

Hot Articles

“March|2017”

Health Science



Title: [Alternative Treatment Regimens With the PCSK9 Inhibitors Alirocumab and Evolocumab: A Pharmacokinetic and Pharmacodynamic Modeling Approach](#)

Author: Nina Scherer, Christiane Dings, Michael Böhm, Ulrich Laufs and Thorsten Lehr

Journal: The Journal of Clinical Pharmacology

Volume: Early View 6 March 2017

Doi: 10.1002/jcph.866

Abstract

Alirocumab and evolocumab are 2 human monoclonal antibodies that inhibit the proprotein convertase subtilisin/kexin type 9 (PCSK9). These antibodies can potentially lower low-density lipoprotein cholesterol (LDLc) serum concentrations. The aims of this analysis were to develop a pharmacokinetic (PK) and pharmacodynamic (PD) model for both antibodies, to simulate and investigate different dosage and application regimens, and finally, to note the effects on LDLc levels. Alirocumab was clinically studied and approved with 2 doses, 75 and 150 mg every 2 weeks (Q2W), whereas evolocumab was tested and approved with 2 dosing intervals, 140 mg Q2W and 420 mg Q4W. Data were digitized from published studies describing alirocumab and evolocumab PK, as well as LDLc levels in humans for various single and multiple doses. Alirocumab dosages ranged between 75 and 300 mg and evolocumab from 7 to 420 mg. The analysis was performed using a nonlinear mixed-effects modeling technique. A 2-compartment model with first-order absorption and saturable elimination described the PK of both antibodies best. LDLc levels were described by a turnover model with zero-order synthesis rate decreased by the antibodies and a first-order degradation rate that was increased by the antibodies. Simulations show a comparable effectiveness for alirocumab 75 mg Q2W and 150 mg Q3W as well as evolucmab 140 mg Q2W and 420 mg Q5W, respectively. This is the first PK/PD model describing the link between alirocumab and evolocumab PK and LDLc concentrations. The model may serve as an important tool to simulate different dosage regimens in order to optimize therapy.

Database

Wiley Online Library

Title: [Cost-utility analysis of methylphenidate and amphetamine/dexamphetamine in adults with attention-deficit hyperactivity disorder](#)

Author: Surbhi Shah, Hongye Wei, Jayani Jayawardhana, Matthew Perri, Ewan Cobran and Henry N. Young

Journal: Journal of Pharmaceutical Health Services Research

Volume: Version of record online: 5 March 2017

Doi: 10.1111/jphs.12173

Abstract

Objectives

Methylphenidate (MPH) and amphetamine/dexamphetamine (AMP/DEX) are the two most common stimulants used to treat attention-deficit hyperactivity disorder (ADHD). Previous economic evaluations of these treatments mainly focused on children and adolescents. The objective of this study was to conduct a cost-utility analysis of MPH and AMP/DEX treatments in adults with ADHD.

Methods

This study was conducted from a third-party payer perspective using the Medical Expenditure Panel Survey from 2011 to 2013. Patients taking MPH or AMP/DEX were identified from the Prescribed Medicines files. The Short Form-12 version 2 questionnaire scores were used to calculate quality-adjusted life years (QALYs). Only direct costs were evaluated from payer's perspective. Incremental cost-utility ratios were calculated, and sensitivity analyses were performed to assess the robustness of the findings at different willingness to pay (WTP) assumptions.

Key findings

Of 305 patients, 68.8% were in the AMP/DEX group and 31.2% were in MPH group. The mean annual cost for the MPH group was \$4355.31, and the cost for the AMP/DEX group was \$6026.40. The mean utilities for MPH and AMP/DEX groups were 0.622 and 0.598 respectively. Sensitivity analyses showed that MPH exceeded AMP/DEX at all WTP values.

Conclusion

Methylphenidate was clearly a dominating therapy over AMP/DEX; however, the QALY difference was found to be 0.024. Further research is needed to assess the long-term impact of using these treatments on various clinical and economic outcomes.

Database

Wiley Online Library

Title: [Role of Wnt/ \$\beta\$ -catenin Signaling Regulatory microRNAs in the Pathogenesis of Colorectal Cancer](#)

Author: Farzad Rahmani, Amir Avan, Seyed Isaac Hashemy and Seyed Mahdi Hassanian

Journal: Journal of Cellular Physiology

Volume: Accepted manuscript online: 7 MAR 2017 06:41AM EST

Doi: 10.1002/jcp.25897

Abstract

Colorectal cancer (CRC) is one of the leading causes of cancer death worldwide. In more than 90% of all CRC patients, the master oncogenic Ras-Wnt signaling axis is over-activated. MicroRNAs (miRNAs) are potential novel diagnostic and prognostic biomarkers as well as therapeutic targets for several cancers including lung, breast, gastric and colorectal cancers. Oncogenic or tumor suppressor miRNAs modulate tumor cells proliferation, cell cycle progression, angiogenesis, invasion and metastasis through regulating oncogenic pathways including Wnt/ β -catenin signaling. This review summarizes the current knowledge about the role of Wnt/ β -catenin signaling regulatory miRNAs in the pathogenesis of colorectal cancer for a better understanding and hence a better management of this disease. This article is protected by copyright. All rights reserved

Database

Wiley Online Library

Title: [Improving medication adherence through calendar packaging: results of a randomized controlled trial among hypertensive patients](#)

Author: Bee Ying Tan, Asrul Akmal Shafie, Mohamed Azmi Ahmad Hassali, Fahad Saleem and Jaya Muneswarao

Journal: Journal of Pharmaceutical Health Services Research

Volume: Version of Record online: 2 MAR 2017

Doi: DOI: 10.1111/jphs.12171

Abstract

Objective

This study aimed to investigate the effect of calendar packaging (CP) on medication adherence among hypertensive patients in Malaysia.

Setting

Outpatient Pharmacy Department, Kulim Hospital.

Methods

This was a parallel randomized controlled trial of CP (intervention group) versus normal pack (control group) for patients who were on daily dose antihypertensive drug (amlodipine). The primary outcome was medication adherence to amlodipine, assessed by medication possession ratio (MPR), percentage of on-time refills and Malay Version Morisky medication adherence scales.

Key findings

Eighty-three patients participated. The mean age (standard deviation) was 55.85 (10.25) and 56.55 (10.42) for intervention and control group respectively. This study found that intervention group has better medication adherence score than the control group measured by MPR, Morisky medication adherence score ($P < 0.05$) and percentage of on-time refills ($P < 0.01$). Intervention group showed a significantly lower systolic and diastolic blood pressure ($P < 0.05$) compared to control group. Intervention group was significantly associated with higher medication adherence measured by MPR ($\beta = 0.006$, $P < 0.05$), Morisky scale ($\beta = 0.365$, $P < 0.05$) and percentage of on-time refill ($\beta = 0.063$, $P < 0.01$); in addition lower systolic blood pressure ($\beta = -4.4$, $P < 0.05$) after controlling for the study period and patient age.

Conclusions

This study found that CP could improve adherence to medication among hypertensive patients. The results also suggest possible improvement in blood pressure with the use of CP.

Database

Wiley Online Library

Title: [Palatability of a novel oral formulation of prednisone in healthy young adults](#)

Author: Shasha Bai, Nathan Dormer, Catherine Shoults, Amanda Meyer, Carol D. Pierce, Kathleen A. Neville and Gregory L. Kearns

Journal: Journal of Pharmacy and Pharmacology

Volume: Version of Record online: 8 MAR 2017

Doi: 10.1111/jphp.12710

Abstract

Objectives

Prednisone is a widely used anti-inflammatory for a variety of conditions. While oral liquid formulations of prednisone enable weight-based dosing, children frequently find them to be objectionable due to bitter taste. This limitation of prednisone can adversely impact patient acceptance and may result in non-compliance. Efforts to mask flavours often result in poorly controlled, heterogeneous particle distributions and can provide ineffective taste masking. The present work utilized a novel drug delivery technology developed by Orbis Biosciences, Inc., to create an oral taste-masked formulation of prednisone.

Methods

The study examined the palatability of Orbis' microsphere prednisone formulation in healthy young adults (n = 24). Four test articles were used in the study including a reference formulation (Roxanne Laboratories), a control and the test formulation (Orbis) prepared in two different ways. Study participants were randomized in a crossover design.

Key findings

Results indicated that the test prednisone formulation was indistinguishable from the control, and both were preferable to the reference formulation in every category of palatability assessed using a validated 9-point Hedonic Scale. The data also suggested that preparing the microsphere suspension immediately before administration results in the most ideal palatability properties.

Conclusions

In conclusion, the novel microsphere formulation technology was effective in taste-masking prednisone.

Database

Wiley Online Library

Title: [The protective effects of social bonding on behavioral and pituitary-adrenal axis reactivity to chronic mild stress in prairie voles](#)

Author: Neal McNeal, Katherine M. Appleton, Alan Kim Johnson, Melissa-Ann L. Scotti, Joshua Wardwell, Rachel Murphy, Christina Bishop, Alison Knecht & Angela J. Grippo

Journal: Stress

Volume: Published online: 05 Mar 2017

Doi: 10.1080/10253890.2017.1295444

Abstract

Positive social interactions may protect against stress. This study investigated the beneficial effects of pairing with a social partner on behaviors and neuroendocrine function in response to chronic mild stress (CMS) in 13 prairie vole pairs. Following 5 days of social bonding, male and female prairie voles were exposed to 10 days of CMS (mild, unpredictable stressors of varying durations, for instance, strobe light, white noise, and damp bedding), housed with either the social partner (paired group) or individually (isolated group). Active and passive behavioral responses to the forced swim test (FST) and tail-suspension test (TST), and plasma concentrations of adrenocorticotrophic hormone (ACTH) and corticosterone, were measured in all prairie voles following the CMS period. Both female and male prairie voles housed with a social partner displayed lower durations of passive behavioral responses (immobility, a maladaptive behavioral response) in the FST (mean \pm SEM; females: 17.3 ± 5.4 s; males: 9.3 ± 4.6 s) and TST (females: 56.8 ± 16.4 s; males: 40.2 ± 11.3 s), versus both sexes housed individually (females, FST: 98.6 ± 12.9 s; females, TST: 155.1 ± 19.3 s; males, FST: 92.4 ± 14.1 s; males, TST: 158.9 ± 22.0 s). Female (but not male) prairie voles displayed attenuated plasma stress hormones when housed with a male partner (ACTH: 945 ± 24.7 pg/ml; corticosterone: 624 ± 139.5 ng/ml), versus females housed individually (ACTH: 1100 ± 23.2 pg/ml; corticosterone: 1064 ± 121.7 ng/ml). These results may inform understanding of the benefits of social interactions on stress resilience.

Lay Summary: Social stress can lead to depression. The study of social bonding and stress using an animal model will inform understanding of the protective effects of social bonds. This study showed that social bonding in a rodent model can protect against behavioral responses to stress, and may also be protective against the elevation of stress hormones. This study provides evidence that bonding and social support are valuable for protecting against stress in humans.

Database

Taylor & Francis Online Journal

Title: [Mental-health and educational achievement: the link between poor mental-health and upper secondary school completion and grades](#)

Author: Annica Brännlund, Mattias Strandh & Karina Nilsson

Journal: Journal of Mental Health

Volume: Published online: 07 Mar 2017

Doi: 10.1080/09638237.2017.1294739

Abstract

Background: Education profoundly affects adult socioeconomic status, so it is important to ensure that all children have the capability and opportunity to achieve educational goals.

Aims: The study aimed to examine the relationship between mental-health during adolescence and upper secondary school completion and grades, which has received comparatively little research attention to date.

Method: Longitudinal administrative and registered data were used to analyse the relationship between school achievement and prescriptions of psycholeptic and psycho-analeptic drugs. The sample consisted of all children born in Sweden in 1990 (n = 109 223), who were followed from birth to age 20. Logistic and OLS regressions were performed separately for boys and girls, controlling for birth health and family characteristics.

Results: A negative relationship between mental-health problems and educational outcomes was found; this result was almost independent of the controls. Only minor differences between the sexes were detected.

Conclusions: Poor mental-health during childhood correlated negatively with educational attainment. Given the strong link between educational success and adult life, more resources are needed to support children with mental-health problems.

Database

Taylor & Francis Online Journal

Title: [Intestinal Micropatches for Oral Insulin Delivery](#)
Author: Amrita Banerjee, Jessica Wong, Rohan Gogoi, Tyler Brown & Samir Mitragotri
Journal: Journal of Drug Targeting
Volume: Accepted author version posted online: 07 Mar 2017
Doi: 10.1080/1061186X.2017.1300664

Abstract

Diabetes mellitus has become a major public health issue that has almost reached epidemic proportions worldwide. Injectable insulin has been typically utilized for management of this chronic disease. However, lack of patient compliance with injectable formulations has spurred the development of oral insulin formulations, which although appealing, face several delivery challenges. We have developed novel mucoadhesive intestinal patches, several hundred micrometers in dimension (micropatches) that address the challenges of oral insulin delivery. The micropatches adhere to the intestinal mucosa, release their drug load rapidly within 30 minutes and are effective in lowering blood glucose levels in vivo. When insulin-loaded micropatches were administered with a permeation enhancer and protease inhibitor, a peak efficacy of 34% drop in blood glucose levels was observed within 3 h. Efficacy further improved to 41% when micropatches were administered in multiple doses. Here, we describe the design of micropatches as an oral insulin formulation and report their in vivo efficacy.

Database

Taylor & Francis Online Journal

Title: [A Review of Clinical and Imaging Findings in Eosinophilic Lung Diseases](#)

Author: Adam Bernheim and Theresa McCloud

Journal: American Journal of Roentgenology

Volume: Feb 22, 2017 (Ahead of Print)

Doi: 10.2214/AJR.16.17315

Abstract

OBJECTIVE. The purpose of this article is to review the clinical and imaging findings associated with eosinophilic lung diseases.

CONCLUSION. The spectrum of eosinophilic lung diseases comprises a diverse group of pulmonary disorders that have an association with tissue or peripheral eosinophilia. These diseases have varied clinical presentations and may be associated with several other abnormalities. Characteristic imaging findings are often detected with chest radiography, and CT best shows parenchymal abnormalities. The integration of clinical, radiologic, and pathologic findings facilitates diagnosis and directs appropriate treatment.

Database

American Roentgen Ray Society

Title: [Detecting Intracranial Hemorrhage Using Automatic Tube Current Modulation With Advanced Modeled Iterative Reconstruction in Unenhanced Head Single- and Dual-Energy Dual-Source CT](#)

Author: Jan-Erik Scholtz, Julian L. Wichmann, Dennis W. Bennett, Doris Leithner, Ralf W. Bauer, Thomas J. Vogl and Boris Bodelle

Journal: American Journal of Roentgenology

Volume: Feb 28, 2017 (Ahead of Print)

Doi: 10.2214/AJR.16.17171

Abstract

OBJECTIVE. The purpose of our study was to determine diagnostic accuracy, image quality, and radiation dose of low-dose single- and dual-energy unenhanced third-generation dual-source head CT for detection of intracranial hemorrhage (ICH).

MATERIALS AND METHODS. A total of 123 patients with suspected ICH were examined using a dual-source 192-MDCT scanner. Standard-dose 120-kVp single-energy CT (SECT; n = 36) and 80-kVp and 150-kVp dual-energy CT (DECT; n = 30) images were compared with low-dose SECT (n = 32) and DECT (n = 25) images obtained using automated tube current modulation (ATCM). Advanced modeled iterative reconstruction (ADMIRE) was used for all protocols. Detection of ICH was performed by three readers who were blinded to the image acquisition parameters of each image series. Image quality was assessed both quantitatively and qualitatively. Interobserver agreement was calculated using the Fleiss kappa. Radiation dose was measured as dose-length product (DLP).

RESULTS. Detection of ICH was excellent (sensitivity, 94.9–100%; specificity, 94.7–100%) in all protocols ($p = 1.00$) with perfect interobserver agreement (0.83–0.96). Qualitative ratings showed significantly better ratings for both standard-dose protocols regarding gray matter–to–white matter contrast ($p \leq 0.014$), whereas highest gray matter–to–white matter contrast-to-noise ratio was observed with low-dose DECT images ($p \geq 0.057$). The lowest posterior fossa artifact index was measured for standard-dose DECT, which showed significantly lower values compared with low-dose protocols ($p \leq 0.034$). Delineation of ventricular margins and sharpness of subarachnoidal spaces were rated excellent in all protocols ($p \geq 0.096$). Low-dose techniques lowered radiation dose by 26% for SECT images (DLP, 575.0 ± 72.3 mGy · cm vs 771.5 ± 146.8 mGy · cm; $p < 0.001$) and by 24% in DECT images (DLP, 587.0 ± 103.2 mGy · cm vs 770.6 ± 90.2 mGy · cm; $p < 0.001$). No significant difference was observed between the low-dose protocols ($p = 1.00$).

CONCLUSION. Low-dose unenhanced head SECT and DECT using ATCM and ADMIRE provide excellent diagnostic accuracy for detection of ICH with good quantitative and qualitative image quality in third-generation dual-source CT while allowing significant radiation dose reduction.

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