomant



Benefit in:
perspiration
energy levels
soft tissue swelling

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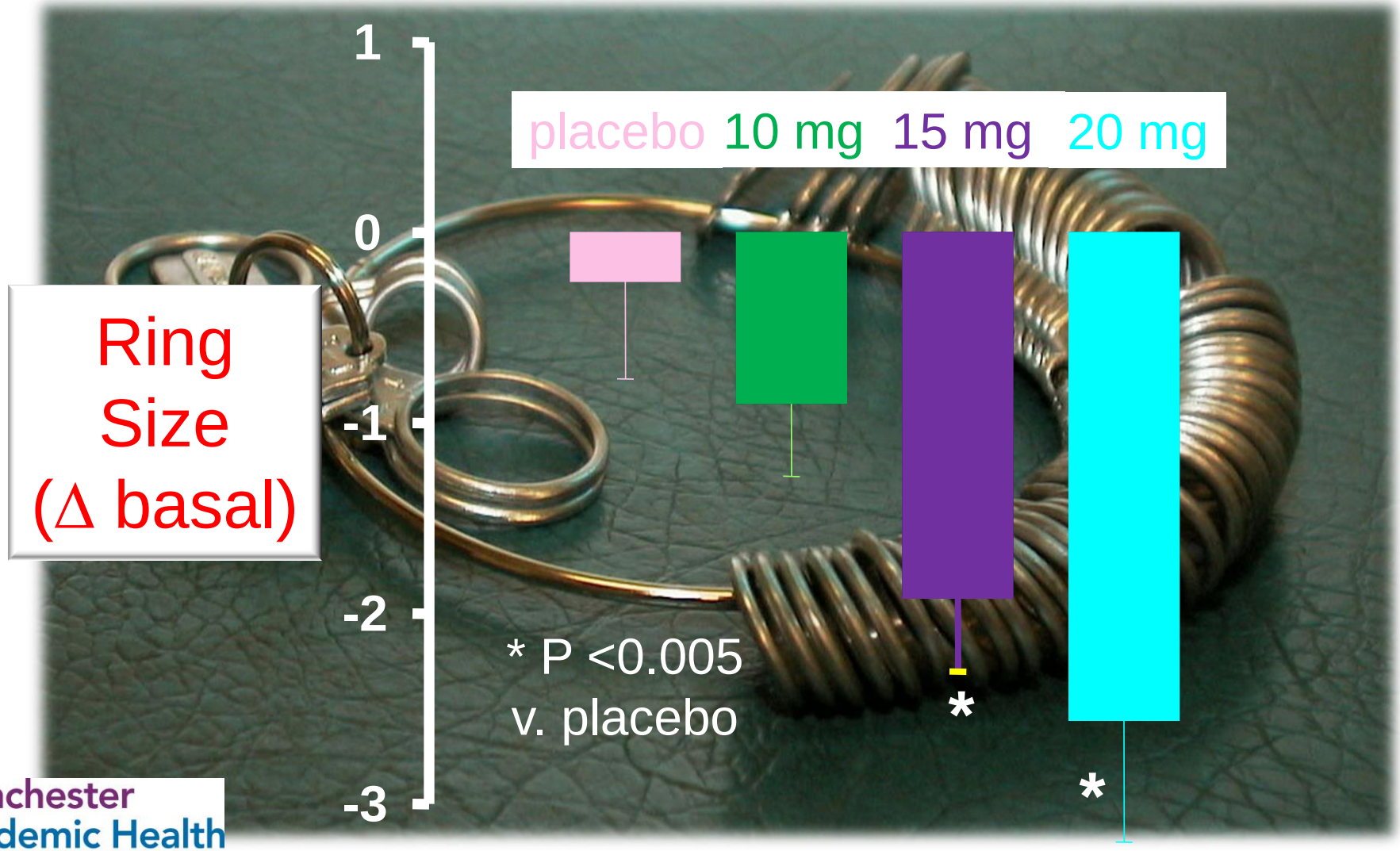
Ring size after 12 weeks of daily pegvisomant



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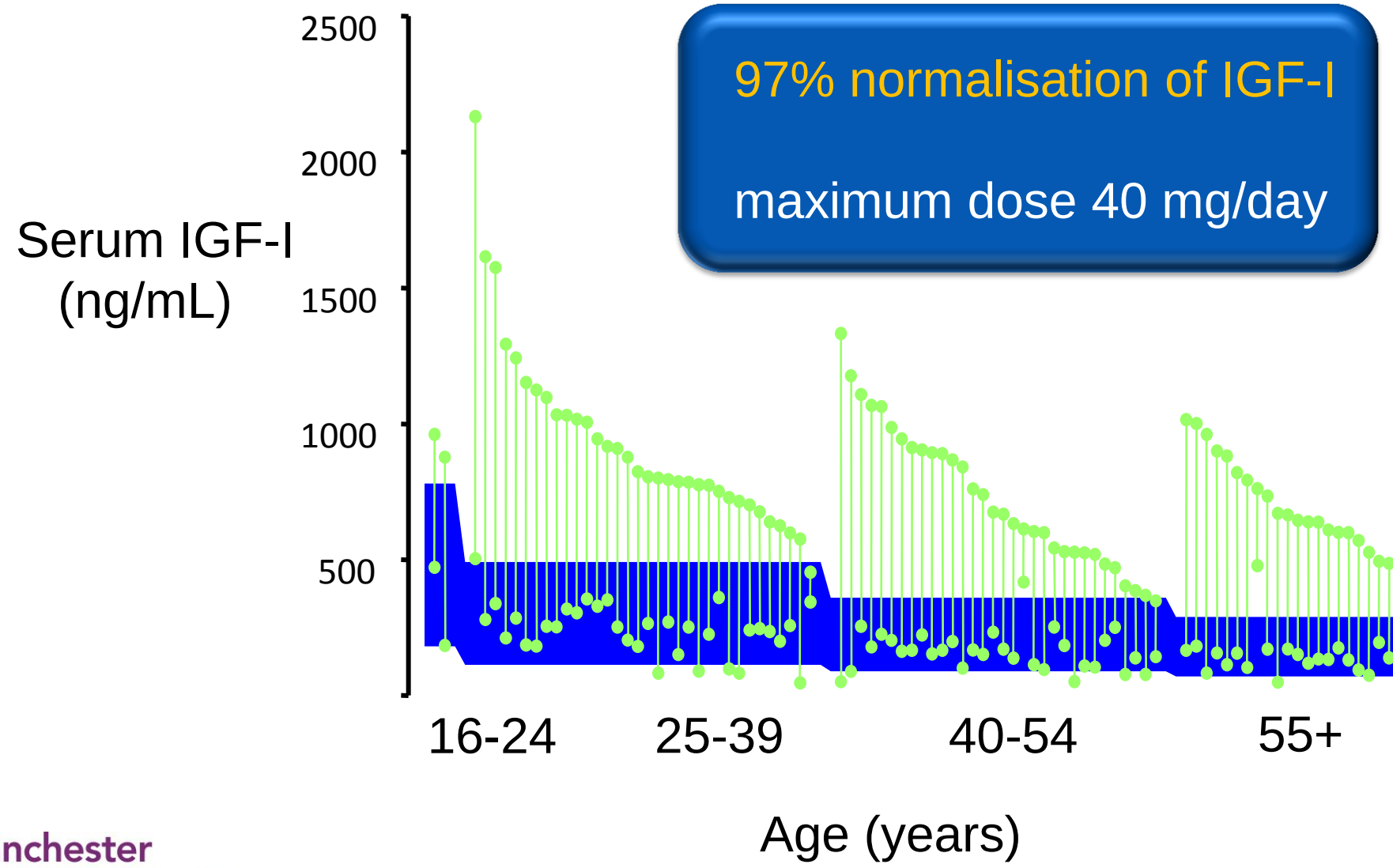
IGF-I at baseline and after 12 months of pegvisomant



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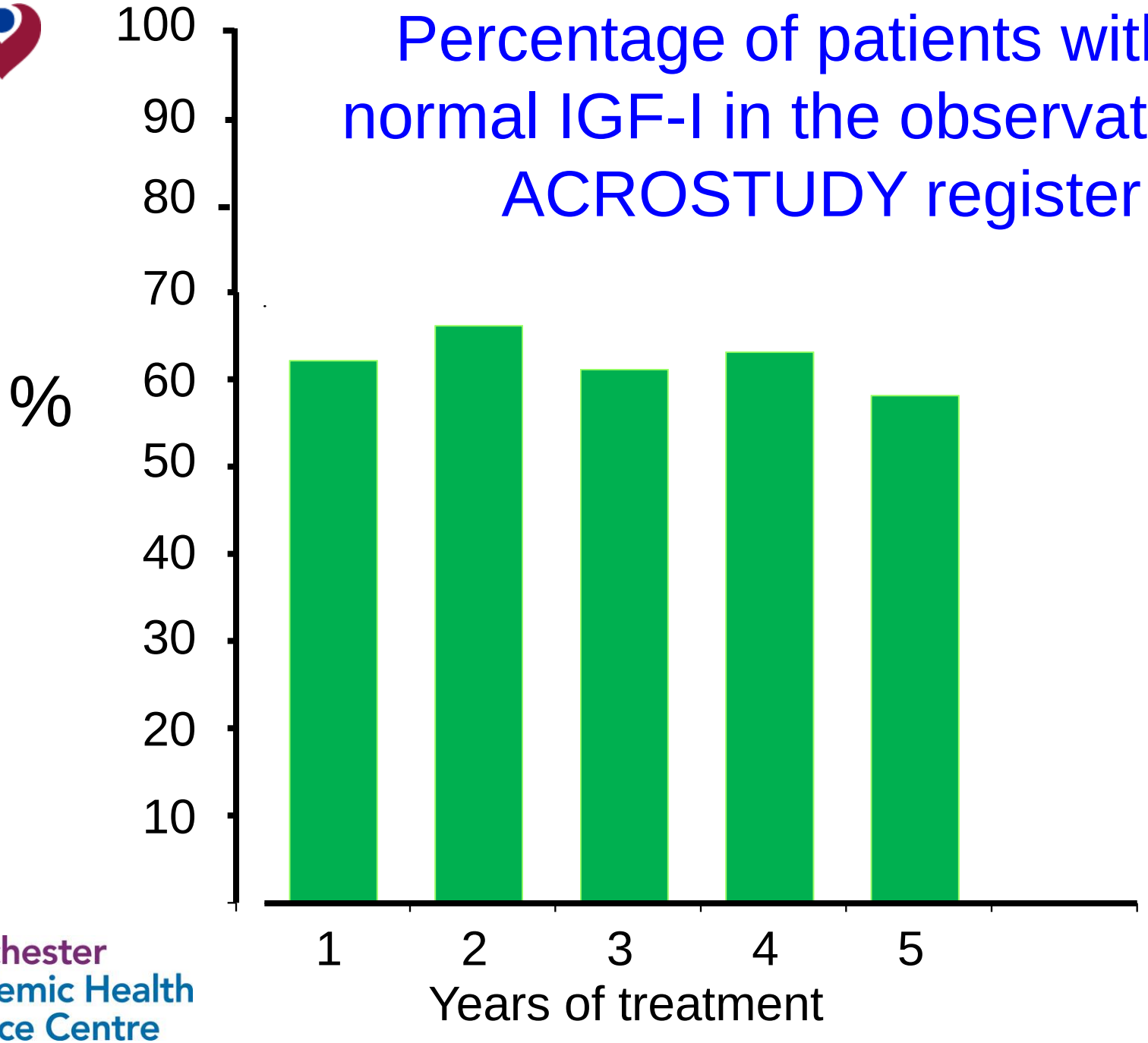
van der Lely Lancet 2001 358 1754

Percentage of patients with a normal IGF-I in the observational ACROSTUDY register



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A Phase II Randomised, Open-Label, Parallel Group Study of the Safety, Tolerability, Pharmacokinetics and Efficacy of Two Subcutaneous Dosing Regimens of ATL1103 in Patients with Acromegaly

PJ Trainer, J Newell-Price, J Ayuk, S Aylwin, A Rees, WM Drake, P Chanson, T Brue, S Webb, C Fajardo, J Aller, A McCormack, D Torpy, G Tachas, L Atley, M Bidlingmaier



antisense THERAPEUTICS

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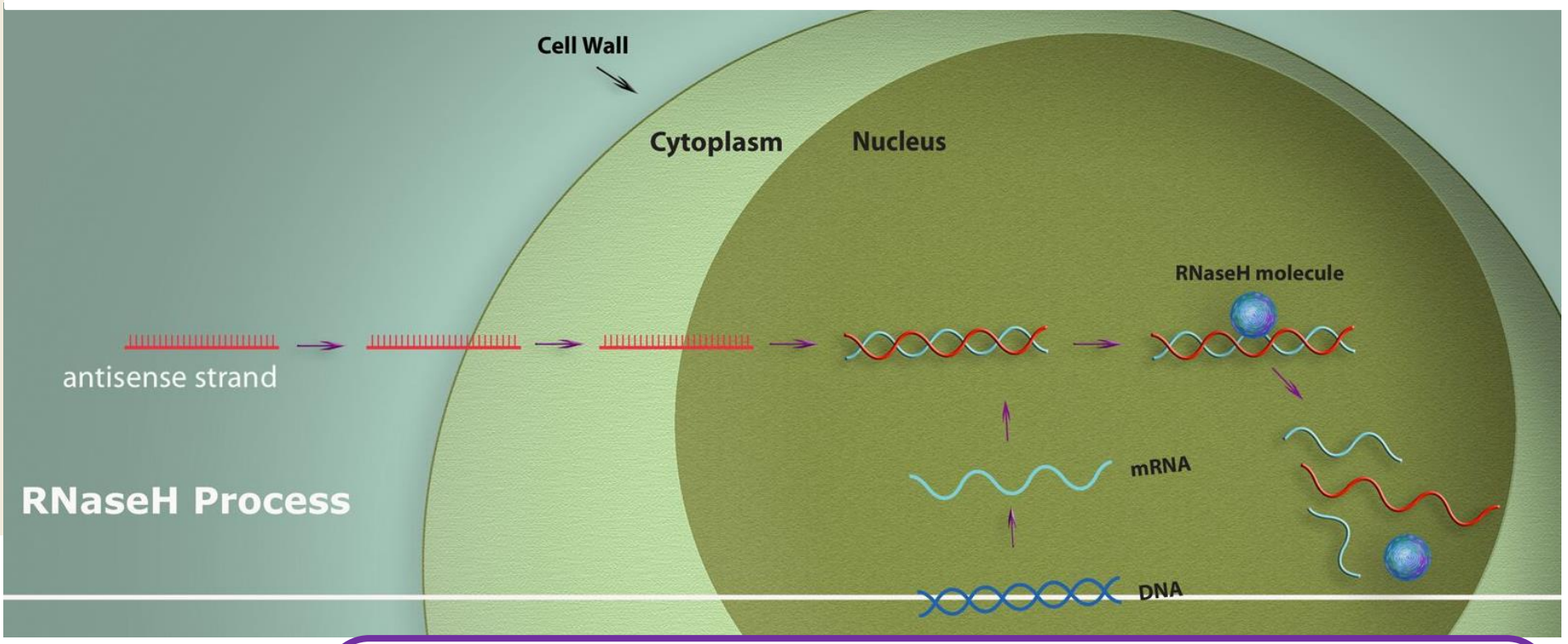
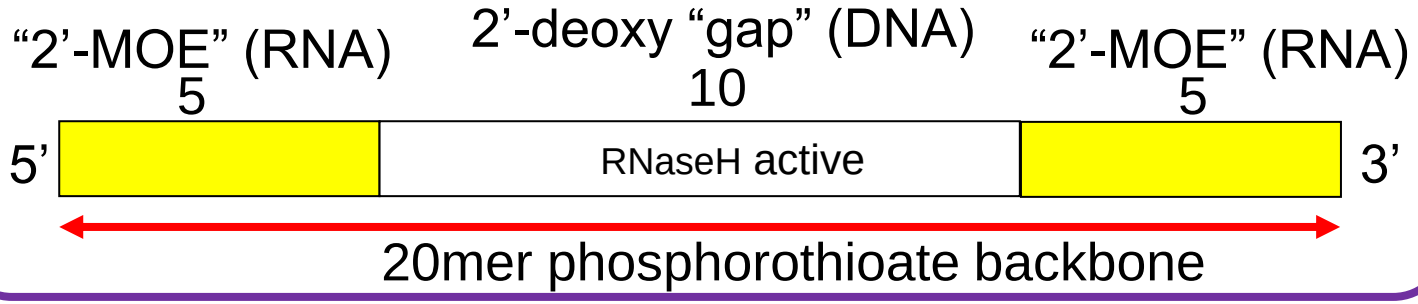
The Christie NHS NHS Foundation Trust

ATL1103 antisense 20mer oligonucleotide directed at GH receptor





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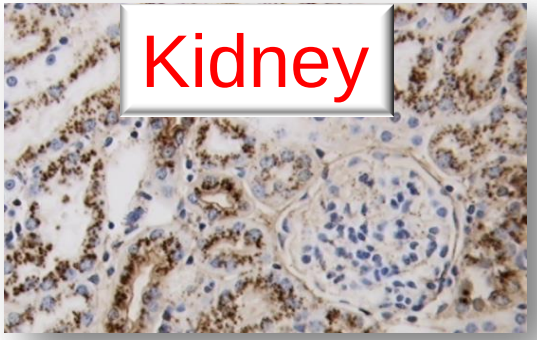
Tissue and Cellular PK of ASOs

Strong PK/PD correlation in

- Kidney
- Liver
- Bone marrow
- Adipose tissue
- Spleen, lymph nodes
- Lung (aerosol)
- Cancer
- Sites of inflammation
- Eye (Intravitreal)
- CNS (ICV or IT)

Liver half-life >3 weeks

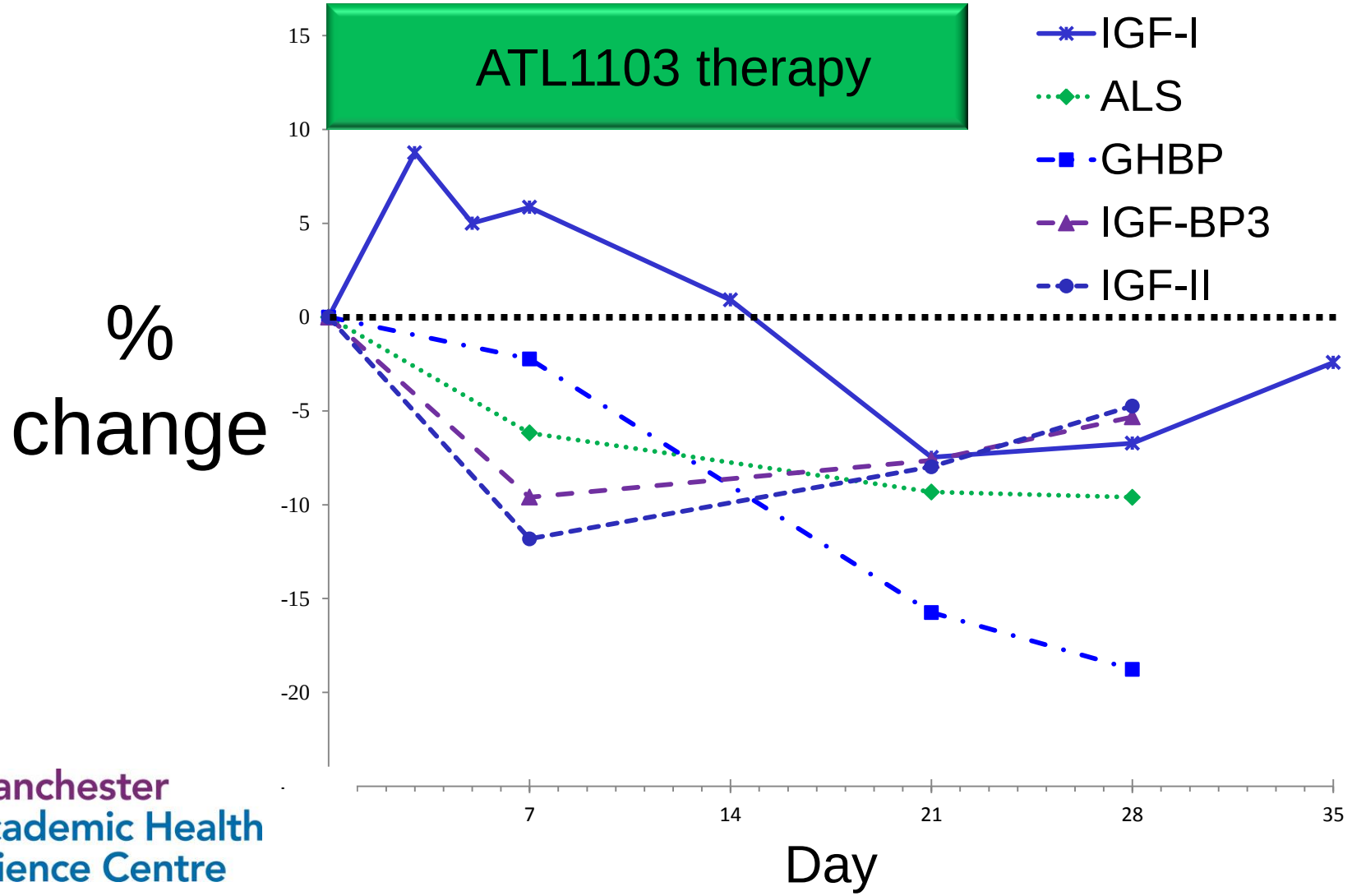






ATL1103 Phase I pharmacodynamic study

250 mg - six doses over 3 weeks (on Day 1, 3, 5, 7, 14 & 21)



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Phase 2, randomised, open-label, parallel group study (EudraCT 2012003147 30)

Ethical approval obtained in each jurisdiction

Powered for 24 patients

Inclusion criteria included:

- active acromegaly (IGF-I >130% ULN)
- washout from medical therapy (Long acting SMS analogues 4 months, DA 6 - 8 weeks)

Exclusion criteria included:

- tumour within 3 mm of optic chiasm
- pituitary surgery within 3 months
- radiotherapy within 1 year

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Protocol

ATL1103 subcutaneously for 13 weeks (3 doses in first week)

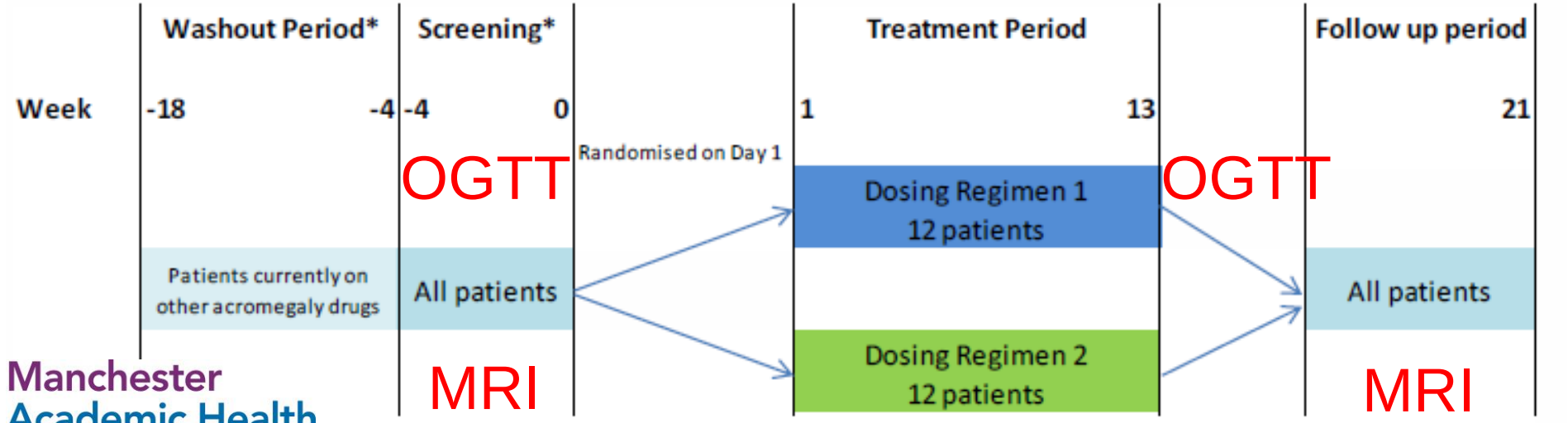
Randomised to:

200 mg once weekly
or
200 mg twice weekly

IGF-I & GH assay

IDS iSYS

Bidlingmaier
JCEM 2014 99 1712



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End-Points

Results presented pending confirmation after database lock

Efficacy

Primary

The percentage change in IGF-I at week 14

Secondary

% of patients with a normal IGF-I at week 14

% of patients with a normal IGF-I at anytime

Changes in GHBP, BP-3, ALS & IGF-II

Changes in AcroQoL, S&S, size of ring finger

Changes in GH, insulin & glucose

Patients

	200 mg once weekly	200 mg twice weekly
N	13	13
Age	48 ± 14	53 ± 17
Gender (M/F)	5/8	6/7
Weight (kg)	97 ± 20	85 ± 25
Prior RT	6 (46%)	5 (38%)
Prior Surgery	13 (100%)	12 (92.3%)

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Results – Safety End Point

	200 mg once weekly	200 mg twice weekly
Withdrawals	1	1
Reason for withdrawal	withdrew consent after last drug dose	withdrew consent after last drug dose
Serious AE	3 (1 patient) - unlikely drug related	1 – not related to drug
Treatment Emergent AE	131 (11 patients)	178 (11 patients)
Patients with ISR	10 (76.9%)	11 (84.6%)
Mild	8	6
Moderate	2	5
Severe	0	0

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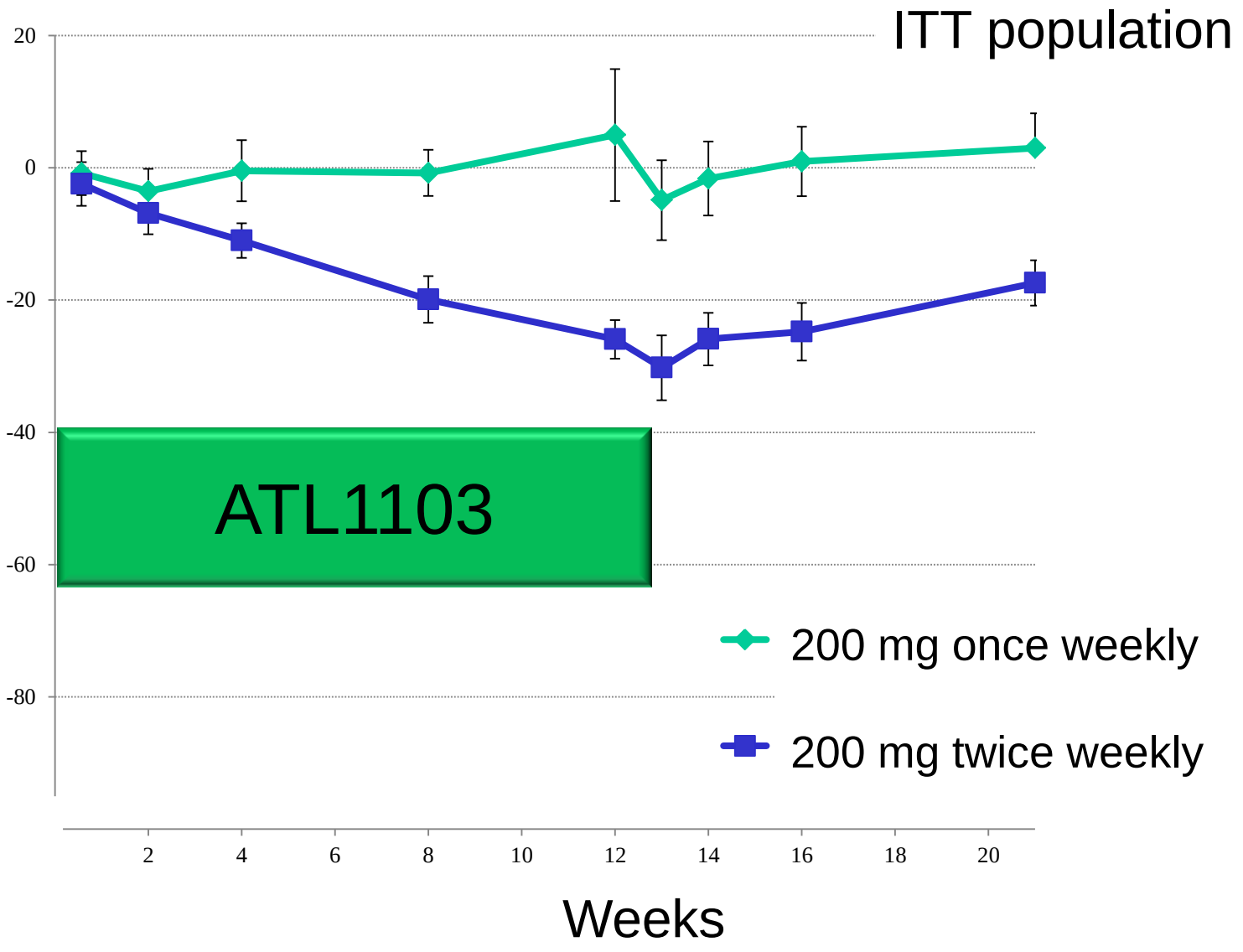
Treatment-Emergent Adverse Events with more than two occurrences

	Regimen 1 (N=13)	Regimen 2 (N=13)	Total (N=26)
	n N (%)	n N (%)	n N (%)
INJECTION SITE ERYTHEMA	11 6 (46.2%)	28 4 (30.8%)	39 10 (38.5%)
INJECTION SITE PRURITUS	3 3 (23.1%)	25 4 (30.8%)	28 7 (26.9%)
INJECTION SITE REACTION (unspecified)	12 2 (15.4%)	11 3 (23.1%)	23 5 (19.2%)
INJECTION SITE PAIN	5 4 (30.8%)	6 3 (23.1%)	11 7 (26.9%)
INJECTION SITE BRUISING	5 2 (15.4%)	4 3 (23.1%)	9 5 (19.2%)
INJECTION SITE SWELLING	0 0	6 3 (23.1%)	6 3 (11.5%)
INJECTION SITE IRRITATION	1 1 (7.7%)	4 2 (15.4%)	5 3 (11.5%)
INJECTION SITE MASS	1 1 (7.7%)	3 2 (15.4%)	4 3 (11.5%)
HEADACHE	21 5 (38.5%)	5 3 (23.1%)	26 8 (30.8%)
ARTHRALGIA	4 3 (23.1%)	4 1 (7.7%)	8 4 (15.4%)
RASH	3 1 (7.7%)	5 2 (15.4%)	8 3 (11.5%)
FATIGUE	3 2 (15.4%)	4 3 (23.1%)	7 5 (19.2%)
CONSTIPATION	3 2 (15.4%)	2 2 (15.4%)	5 4 (15.4%)
DIARRHOEA	3 2 (15.4%)	2 2 (15.4%)	5 4 (15.4%)
HYPERHIDROSIS	1 1 (7.7%)	4 2 (15.4%)	5 3 (11.5%)
LETHARGY	0 0	4 1 (7.7%)	4 1 (3.8%)
PARAESTHESIA	4 1 (7.7%)	0 0	4 1 (3.8%)
URINARY TRACT INFECTION	3 2 (15.4%)	0 0	3 2 (7.7%)
DIZZINESS	0 0	3 2 (15.4%)	3 2 (7.7%)

Change in IGF-I with 13 weeks of ATL1103



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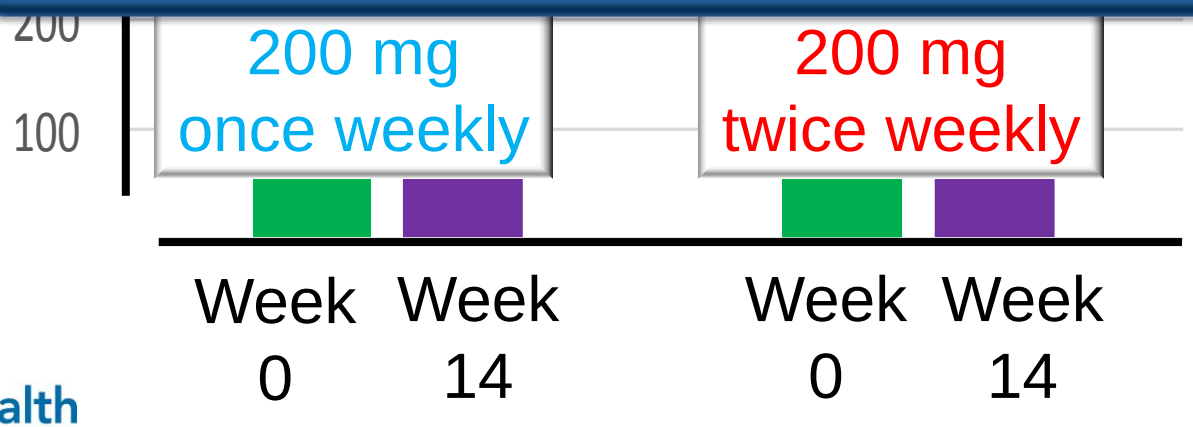
Change in IGF-I with 13 weeks of ATL1103

mean

IGF-
(ng/m

Rate of IGF-I normalisation

	200 mg once weekly	200 mg twice weekly
Week 14	1	1
Anytime	1	2 (15.4%)



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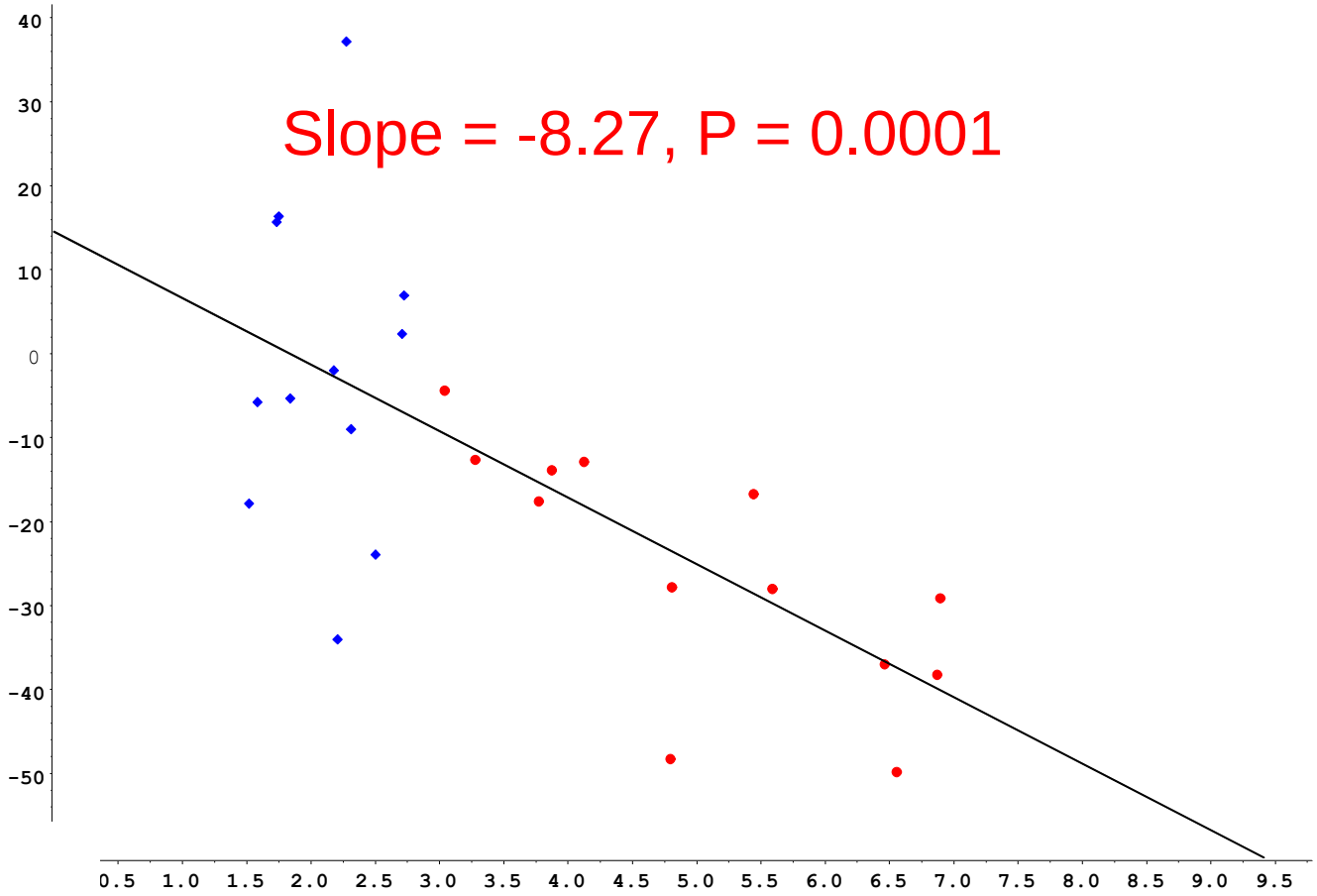
Scatterplot of % change in IGF-I vs dose/kg

- ATL1103 200 mg/wk
- ATL1103 400 mg/wk



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Scatterplot of % change in IGF-I vs dose/kg

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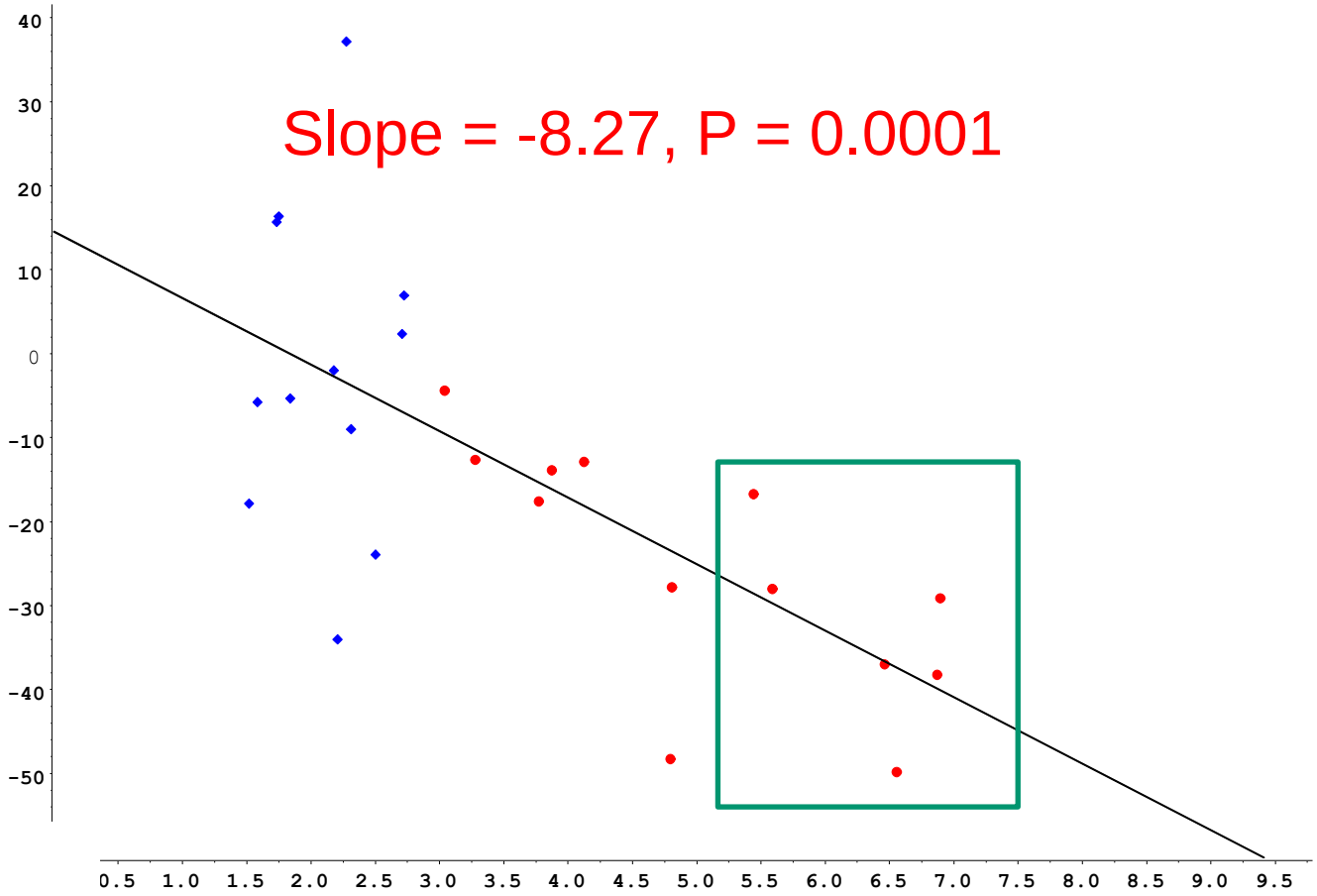

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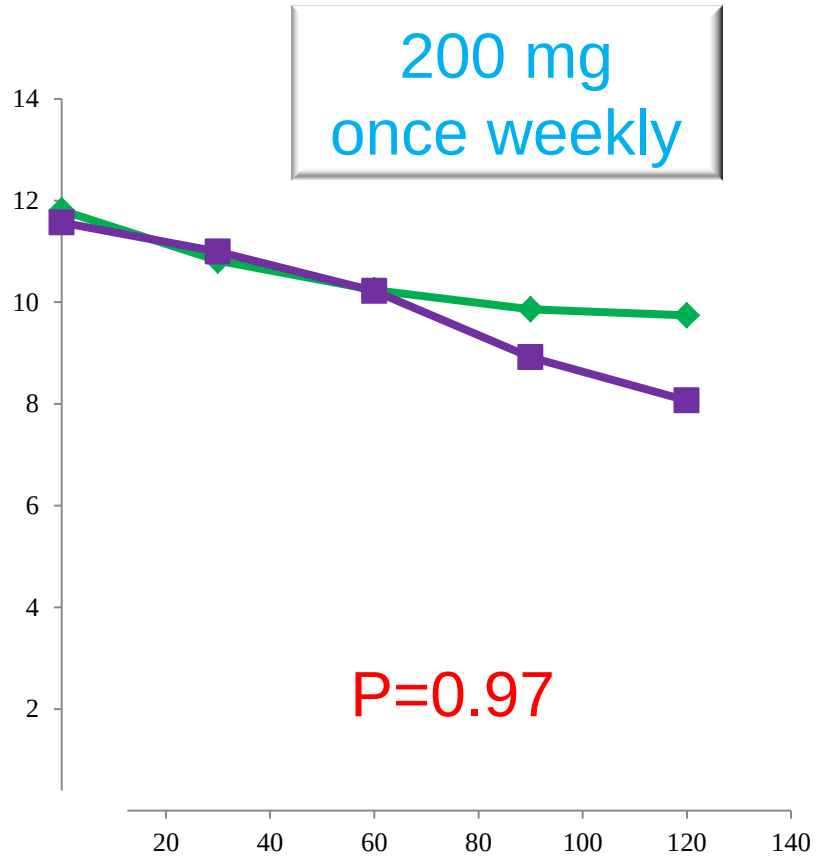
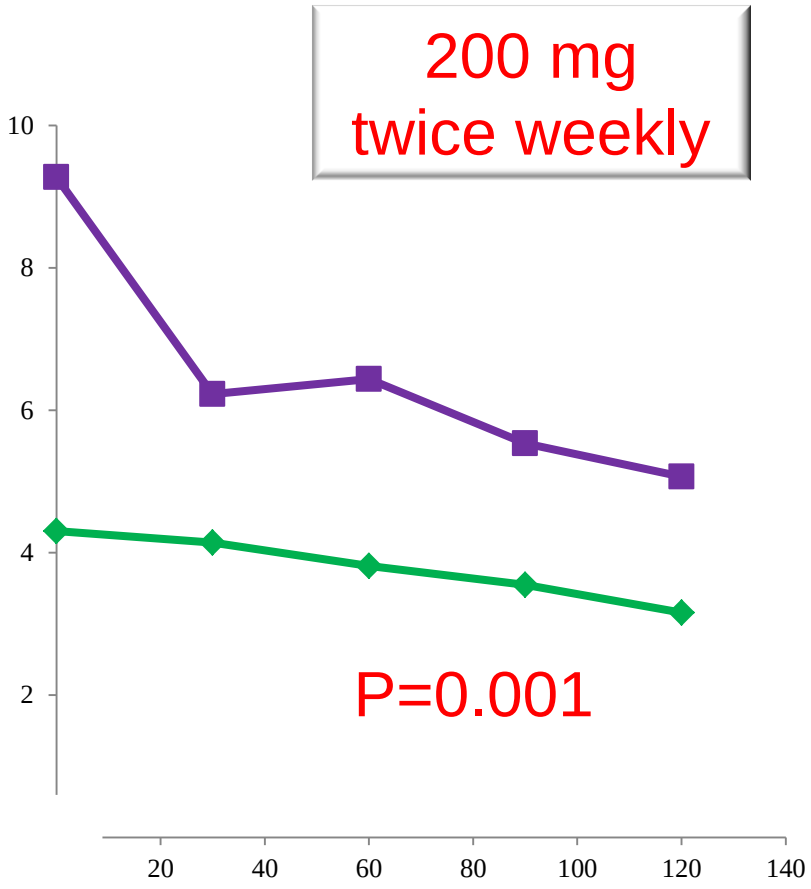
GH levels during a 75 gm oral glucose tolerance test





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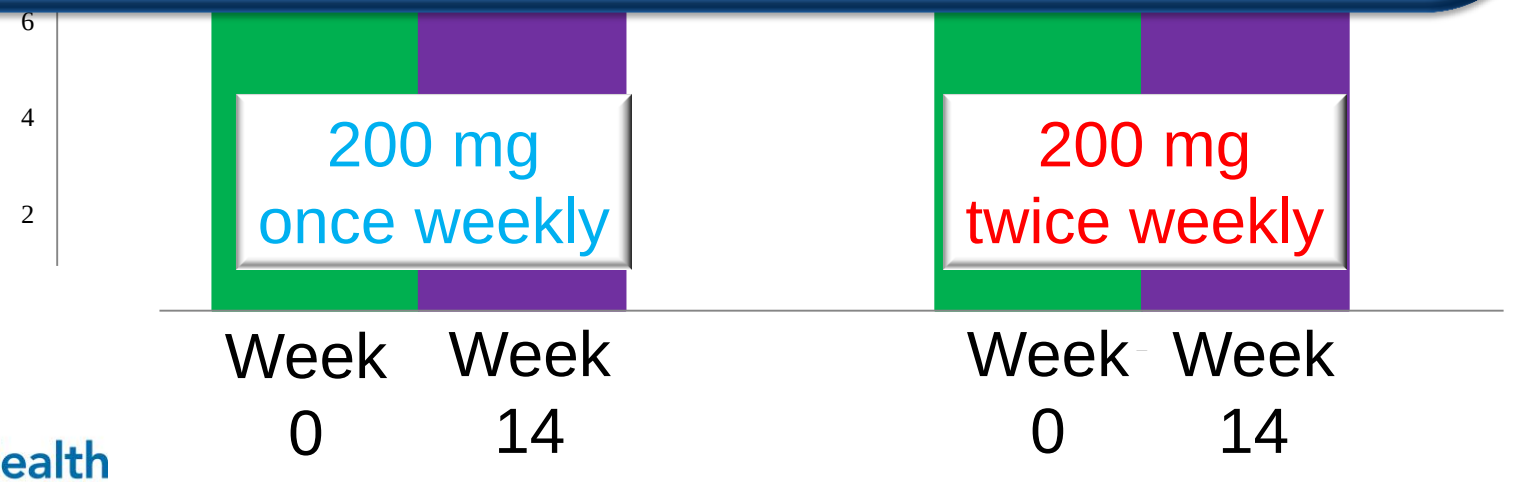
Change in Signs & Scores with ATL1103

Ring size	200 mg once weekly	200 mg twice weekly
Mean change	-0.62	-0.92
	P=0.17	P=0.02

S&



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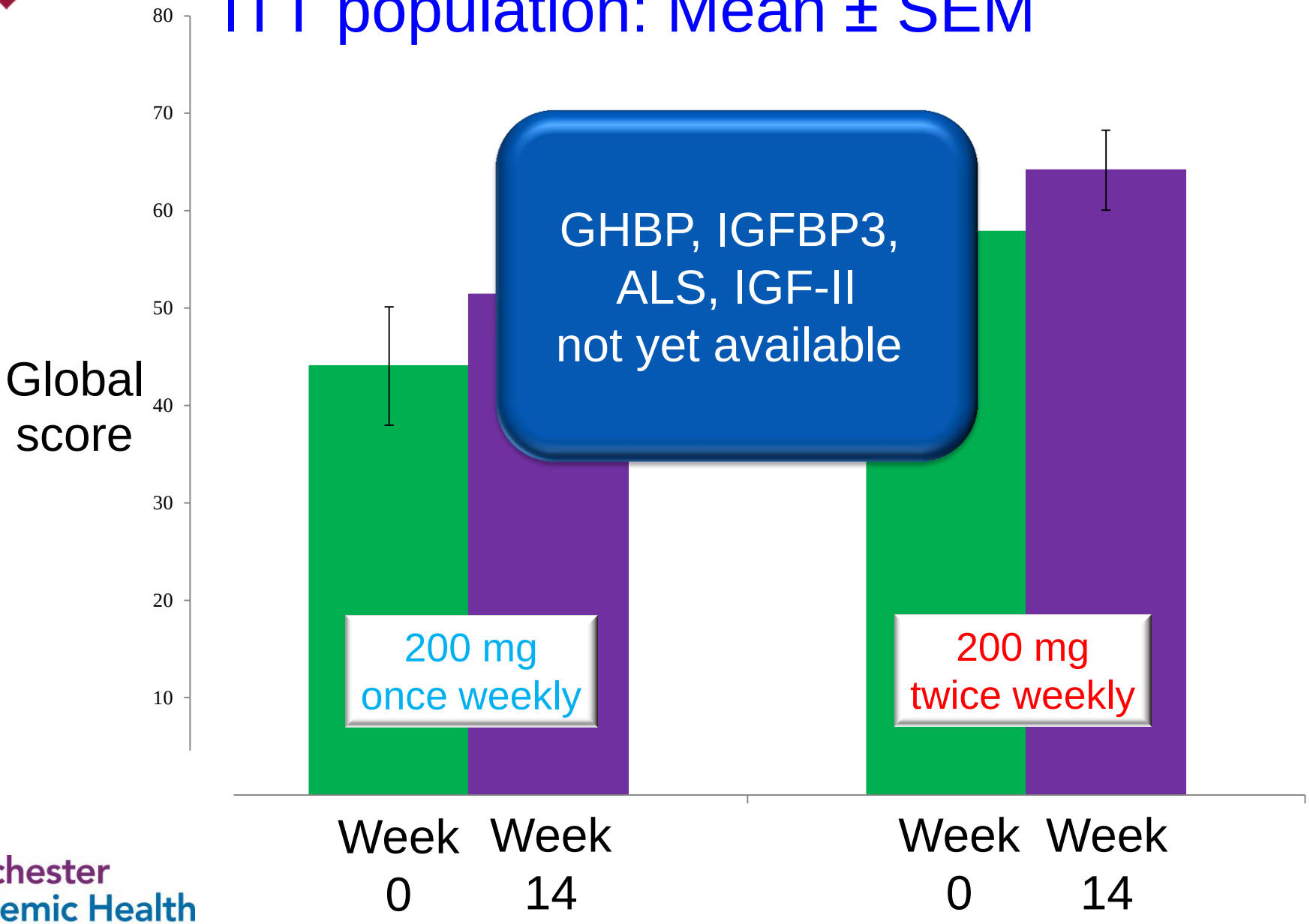
AcroQol: Global score
ITT population: Mean ± SEM



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Summary: Safety endpoints

No patient withdrawals or SAEs related to ATL1103

Well tolerated

Injections site reactions most reported adverse event (AE):

- all mild to moderate

No flu-like symptoms

Liver enzymes elevations in two patients

Transient platelet reductions in one patient

Positive safety profile suggests ATL1103 may be tolerated at higher doses

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Summary: Efficacy endpoint (IGF-I)

200 mg once weekly for 13 weeks did not result in a change in mean IGF-I

2 x 200 mg/week ATL1103

26% mean reduction of IGF-I one week after 13 weeks (P <0.0001)

IGF-I had not reached nadir by week 13

IGF-I “normalised” in two patients

Dose-response relationship with ATL1103 (mg/kg/week) *vs* change in IGF-I

Conclusions

The data indicate that a larger dose of ATL1103 administered for longer should be well tolerated and result in normalisation of IGF-I in a significant number of patients with acromegaly

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Antisense Therapeutics Ltd

ASX:ANP

Investor Update – October 2014

Forward Looking Statements

This presentation contains forward-looking statements regarding the Company's business and the therapeutic and commercial potential of its technologies and products in development. Any statement describing the Company's goals, expectations, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, particularly those risks or uncertainties inherent in the process of developing technology and in the process of discovering, developing and commercializing drugs that can be proven to be safe and effective for use as human therapeutics, and in the endeavor of building a business around such products and services. Actual results could differ materially from those discussed in this presentation. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the Antisense Therapeutics Limited Annual Financial Report for the year ended 30 June 2014 copies of which are available from the Company or at www.antisense.com.au.

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Antisense Therapeutics Ltd

- ✓ Long standing strategic collaboration with Isis Pharmaceuticals Inc, world leaders in antisense drug development (Isis partnered with GSK, Pfizer, Genzyme, Biogen Idec)
- ✓ Isis collaboration provides ANP with access to ribonucleic acid (RNA) targeted antisense drugs (ATL1103 for acromegaly, ATL1102 for MS, ATL1101 for cancer)
- ✓ Renewed global interest in RNA targeted technologies from investors and Big Pharma Co's
- ✓ ANP developing drugs for diseases with large unmet medical need and with potential significant competitive advantages based on the Isis 2nd generation antisense technology
- ✓ Advanced development pipeline for multiple disease applications including Acromegaly, Multiple Sclerosis, and Cancer
- ✓ **Only Australian Biotech company with two drugs with positive Phase II clinical data**

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Key Achievements 2014

- ATL1103 for Acromegaly
  - ✓ *Phase 2 clinical trial – completion of trial and reporting of successful efficacy results*
  - ✓ *Positioned to move into Phase III stage of development with partner*
  - ✓ *Phase II data presented at International Scientific Congress by Chief Investigator*
  - ✓ *Canadian patent granted*
- ATL1102 for MS
  - ✓ *Request submitted for US FDA Pre-IND assessment for a Phase 2b clinical trial*
  - ✓ *ATL1102 Phase 2a MS trial results published in the leading Medical Journal Neurology*
  - ✓ *US and EU patent allowances*
- Corporate
  - ✓ *Engaged US-based Advisory firm Destum Partners to advance project partnering plans*
  - ✓ *Strengthened Balance sheet with Capital Raising and receipt of R&D Tax credit*

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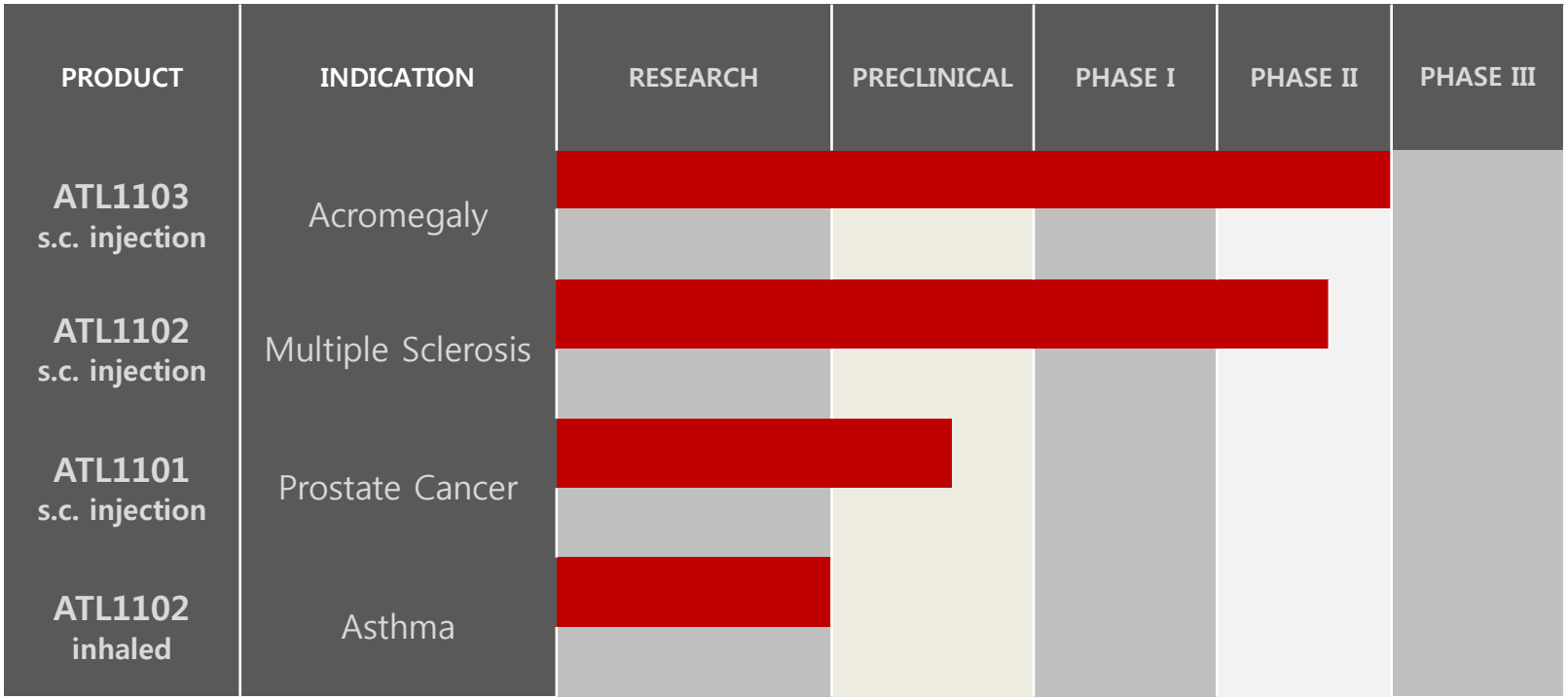
Pipeline Program



- ✓ Pipeline drugs are all antisense compounds via the Isis collaboration

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ATL1103 improving on current treatments

Comparing second line therapy Somavert® to ATL1103 est. sales of > US$200m/year

Pegvisomant (Somavert®)	ATL1103 Target Product Profile (TPP)
In clinical trial effective in greater % of patients in normalising sIGF-I than somatostatins	✓ Broad based efficacy like Somavert
Average treatment cost of $60K/annum (up to $90K/annum)	✓ Lower cost of therapy due to less expensive cost of manufacture
Limited by high cost, inconvenient administration • lyophilized powder requiring reconstitution and daily dosing regimen	✓ More convenient dosing/administration regimen • prefilled syringe; once/twice weekly dosing for improved patient compliance

- Low Somavert® market penetration (est. ~25% of 1st line treatment failures) likely due to high cost, inconvenient administration, and daily dosing
- ATL1103 has potential to convert share from Somavert® and for use with currently untreated patients

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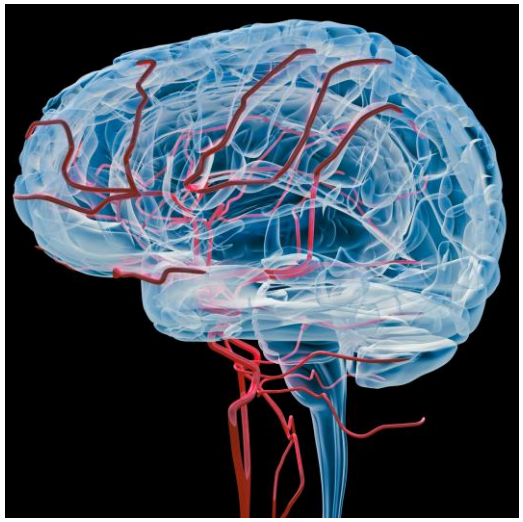
ATL1102 for Multiple Sclerosis

Multiple Sclerosis (MS) is a chronic, progressive, and debilitating autoimmune disease that affects central nervous system, brain and spinal cord



- Affects 400,000 people in the U.S. and > 2.1 million worldwide
- Global sales for MS drugs in 2013 were US$14 Billion
- ATL1102 is an antisense inhibitor of VLA-4 protein a clinically validated target in MS by drug Tysabri® (monoclonal antibody drug to same target)
- Tysabri® current efficacy benchmark (most potent) for treatment of RR-MS; 2013 sales of US$1.6 Billion
- Tysabri® can cause a potential lethal viral brain infection - progressive multi focal leukoencephalopathy (PML)

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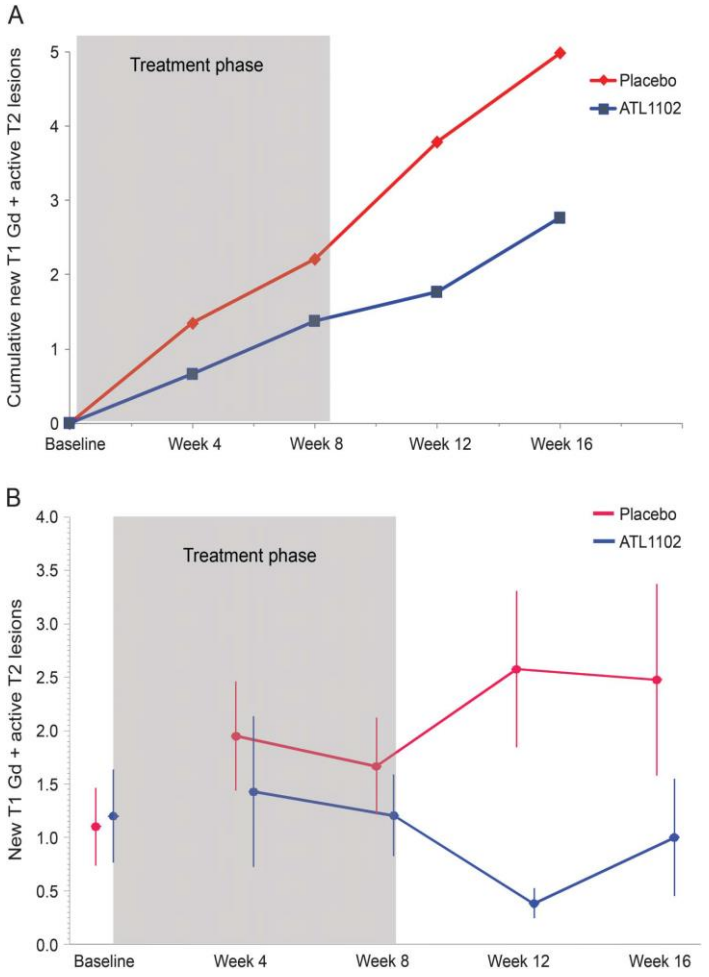
ATL1102 for Multiple Sclerosis

ATL1102 Development status

- Successful Phase 2a trial completed in patients with Relapsing Remitting-MS
- Met primary end point after only two months of dosing reducing the cumulative number of new active brain lesions by 54.4% (p=0.01) compared to placebo
- ATL1102 demonstrated comparable/potentially superior activity to Tysabri® at same stage development
- Results recently published in the Journal of the American Academy of Neurology

(A) Cumulative number of new active lesions and (B) number of new active lesions



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ATL1102 Opportunity in MS

ATL1102 has the potential to be well differentiated from Tysabri®

Parameter	ATL1102	Tysabri®
Efficacy	✓ Highly potent	✓ Highly potent
Safety	✓ Well tolerated	Safety concerns
Route of administration	✓ Self-administered	IV infusion
Manufacturing	✓ Less expensive	More expensive

New US and EU patents granted to 2029 and potentially extendable to 2034

Next step - potential Phase 2b study of ATL1102 in MS patients

FDA Pre-IND assessment of ANP's Phase 2b clinical trial design: Goal date was 17 October 2014

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Corporate Structure

Key Financials	
Market Capitalisation	A$16 million
Cash as at 30 June 2014 *	A$1.3 million
Ordinary shares on Issue	152 million
Share price	$0.105

Top 5 Shareholders		%
CIRCADIAN TECHNOLOGIES	14,331,583	9.4%
LEON SERRY & ASSOCIATED COMPANIES	6,512,794	4.3%
MR J & MRS C CONSTABLE	5,890,000	3.9%
ISIS PHARMACEUTICALS INC	5,880,833	3.9%
CITICORP NOMINEES PTY LIMITED	2,766,736	1.8%

*** Capital Position (post 30 June)**

- ✓ Share Placement - $840K - September
- ✓ R&D Tax Incentive - $1.14M - October
- ✓ Board participation in placement - $100K - November
- ✓ Share Purchase Plan - $1.5M - November

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Top 20 Shareholders as at 17 October	
POLYCHIP PHARMACEUTICALS PTY LTD	10,190,649
ISIS PHARMACEUTICALS INC	5,880,833
MR JASON ERIC CONSTABLE & MRS CATHERINE CONSTABLE	5,500,000
SYNGENE LIMITED	4,140,934
CITYCASTLE PTY LTD	3,949,999
CITICORP NOMINEES PTY LIMITED	2,766,736
BAYSPEC PTY LTD	2,400,000
SKED PTY LTD <SUPER FUND A/C>	2,289,462
FLINTBERG PTY LTD <OR SUPERANNUATION FUND A/C>	2,027,500
MRS LORRAINE SANDRA MOSES	1,600,000
MR NORMAN CHI WING TANG & MRS TERESA KIT CHING TANG	1,350,000
SYED CORPORATION PTY LTD	1,162,179
MR MICHAEL ANDREW CLARK	1,114,938
MR LESLIE SMITH	1,100,000
MR MARK DIAMOND	1,053,567
MR JAMES EDWARDS	1,051,500
DR HUY TRAN	1,016,000
ARMDIG PTY LTD	1,000,000
MR LARRY HUI	1,000,000
DABCO HOLDINGS PTY LTD	925,000

Share Purchase Plan (SPP)

- The Company intends to raise approximately A$1.5 million via the SPP (first $1 million underwritten)
- The purpose of the SPP is to provide eligible shareholders with the opportunity to invest in ANP ordinary shares at the same offer price as the recent placement, without brokerage or other transaction costs
- The capital raised under the placement and the SPP will be utilised to progress partnering plans for ATL1103 for acromegaly, FDA interactions on a potential Phase IIb study for ATL1102 for MS, and the planned higher dose clinical trial of ATL1103 in acromegalic patients

Timetable

Event	Date
Record date of SPP	Wednesday 24 September 2014
Announcement of the SPP	Thursday 25 September 2014
Opening date for the SPP and Mail out of SPP Documentation	Tuesday 7 October 2014
Closing Date of the SPP	Friday 31 October 2014
Annual General Meeting of Shareholders	Thursday 6 November 2014
Allotment and Issue of SPP Shares	10am (AEDST) Wednesday 12 November 2014

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Investment Highlights

- ✓ RNA based technologies continuing to see investor and Big Pharma interest
- ✓ Commercialising platform technology with world leader in RNA therapeutics, Isis Pharmaceuticals
- ✓ Antisense technology validation provided by successful clinical progress (1 drug on market and 32 drugs in development) and licensing deals with Big Pharma
- ✓ 2 advanced development programs with significant commercial potential
  - ***ATL1103 in Acromegaly***
    - *Primary efficacy endpoint met in Phase II clinical trial*
    - *Discussions underway with potential partners for Phase III development*
  - ***ATL1102 in MS***
    - *Successful Phase 2a trial in RR-MS patients – results recently published in leading Scientific Journal NEUROLOGY*
    - *FDA's Pre-IND assessment of ANP's proposed Phase 2b clinical trial design – FDA written response due any time now!*

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