บทความที่น่าสนใจประจำเดือน กรกฎาคม 2559

สาขาวิทยาศาสตร์สุขภาพ

Title :	A Phase 1 Dose-Escalation Study of ASP2409, a Selective T-Cell Costimulation Inhibitor, in Stable Rheumatoid Arthritis Patients on Methotrexate Therapy
Author :	Wenhui Zhang, Robert M. Kernstock, Erik E. Karrer, Stanley B. Cohen, Vishala L. Chindalore, Alan J. Kivitz, Paul C. Blahunka, Leticia Delgado-Herrera, Bernhardt G. Zeiher, Nancy L. Samberg and Jay P. Garg
Journal :	Clinical Pharmacology in Drug Development: Volume 5, Issue 4, pages 259–268, July/August 2016
Abstract :	ASP2409 represents a new class of CTLA4-Ig molecules with higher binding avidity and selectivity to CD86. This first-in-human study was to assess the safety, tolerability, pharmacokinetics (PK), and pharmacodynamics of ASP2409 in stable rheumatoid arthritis patients on methotrexate therapy with a randomized, double-blind, placebo-controlled dose-escalation study design. Patients were enrolled and randomized in each of 8 dose-escalation cohorts ranging from 0.001 to 3.0 mg/kg to receive either ASP2409 or placebo in a sequential manner. Escalation to higher dose levels occurred in the absence of dose-limiting toxicity. A total of 57 patients completed the study. ASP2409 showed nonlinear PK over the dose range of 0.01 to 3.0 mg/kg following a single intravenous administration, indicating target-mediated drug disposition. Area under the concentration–time curve (AUC) and maximum concentration (Cmax) increased at a greater than dose-proportional rate. The half-life of ASP2409 increased dose dependently and ranged from 1.57 to 6.68 days. ASP2409 showed a dose-dependent increase in the extent and duration of CD86 receptor occupancy. There were no clinically relevant safety issues up to a single dose of 3.0 mg/kg. No maximum tolerated dose was reached. The incidence and duration of antidrug antibodies did not correlate with adverse events. ClinicalTrials.gov identifier: NCT02171143
Database :	Wiley Online Library

Title :	Improving Screening Mammography Outcomes Through Comparison With Multiple Prior Mammograms
Author :	Jessica H. Hayward, Kimberly M. Ray, Dorota J. Wisner, John Kornak, Weiwen Lin, Bonnie N. Joe and Edward A. Sickles
Journal :	American Journal of Roentgenology: 1-7. 10.2214/AJR.15.15917 (Ahead of Print)
Abstract :	OBJECTIVE. The objective of the present study is to evaluate the effect of comparison with multiple prior mammograms on the outcomes of screening mammography relative to comparison with a single prior mammogram. MATERIALS AND METHODS. We retrospectively analyzed 46,288 consecutive screening mammograms performed at our institution for 22,792 women. We divided these examinations into three groups: those interpreted without comparison with prior mammograms, those interpreted in comparison with one prior examination, and those interpreted in comparison with two or more prior examinations. For each group, we determined the rate of examination recall. We also calculated the positive predictive value of recall (i.e., positive predictive value level 1 [PPV1]) and the cancer detection rate (CDR) for both the group of examinations compared with a single prior mammogram and the group compared with multiple prior mammograms. Generalized estimating equations with the logistic link function were used to determine the relative odds ratio of recall as a function of the number of comparisons, with adjustment made for age as a confounding variable. The Fisher exact test was performed to compare the PPV1 and the CDR in the different cohorts. RESULTS. The recall rate for mammograms interpreted without comparison with prior examinations was 16.6%, whereas that for mammograms compared with one prior examination was 7.8% and that for mammograms compared with two or more prior examinations was 6.3%. After adjustment was made for age, the odds ratio of recall for the group with multiple prior examinations relative to the group with a single prior examination was 0.864 (95% CI, 0.776–0.962; p = 0.0074). Statistically significant increases in the PPV1 of 0.05 (p = 0.0009) and in the CDR of 2.3 cases per 1000 examinations (p = 0.0481) were also noted for mammograms compared with multiple prior examinations relative to those compared with a single prior examination.

	CONCLUSION. Comparison with two or more prior mammograms resulted in a statistically significant reduction in the screening mammography recall rate and increases in the CDR and PPV1 relative to comparison with a single prior mammogram.
Database :	American Roentgen Ray Society (Publisher)

Title :	Preparation and in-vitro/in-vivo evaluation of curcumin nanosuspension with solubility enhancement
Author :	Xin Li, Huiling Yuan, Caiyun Zhang, Weidong Chen, Weiye Cheng, Xin Chen and Xi Ye
Journal :	Journal of Pharmacy and Pharmacology: Volume 68, Issue 8, pages 980–988, August 2016
Abstract :	Objectives: We developed Cur nanosuspension (Cur-NS) with PVPK30 and SDS as stabilizers to improve poor water solubility and short biological half-time of Cur. Methods: Physicochemical characterization of Cur-NS was characterized systematically. The in-vitro dissolution, cytotoxicity and in-vivo pharmacokinetic experiments of Cur-NS were also evaluated. Key findings: Scanning electron microscope indicated that the morphologies of Cur-NS were spherical or ellipsoidal in shape. X-ray diffraction verified that Cur was successfully developed as nanoparticles with an amorphous phase in Cur-NS. Fourier transform infrared spectroscopy suggested there was no degradation about Cur in the Cur-NS. Furthermore, the in-vitro study showed that the cumulative release of the Cur-NS was 82.16 ± 2.62% within 34 h and the cytotoxicity of the Cur-NS against HepG2 cells was much better than raw Cur. Besides, in-vivo pharmacokinetics in rats by intravenous injection displayed that the in-vivo process of Cur-NS pertained to two-compartment model. Meanwhile, the t1/2 and AUC0–t of Cur-NS were enhanced by 11.0-fold and 4.2-fold comparing to Cur solution. Conclusions: The Cur-NS significantly increased the water solubility and half-time of Cur, suggesting its potential as a nanocarrier in the delivery of Cur for future clinical application.
Database :	Wiley Online Library

Title :	What do patients need to know? A study to assess patients' satisfaction with information about medicines
Author :	Michael J. Twigg, Debi Bhattacharya, Allan Clark, Rina Patel, Hannah Rogers, Hattie Whiteside, Mahavish Yaqoob and David J. Wright
Journal :	International Journal of Pharmacy Practice: Version of Record online: 15 FEB 2016 | DOI: 10.1111/ijpp.12252
Abstract :	Objectives: This study aimed to determine the information needs and reported adherence of patients prescribed medicines for chronic conditions in those who have received a community pharmacy advanced service and those who have not. Methods: A questionnaire was constructed using validated tools to measure medication information satisfaction and adherence together with questions eliciting information regarding the use of pharmacy services and demographic characteristics. This questionnaire was distributed from four community pharmacies to a convenience sample of 400 patients as they collected their medicines. Patients were eligible if prescribed more than one regular medicine and attending the pharmacy for longer than 3 months. The questionnaire was returned directly to the university. Key Findings: Two hundred and thirty-two (58%) questionnaires were returned. All respondents desired further information about their prescribed medicines, particularly about potential medication problems. Dissatisfaction centred on side effects, interactions and certain medicine characteristics such as how long it will take to act. Satisfaction with information about medicines and adherence were significantly greater in a subgroup reporting that they had received an advanced pharmacy service, e.g. medicine use review (MUR). Conclusion: Patients who had received an advanced service reported greater adherence and satisfaction with medicine-related information. This was a small, observational study, using a convenience sample of four pharmacies; in order to draw definitive conclusions, a larger study with participants randomised to receive an advanced service is required.
Database :	Wiley Online Library

Title :	You have full text access to this contentInfluence of particle shedding from silicone tubing on antibody stability
Author :	Verena Saller, Constanze Hediger, Julia Matilainen, Ulla Grauschopf, Karoline Bechtold-Peters, Hanns-Christian Mahler and Wolfgang Friess
Journal :	Journal of Pharmacy and Pharmacology: Version of Record online: 1 JUL 2016 | DOI: 10.1111/jphp.12603
Abstract :	Objectives: Peristaltic pumps are increasingly employed during fill & finish operations of a biopharmaceutical drug, due to sensitivity of many biological products to rotary piston pump-related stresses. Yet, possibly also unit operations using peristaltic pumps may shed particulates into the final product due to abrasion from the employed tubing. It was the aim of this study to elucidate the potential influence of particles shed from peristaltic pump tubing on the stability of a drug product. Methods: Spiking solutions containing shed silicone particles were prepared via peristaltic pumping of placebo under recirculating conditions and subsequently characterized. Two formulated antibodies were spiked with two realistic, but worst-case levels of particles and a 6-month accelerated stability study with storage at 2–8, 25 and 40°C were conducted. Key findings: Regarding the formation of aggregates and fragments, both mAbs degraded at their typically expected rates and no additional impact of spiked particles was observed. No changes were discerned however in turbidity, subvisible and visible particle assessments. Flow imaging data for one of the mAb formulations with spiked particles suggested limited colloidal stability of shed particles as indicated by a similar increase in spiked placebo. Conclusions: Shed silicone particles from peristaltic pump tubing are assumed to not impair drug product stability.
Database :	Wiley Online Library

Title :	Retrospective Evaluation of Ultrasound Features of Thyroid Nodules to Assess Malignancy Risk: A Step Toward TIRADS
Author :	Adnan R. Zayadeen, Monzer Abu-Yousef and Kevin Berbaum
Journal :	American Journal of Roentgenology: 1-10. 10.2214/AJR.15.15121 (Ahead of Print)
Abstract :	OBJECTIVE. The aim of this retrospective study was to develop a thyroid nodule scoring system for malignancy potential to better select nodules for ultrasound (US)-guided fine needle aspiration (FNA). MATERIALS AND METHODS. US-guided FNA was performed on 2375 thyroid nodules in successive patients. Cytologic or histopathologic confirmation of disease state in 2002 lesions showed that 148 were malignant. We developed an extended scoring system to provide more decision levels than standard scoring by including weak (macrocalcification, eggshell calcification, hypoechogenicity, solid consistency) as well as strong indicators of malignancy (microcalcification, hypoechogenicity, lobulated or ill-defined margins, taller-than-wide shape, suspicious lymph nodes) and by including contraindications (hyperechogenicity, comet-tail artifact, complete halo, cystic or microcystic). ROC analysis was used to compare detection accuracy and decision thresholds resulting from standard scoring using five major features with extended scoring. RESULTS. Although an accuracy advantage was found for the extended scoring over standard scoring, we discount this finding because our scoring involved a preliminary analysis. However, the extended scoring offers more reporting options for certainty of malignancy: standard scoring gave four potential thresholds for reporting; extended scoring gave nine. The most useful of the additional thresholds captured nearly 88% of malignancies but resulted in only 28% of patients without malignancy undergoing biopsy. CONCLUSION. Our extended Thyroid Imaging Reporting and Data System scoring provides more operating points to support treatment decisions. A simplified decision rule—biopsy every nodule with at least two weak features or one strong feature—preserves the most useful of the new decision thresholds from extended scoring
Database :	American Roentgen Ray Society (Publisher)

Title :	Co-administration of Rifampin Significantly Reduces Odanacatib Concentrations in Healthy Subjects
Author :	S. Aubrey Stoch, Jeanine Ballard, Christopher Gibson, Filippos Kesisoglou, Rose Witter, Kelem Kassahun, Stefan Zajic, Anish Mehta, Christine Brandquist, Cynthia Dempsey, Daria Stypinski and Marc L. Reitman
Journal :	The Journal of Clinical Pharmacology: Accepted manuscript online: 20 JUN 2016 03:35AM EST | DOI: 10.1002/jcph.780
Abstract :	This open-label, 2-period study assessed the effect of multiple-dose administration of rifampin, a strong cytochrome P450 3A (CYP3A) and P-glycoprotein (P-gp) inducer, on the pharmacokinetics of odanacatib, a cathepsin K inhibitor. In Period 1, 12 healthy male subjects (mean age 30 years) received a single dose of odanacatib 50 mg on Day 1 followed by a 28-day washout. In Period 2, subjects received rifampin 600 mg/day for 28 days; odanacatib 50 mg was co-administered on Day 14. Blood samples for odanacatib pharmacokinetics were collected at predose and Day 1 of Period 1 and Day 14 of Period 2. Co-administration of odanacatib and rifampin significantly reduced odanacatib exposure. The odanacatib AUC0-∞ geometric mean ratio (GMR) (90% confidence interval [CI]) [odanacatib + rifampin/odanacatib alone] was 0.13 (0.11, 0.16). The harmonic mean (jack-knife standard deviation) apparent terminal half-life (t½) was 71.6 (10.2) hours for odanacatib alone and 16.0 (3.4) hours for odanacatib + rifampin, indicating greater odanacatib clearance following coadministration with rifampin. Samples were collected in Period 2 during rifampin dosing (Days 1, 14, and 28) and after rifampin discontinuation (Days 35, 42, and 56) to evaluate the ratio of plasma 4β-hydroxycholesterol to total serum cholesterol as a CYP3A4 induction biomarker; the ratio increased ~5 fold over 28 days of daily dosing with 600 mg rifampin, demonstrating sensitivity to CYP3A4 induction.
Database :	Wiley Online Library

Title :	Reversibility of Apixaban Anticoagulation with a Four-Factor Prothrombin Complex Concentrate in Healthy Volunteers
Author :	S Nagalla, L Thomson, Y Oppong, B Bachman, I Chervoneva and WK Kraft
Journal :	Clinical and Translational Science: Volume 9, Issue 3, pages 176–180, June 2016
Abstract :	It was hypothesized that the four-factor prothrombin complex concentrate (4F-PCC) Kcentra 25 unit/kg would reverse impairment of thrombin generation in healthy volunteers dosed with apixaban to steady state. In this randomized, two-period crossover, assessor-blinded trial, 12 healthy subjects received 5 mg apixaban every 12 h. Three h after the fifth dose, four-factor prothrombin complex concentrate (4F-PCC) 25 unit/kg or saline were infused. Serial blood samples were assessed for thrombin generation using PPP-reagent and PPP-reagent low, anti-Xa, PT, and PTT assays. Geometric mean ratio was calculated at 30 min postinfusion, and at 24, 48, and 72 h. Peak thrombin generation was 76% higher at 30 min postinfusion with 4F-PCC ($p = 0.025$). The difference declined to 24% at 24 h and resolved by 48 h. Other thrombin generation parameters were also partially normalized. There was no difference between 4F-PCC and saline in anti-Xa assessment at 30 min or later time points.
Database :	Wiley Online Library

Title :	Evidence for the Role of BAG3 in Mitochondrial Quality Control in Cardiomyocytes
Author :	Farzaneh G. Tahrir, Tijana Knezevic, Manish K. Gupta, Jennifer Gordon, Joseph Y. Cheung, Arthur M. Feldman and Kamel Khalili
Journal :	Journal of Cellular Physiology: Accepted manuscript online: 6 JUL 2016 06:50AM EST | DOI: 10.1002/jcp.25476
Abstract :	Mitochondrial abnormalities impact the development of myofibrillar myopathies. Therefore, understanding the mechanisms underlying the removal of dysfunctional mitochondria from cells is of great importance toward understanding the molecular events involved in the genesis of cardiomyopathy. Earlier studies have ascribed a role for BAG3 in the development of cardiomyopathy in experimental animals leading to the identification of BAG3 mutations in patients with heart failure which may play a part in the onset of disease development and progression. BAG3 is co-chaperone of heat shock protein 70 (HSP70), which has been shown to modulate apoptosis and autophagy, in several cell models. In this study, we explore the potential role of BAG3 in mitochondrial quality control. We demonstrate that siRNA mediated suppression of BAG3 production in neonatal rat ventricular cardiomyocytes (NRVCs) significantly elevates the level of Parkin, a key component of mitophagy. We found that both BAG3 and Parkin are recruited to depolarized mitochondria and promote mitophagy. Suppression of BAG3 in NRVCs significantly reduces autophagy flux and eliminates expression of Tom20, an essential import receptor for mitochondria proteins, after induction of mitophagy. These observations suggest that BAG3 is critical for the maintenance of mitochondrial homeostasis under stress conditions, and disruptions in BAG3 expression impact cardiomyocyte function.
Database :	Wiley Online Library

Title :	Particulate Respirators Functionalized with Silver Nanoparticles Showed Excellent Real-Time Antimicrobial Effects against Pathogens
Author :	Clark Renjun Zheng, Shuai Li, Chengsong Ye, Xinyang Li, Chiqian Zhang, Xin Yu,
Journal :	Environ. Sci. Technol. 2016 , 50 (13), pp 7144–7151: DOI: 10.1021/acs.est.6b00788
Abstract :	Particulate respirators designed to filtrate fine particulate matters usually do not possess antimicrobial functions. The current study aimed to functionalize particulate respirators with silver nanoparticles (nanosilver or AgNPs), which have excellent antimicrobial activities, utilizing a straightforward and effective method. We first enhanced the nanosilver-coating ability of nonwoven fabrics from a particulate respirator through surface modification by sodium oleate. The surfactant treatment significantly improved the fabrics' water wet preference where the static water contact angles reduced from 122° to 56°. Both macroscopic agar-plate tests and microscopic scanning electron microscope (SEM) characterization revealed that nanosilver functionalized fabrics could effectively inhibit the growth of two model bacterial strains (i.e., Staphylococcus aureus and Pseudomonas aeruginosa). The coating of silver nanoparticles would not affect the main function of particulate respirators (i.e., filtration of fine air-borne particles). Nanosilver coated particulate respirators with excellent antimicrobial activities can provide real-time protection to people in regions with severe air pollution against air-borne pathogens.
Database :	ACS (American Chemical Society)