

Cover Page



Universiteit Leiden



The handle <http://hdl.handle.net/1887/30244> holds various files of this Leiden University dissertation.

Author: Claessen, Kim Maria Johanna Aldegonda

Title: Pathophysiology of the GH/IGF-1 axis : long-term consequences on joints and bone

Issue Date: 2014-12-17

PATHOPHYSIOLOGY OF THE GH / IGF-I AXIS:

Long-term consequences on joints and bone

Kim M.J.A. Claessen

PROEFSCHRIFT
ter verkrijging van
de graad van Doctor aan de Universiteit Leiden
op gezag van Rector Magnificus Prof. mr. C.J.J.M. Stolk
volgens besluit van het College voor Promoties
te verdedigen op woensdag 17 december 2014
klokke 16:15 uur

DOOR
Kim Maria Johanna Aldegonda Claessen
Geboren te Roosendaal
In 1989

The studies described in this thesis were performed at the Department of Endocrinology & Metabolism in collaboration with the Departments of Rheumatology, Radiology and Molecular Epidemiology of the Leiden University Medical Center, Leiden, The Netherlands

ISBN

Author Kim M.J.A. Claessen
Cover design & lay-out Jelmer Buurma (*ep.buurma@gmail.com*)
Cover image Photographer: Paul. C. Johannesma. With special thanks to one of our acromegaly patients.
Printed by Gildeprint Drukkerijen, Enschede, The Netherlands

Copyright © 2014, Kim Maria Johanna Aldegonda Claessen, Amsterdam, The Netherlands

All rights reserved. No part of this thesis may be reproduced, stored in a retrieval system of any nature, or transmitted in any form or by any means without prior permission of the author.

For publication of this thesis financial support of Ferring B.V., Pfizer B.V., Novartis Pharma B.V., Novo Nordisk B.V., Ipsen Farmaceutica B.V., Sanofi-Aventis Netherlands B.V., ABN AMRO and the Dept. of Endocrinology & Metabolism is gratefully acknowledged.

PROMOTIECOMMISSIE

Promotores Prof. dr. A.M. Pereira
Prof. dr. M. Kloppenburg

Copromotor Dr. N.R. Biermasz

Overige leden Prof. dr. J.A. Romijn (*AMC, Amsterdam*)
Prof. dr. A.J. van der Lely (*EMC, Rotterdam*)
Prof. dr. H. Pijl
Prof. dr. A.J. Rabelink

Appelboompjes

*Voller wordend met de dagen,
vastgegroeid in 't ogenblik,
bestemd, mijn zustertjes, – als ik –
te wortelen, rijpen en vrucht te dragen.*

M. Vasalis (1909-1998)

TABLE OF CONTENTS

Chapter I	General Introduction & Outline of Thesis	10	Part C: Long-term outcome of recombinant human GH therapy in GH deficient adults		
Part A: Long-term effects of acromegaly on joints and bone					
Chapter II	Progression of acromegalic arthropathy despite long-term biochemical control: a prospective, radiological study.	44	Chapter X	Therapy of Endocrine Disease: Long-term effects of recombinant human Growth Hormone (rhGH) replacement in adults with Growth Hormone Deficiency (GHD): a Systematic Review.	206
Chapter III	Increased clinical symptoms of acromegalic arthropathy in patients with long-term disease control: a prospective follow-up study.	66	Chapter XI	Metabolic profile in Growth Hormone Deficient (GHD) adults after long-term recombinant human Growth Hormone (rhGH) therapy.	240
Chapter IV	Acromegalic arthropathy in various stages of the disease: a Magnetic Resonance Imaging (MRI) study.	86	Chapter XII	Abnormal metabolic profile in middle-aged GH-deficient adults despite long-term recombinant human GH replacement.	260
Chapter V	Two phenotypes of arthropathy in long-term controlled acromegaly? A comparison between patients with and without joint space narrowing (JSN).	112	Chapter XIII	Effects of up to 15 years of recombinant human GH (rhGH) replacement on bone metabolism in adults with Growth Hormone Deficiency (GHD): The Leiden Cohort Study.	280
Chapter VI	Progression of vertebral fractures despite long-term biochemical control of acromegaly: a prospective follow-up study.	130	Chapter XIV	General Discussion & Summary	302
Part B: The role of the GH / IGF-I axis in primary OA					
Chapter VII	Relationship between Insulin-like Growth Factor-1 and radiographic disease in patients with primary osteoarthritis: a Systematic Review.	152	Chapter XV	Nederlandse samenvatting	320
Chapter VIII	High serum Insulin-like Growth Factor-1 (IGF-1) levels are associated with the presence of primary osteoarthritis, but not with radiographic progression: the GARP Study.	172	Curriculum Vitae		334
Chapter IX	Relationship between the functional exon 3 deleted growth hormone receptor polymorphism and symptomatic osteoarthritis in women.	186	List of published abstracts		336
			List of scientific publications		338
			Appendices		340
			Dankwoord		