Hot Articles

“August|2019”

Health Science

[Health Science]

Title: Policies influencing access to new targeted oncologic drugs in Ecuadorian hospitals: an interrupted time series analysis

Author: Carlos E. Durán Monique Elseviers Robert Vander Stichele Sylvie Rottey Patricia Granja Thierry Christiaens

Journal: Journal of Pharmaceutical Health Services Research

Volume: First published: 07 August 2019 (Version of Record online)

Doi: https://doi.org/10.1111/jphs.12317

Abstract

Objective and methods: An interrupted time series analysis was performed to measure the impact of two policy interventions on the accessibility to new targeted oncologic drugs in Ecuador. The first intervention decentralized the selection process allowing drug and therapeutic committees (DTCs) to directly select new drugs. The second brought back the final decision to a central body but kept the first decision level in hospitals. Five - year (2010 – 2014) individual dispensing data from the six largest Ecuadorian cancer hospitals were analysed. Monthly incidence rate of targeted oncologic drug users (per 1000 cancer patients) was defined as the unit of analysis. Level and slope changes after policy interventions were studied; P value <0.05 was considered statistically significant.

Key findings: In public hospitals, incidence rate immediately dropped (level) after the first policy intervention ($P < 0.05$). The slope increased not significantly until the second policy. After the second intervention, the incidence level dropped, and the slope was negative (both not significant). In private hospitals, the incidence level dropped significantly after the first policy, followed by a significant slope increase. After the second intervention, the incidence level dropped, and the slope was negative (both significant).

Conclusions: Transferring to DTCs the responsibility to select new drugs produced an increase in prescription intensity of targeted oncologic drugs, mainly in the private sector. The second intervention changed this trend. Combination of different levels of decision, meaning a DTC analysis plus a reanalysis by a central body, seems to limit new prescriptions of targeted oncologic drugs.

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[Health Science]

Title: Effects of Maribavir on P - Glycoprotein and CYP2D6 in Healthy Volunteers

Author: Ivy H. Song, Katarina Ilic, MPH Joseph Murphy, Kenneth Lasseter, Patrick Martin

Journal: The Journal of Clinical Pharmacology

Volume: First published: 06 August 2019 (Version of Record online)

Doi: https://doi.org/10.1002/jcph.1504

Abstract

Maribavir is an investigational drug being evaluated in transplant recipients with cytomegalovirus infection. To understand potential drug - drug interactions, we examined the effects of multiple doses of maribavir on cytochrome P450 (CYP) 2D6 and P - glycoprotein (P - gp) activity using probe substrates in healthy volunteers. During this phase 1 open - label study (NCT02775240), participants received the probe substrates digoxin (0.5 mg) and dextromethorphan (30 mg) before and after maribavir (400 mg twice daily for 8 days). Serial plasma samples were analyzed for digoxin, dextromethorpha, dextrorphan, and maribavir concentrations. Pharmacokinetic parameters were calculated (noncompartmental analysis) and analyzed with a linear mixed - effects model for treatment comparison to estimate geometric mean ratios (GMRs) and 90% confidence intervals (CIs). CYP2D6 polymorphisms were genotyped using polymerase chain reaction. Overall, 17 of 18 participants (94.4%) completed the study. All participants were genotyped as CYP2D6 intermediate/extensive metabolizers. GMR (90%CI) of digoxin Cmax, AUClast, and AUC0 - ∞ with and without maribavir was 1.257 (1.139 - 1.387), 1.187 (1.088 - 1.296), and 1.217 (1.110 - 1.335), respectively, outside the "no - effect" window (0.8 - 1.25). GMR (90%CI) of dextromethorphan AUClast and AUClast ratio of dextromethorphan/dextrorphan were 0.877 (0.692 - 1.112) and 0.901 (0.717 - 1.133), respectively, marginally outside the no - effect window, although large variability was observed in these pharmacokinetic parameters. Pharmacokinetic parameters of dextrorphan were unaffected. Maribavir inhibited P - gp activity but did not affect CYP2D6 activity. Maribavir's effect on the pharmacokinetics of P - gp substrates should be evaluated individually, and caution should be exercised with P - gp substrates with narrow therapeutic windows.

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[Health Science]

Title: miR - 140 - 5p is negatively correlated with proliferation, invasion, and tumorigenesis in malignant melanoma by targeting SOX4 via the Wnt/ β - catenin and NF - κ B cascades

Author: Ge Zhao Yakun Yin Bin Zhao

Journal: Journal of Cellular Physiology

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Doi: https://doi.org/10.1002/jcp.29122

Abstract

MicroRNAs (miRNAs) have been validated as critical regulators in the development of melanoma. miR - 140 was abnormally downregulated in uveal melanoma samples. However, the expression level and roles of miR - 140 - 5p remain unclear in melanoma for now. We speculate that miR - 140 - 5p is abnormally expressed and may play an important role in melanoma. The expressions of miR - 140 - 5p and SOX4 messenger RNA were determined by quantitative real - time polymerase chain reaction assays. Western blot assays were employed to detect the expression levels of SOX4, Ki67, MMP - 2, MMP - 7, p - β - catenin, c - Myc, cyclin D1, p65, and I κ B α . Luciferase reporter assays were employed to elucidate the interaction between SOX4 and miR - 140 - 5p. MTT (3 - (4,5 - dimethyl - 2 - thiazolyl) - 2,5 - diphenyl - 2H - tetrazolium bromide) and transwell invasion assays were applied to evaluate capabilities of cell proliferation and invasion, respectively. Xenograft models of melanoma were established to verify the role and molecular basis of miR - 140 - 5p. Immunohistochemical (IHC) assays were employed to measure the Ki67 and SOX4 at the protein level in xenografted melanoma tissues. Herein, these observations showed that, miR - 140 - 5p was abnormally downregulated in melanoma tissues and cells, while SOX4 was upregulated. miR - 140 - 5p directly targeted SOX4 and inhibited its expression in melanoma cells. miR - 140 - 5p overexpression repressed melanoma cell proliferation and invasion and its effects were partially restored SOX4 overexpression. Moreover, miR - 140 - 5p hindered melanoma growth in vivo by downregulating SOX4. Mechanistically, miR - 140 - 5p suppressed activation of the Wnt/ β - catenin and NF - κ B pathways by targeting SOX4. Our study concluded that miR - 140 - 5p hindered cell proliferation, invasion, and tumorigenesis by targeting SOX4 via inactivation of the Wnt/ β - catenin and NF - κ B signaling pathways in malignant melanoma, which provides an underlying molecular mechanism for the treatment for melanoma with miRNAs.

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[Health Science]

Title: A population - based study of prescribing trends in a potentially vulnerable paediatric population from 1999 to 2012

Author: Kim Sears, Sherri Elms, Marlo Whitehead, Joan E. Tranmer, Dana S. Edge, Elizabeth G. VanDenKerkhof

Journal: International Journal of Pharmacy Practice

Volume: First published: 02 August 2019 (Version of Record online)

Doi: https://doi.org/10.1111/ijpp.12565

Abstract

Objectives: There is a limited understanding of paediatric medication prescribing trends and patterns, thus poorly positioning decision - makers to identify quality and safety concerns related to medication use. The objective of this study was to determine overall medication prescribing trends and patterns among children receiving Ontario Drug Benefits over a thirteen - year period in the province of Ontario, Canada.

Methods: Administrative health databases housed within the Institute for Clinical Evaluative Sciences (ICES), Ontario, Canada, were used to identify outpatient prescriptions dispensed from 1999 to 2012 through a publicly funded programme to children ⩽18 years of age. Medications were classified according to the American Hospital Formulary Service Pharmacologic - Therapeutic Classification system. Descriptive statistics were used to summarize prescribing patterns.

Key findings: This study identified 457 037 children who were dispensed a new prescription between 1999 and 2012. About 56% received their first prescription before 6.5 years of age, and 85% of the children in this study were from families who received social assistance. The most commonly prescribed drugs were antiinfectives (56.1%). Prescriptions for several central nervous system agents, including antipsychotics and agents for attention - deficit/hyperactivity disorder, increased across the study period. Changes in prescribing patterns within opioids, hormones and autonomic agents were noted. The results suggest that historically, prescribing trends have shifted with public policy, pharmaceutical marketing and diagnostic patterns, thus identifying them as a possible tool to measure the impact of policydriven practice changes. Anti - infective prescribing increased markedly with the global H1N1 pandemic. Pharmaceutical marketing, formulary decisions and diagnostic trends may affect the prescribing of ADHD medications globally. .....

Conclusions: This study presents the first overview of Canadian prescribing trends for children, the majority of which are of low socioeconomic status and represent a potentially vulnerable population. Our analysis suggests that future research is required to determine whether prescribing trends could be used as indicators of policy effectiveness, pharmacovigilance and diagnostic trends.

Database

Wiley Online Library

[Health Science]

Title: Therapeutic effects of iontophoresis with gold nanoparticles in the repair of traumatic muscle injury

Author: Franciani Rodrigues da Rocha, Daniela dos Santos Haupenthal, Rubya Pereira Zaccaron, Maria Eduarda Anastácio Borges Corrêa, Natalia dos Santos Tramontin, Jeandro Paes Fonseca, Renata Tiscoski Nesi, Alexandre Pastoris Muller, Ricardo Aurino Pinho, Marcos Marques da Silva Paula & Paulo Cesar Lock Silveira

Journal: Journal of Drug Targeting

Volume: Accepted author version posted online: 03 Aug 2019

Doi: https://doi.org/10.1080/1061186X.2019.1652617

Abstract

Studies have shown the benefits of gold nanoparticles (GNPs) in muscle and epithelial injury models. In physiotherapy, the use of the microcurrent apparatus is associated with certain drugs (Iontophoresis) to increase the topical penetration and to associate the effects of both therapies. Therefore, the objective of this study was to investigate the effects of iontophoresis along with GNPs in the skeletal muscle of rats exposed to a traumatic muscle injury. We utilized 50 Wistar rats randomly divided in to five experimental groups (n = 10): Control group (CG); Muscle injury group (MI); MI + GNPs (20 nm, 30mg/kg); MI + Microcurrent (300 μA); and MI + Microcurrent + GNPs. The treatment was performed daily for 7 days, with the first session starting at 24h after the muscle injury. The animals were sacrificed and the gastrocnemius muscle was surgically removedand stored for the proper evaluations. The group that received iontophoresis with GNPs showed significant differences in inflammation and oxidative stress parameters and in the histopathological evaluation showed preserved morphology. In addition, we observed an improvement in the locomotor response and pain symptoms of these animals. These results suggest that the association of boththerapies accelerates the inflammatory response of the injured limb.

Database

Taylor & Francis Online Journals

[Health Science]

Title: Application device for THC:CBD oromucosal spray in the management of resistant spasticity: pre-production testing

Author: Paloma Montero-Escribano & Carlos Vila Silván

Journal: Expert Review of Medical Devices

Volume: Accepted author version posted online: 08 Aug 2019

Doi: https://doi.org/10.1080/17434440.2019.1653182

Abstract

Background: Patients with multiple sclerosis spasticity (MSS) and upper limb/hand impairment who are taking 9-delta-tetrahydrocannabinol:cannabidiol (THC:CBD) oromucosal spray (Sativex®) may have difficulty self-administering their medication, possibly limiting adherence and treatment effectiveness. A Class I EU device is available to support administration of THC:CBD spray. Pre-production testing was undertaken in a patient sample.

Methods: Current users of THC:CBD spray were recruited to review the instruction leaflet and test the device. Patients and observing healthcare professionals (HCP) completed a purpose-designed questionnaire which captured user experience and HCP opinion.

Results: Fifteen patients participated. Mean treatment time with THC:CBD spray was 4 (range: 0.1–6.1) years. 87% of participants 'always', 'often' or 'sometimes' had hand impairment, and 53% reported difficulty administering THC:CBD spray. Participants reported better application using the device (73%), with less strength required (54%). Most participants (93%) considered the instruction leaflet to be clear and many (66%) expressed interest in using the device. Most HCPs (93%) did not foresee any difficulties in use of the device.

Conclusion: The proposed adherence device was useful to address self-application difficulties with THC:CBD spray in our sample. Providing the device to MSS patients with upper limb/hand spasticity impairment may restore autonomy and support adherence to THC:CBD spray.

Database

Taylor & Francis Online Journals

[Health Science]

Title: An up-date on emerging drugs in osteosarcoma: towards tailored therapies?

Author: Claudia Maria Hattinger, Maria Pia Patrizio, Federica Magagnoli, Silvia Luppi & Massimo Serra

Journal: Expert Opinion on Emerging Drugs

Volume: Accepted author version posted online: 12 Aug 2019

Doi: https://doi.org/10.1080/14728214.2019.1654455

Abstract

Introduction: Current treatment of conventional and non-conventional high-grade osteosarcoma (HGOS) is based on the surgical removal of primary tumor and, when possible, of metastases and local reccurrence, together with systemic pre- and post-operative chemotherapy with drugs that have been used since decades.

Areas covered: This review is intended to summarize the new agents and therapeutic strategies that are under clinical evaluation in HGOS, with the aim to increase the cure probability of this highly malignant bone tumor, which has not significantly improved during the last 30-40 years. The list of drugs, compounds and treatment modalities presented and discussed here has been generated by considering only those that are included in presently ongoing and recruiting clinical trials, or which have been completed in the last two years with reported results, on the basis of the information obtained from different and continuously updated data bases.

Expert opinion: Despite HGOS is a rare tumor, several clinical trials are presently evaluating different treatment strategies, which may hopefully positively impact on outcome of patients who experience unfavourable

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Taylor & Francis Online Journals

[Health Science]

Title: Selected application of peptide molecules as pharmaceutical agents and in cosmeceuticals

Author: Manica Negahdaripour, Hajar Owji, Mahboobeh Eslami, Mozhdeh Zamani, Bahareh Vakili, Soudabeh Sabetian, Navid Nezafat & Younes Ghasemi

Journal: Expert Opinion on Biological Therapy

Volume: Published online: 13 Aug 2019

Doi: https://doi.org/10.1080/14712598.2019.1652592

Abstract

Introduction: Peptide molecules are being vastly investigated as an emerging class of therapeutic molecules in recent years. Currently, 60 peptides have been approved by the US Food and Drug Administration (FDA), and more would enter the market in near future. Peptides have already opened their ways into cosmeceutical and food industries as well.

Areas covered: Antibodies, vaccines, and antimicrobial agents are the major classes of therapeutic peptides. Additionally, peptides may be employed in drug development to support cell penetration or targeting. The interest in antimicrobial peptides is surging due to the increasing risk of antibiotic-resistant pathogens. Peptide vaccines with their significant advantages compared with traditional vaccines, are expected to find their place in coming years, especially for cancer, microbial and allergen-specific immunotherapy. The usage of peptides in cosmeceuticals is also growing rapidly.

Expert opinion: Peptide synthesis has become accessible, and advances in peptide engineering, sequencing technologies, and structural bioinformatics have resulted in the rational designing of novel peptides. All these advancements would lead to the more prominent roles of peptides in the mentioned areas. In this review, we discuss applications of peptides in different fields including pharmaceuticals, cosmeceuticals, besides the critical factors in designing efficient peptide molecules.

Database

Taylor & Francis Online Journals

[Health Science]

Title: Novel deep learning model for more accurate prediction of drug-drug interaction effects

Author: Geonhee Lee, Chihyun Park and Jaegyoon Ahn

Journal: BMC Bioinformatics

Volume: 20 **Issue:** 1 **Page:** 415 (6 August 2019)

Doi: 10.1186/s12859-019-3013-0

Abstract

Background: Predicting the effect of drug-drug interactions (DDIs) precisely is important for safer and more effective drug co-prescription. Many computational approaches to predict the effect of DDIs have been proposed, with the aim of reducing the effort of identifying these interactions in vivo or in vitro, but room remains for improvement in prediction performance.

Results: In this study, we propose a novel deep learning model to predict the effect of DDIs more accurately.. The proposed model uses autoencoders and a deep feed-forward network that are trained using the structural similarity profiles (SSP), Gene Ontology (GO) term similarity profiles (GSP), and target gene similarity profiles (TSP) of known drug pairs to predict the pharmacological effects of DDIs. The results show that GSP and TSP increase the prediction accuracy when using SSP alone, and the autoencoder is more effective than PCA for reducing the dimensions of each profile. Our model showed better performance than the existing methods, and identified a number of novel DDIs that are supported by medical databases or existing research.

Conclusions: We present a novel deep learning model for more accurate prediction of DDIs and their effects, which may assist in future research to discover novel DDIs and their pharmacological effects.

Database

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[Health Science]

Title: MRI for Restaging Locally Advanced Rectal Cancer: Detailed Analysis of Discrepancies With the Pathologic Reference Standard

Author: Xiaoxuan Jia, Yinli Zhang, Yi Wang, Caizhen Feng, Danhua Shen, Yingjiang Ye and Nan Hong

Journal: American Journal of Roentgenology

Volume: Ahead of Print (Aug 6, 2019)

Doi: 10.2214/AJR.19.21383

Abstract

OBJECTIVE. The purpose of this study was to analyze causes of discrepancies between restaging MRI and pathologic findings in the assessment of morphologic indicators of tumor response in patients with rectal cancer who have undergone neoadjuvant treatment.

MATERIALS AND METHODS. MRI and pathologic data from 57 consecutively registered patients who underwent neoadjuvant treatment and total mesorectal excision between August 2015 and July 2018 were retrospectively analyzed. The sensitivity and specificity of restaging MRI in determining tumor regression grade, T category, N category, circumferential resection margin, and extramural vascular invasion were calculated with pathologic results as the reference standard. One-by-one comparisons between MRI and pathologic findings were conducted to identify causes of discrepancies.

RESULTS. The sensitivity of MRI in determining tumor regression grades 3–5 was 77.1%; T3 and T4 category, 100.0%; node-positive disease, 75.0%; circumferential resection margin, 87.5%; and extramural vascular invasion, 91.7%. The specificity values were 72.7%, 62.5%, 70.7%, 85.7%, and 64.4%. Overstaging was mainly caused by misinterpretation of fibrotic areas as residual tumor. Inflammatory cell infiltration could appear as high signal intensity in fibrotic areas on DW images, an appearance similar to that of residual tumor. Edematous mucosa and submucosa adjacent to the tumor and muscularis propria could also be mistaken for residual tumor because of their intermediate signal intensity on T2-weighted MR images.

CONCLUSION. MRI was prone to overstaging of disease. Discrepancies between MRI and pathologic findings were mainly caused by misinterpretation of fibrosis. Inflammatory cell infiltration, pure mucin, edematous mucosa and submucosa adjacent to the tumor, and muscularis propria could also be misinterpreted as residual tumor.

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