controlled release of the encapsulated drug. This investigation focuses on preparation and characterization of nanoparticles of propyl starch, a novel hydrophobic polymer [1], for encapsulating and modulating the release of docetaxel. Docetaxel was selected due to its evident efficacy in numerous cancers limited by its low aqueous solubility and severe toxicity.
Material and Methods: Docetaxel nanoparticles were formulated using solvent emulsification-diffusion technique and optimized with respect to relative amounts of docetaxel and propyl starch, influence of various stabilizers and their quantity. Optimum nanoparticles were characterized with regards to particle size, morphology, surface charge, docetaxel encapsulation and it's *in vitro* release profile. Cytotoxicity assays in cancer cells (Caco-2) were conducted to determine the safety and efficacy of nanoparticles. Cellular internalization of nanoparticles was observed by Confocal laser scanning microscopy. Results in Caco-2 cells were compared with those in non-cancer cells (NHDF-p) to confirm their benignity towards the latter.
Results: Nanometric, homogenous and spherical nanoparticles were formulated with a mean particle size of ~250 nm and a negative surface charge of −23 mV. Encapsulation efficiency of docetaxel was greater than 80% with a controlled release being observed from the selected polymer indicating probability of increased concentration and duration at the affected area. Cytoxicity tests of un-loaded particles in Caco-2 and NHDF-p cells exhibited their safety for cellular evaluations. Cytotoxicity of encapsulated drug was higher than free drug control indicating nanoparticle efficacy attributable to their enhanced internalization. Further, a superior action was observed in cancer versus non-cancer cells. Internalization studies confirmed these results by exhibiting a better uptake of nanoparticles into the cancer cells with a distinct evidence of their peri-nuclear localization.
Conclusions: Docetaxel nanoparticles may be regarded as a safe yet efficacious therapeutic with probability of enhanced drug bioavailability as a direct consequence of the 'nano' dimensions of its carrier.
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1225 POSTER

A Randomised, Double-blind, Placebo Controlled, Multi-site Study of Subcutaneous Ketamine in the Management of Cancer Pain

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Background: Ketamine is used commonly as an adjunct to opioids in the management of pain. The evidence to support this practice is limited. The aim of this study was to evaluate the role of subcutaneous ketamine in cancer pain.
Materials and Methods: Patients with pain related to malignant disease or its treatment, rated as $\geqslant$3/10 despite adequate co-analgesia, were eligible if there has been no change in baseline opioid dose within the previous 48 hours. Participants were randomised to either ketamine or placebo, delivered subcutaneously at a dose titrated from 100 to 500 mg/24hours, according to response and toxicity. Response was defined as a $\geqslant$2 point reduction in average Brief Pain Inventory (BPI) pain score from baseline with $\leqslant$4 breakthrough doses of analgesia. The primary endpoint was average pain score at start day 6. Secondary endpoints included adverse events, response at days 2−5 and quality of life. Ketamine would be considered superior to placebo if the response rate at start day 6 was 25% greater than that of placebo (assuming a placebo response rate of 30%).
Results: One hundred and eighty five participants were randomised from March 2008 to February 2011 to complete the planned sample size of 150. Primary analysis has confirmed the high placebo response rate (26/92 = 28%) with no difference between active and placebo arms ($p = 0.78$).
Conclusion: This adequately powered, randomized controlled trial demonstrates the power of placebo and does not support the role of subcutaneous ketamine in the treatment of cancer pain in advanced cancer.

1226 POSTER

An ErbB-3 Antibody, MP-RM-1, Inhibits Tumour Growth by Blocking Ligand-dependent and Independent Activation of ErbB-3/Akt Signaling

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Background: The ErbB receptors, such as ErbB-1 and ErbB-2, have been intensely pursued as targets for cancer therapeutics. Although initially efficacious in a subset of patients, drugs targeting these receptors led invariably to resistance which is often associated with reactivation of the ErbB-3-PI3K-Akt signaling. This may be overcome by an ErbB-3 ligand binding molecule that abrogates ErbB-3 mediated signaling.
Materials: Toward this end, we have generated a mouse monoclonal antibody, MP-RM-1, against the extracellular domain (ECD) of ErbB-3 receptor. The ability of the antibody to suppress NRG-1b-dependent and independent ErbB-3 signaling was evaluated in vitro by western blotting using a panel of human tumour cell lines (breast, melanoma, stomach and prostate) as well as early passage tumour cells obtained from patients. The effect on tumour growth in vitro was evaluated with clonogenic assay and in vivo using human tumour xenograft nude mouse models.
Results: Assessment of human tumour cell lines as well as early passage tumour cells collected from patients revealed that MP-RM-1 effectively inhibited both NRG-1β stimulated and basal ErbB-3 activation. MP-RM-1 treatment led, in most instances, to decreased ErbB-3 expression. In addition, MP-RM-1 was able to inhibit the colony formation ability of tumour cells and tumour growth in two human tumour xenograft nude mouse models. Treatment with the antibody was associated with a decreased ErbB-3 and Akt phosphorylation and ErbB-3 expression in the excised tumour tissue.
Conclusions: Collectively these results indicate that MP-RM-1 has the potential to interfere with signaling by ErbB-3 and reinforce the notion that ErbB-3 could be a key target in cancer drug design.

1227 POSTER

Molecular Portrait of Breast Cancer Cell Lines and Response to Artemisinin

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Background: Artemisinin (ART) is a sesquiterpene lactone originally used as an antimalarial drug. Broad anti-cancer activities of ART have been documented in the last decade, including activity against breast cancer (BC). The molecular mechanism of ART against BC, especially its selectivity for different BC subtypes, is largely unknown. In this study we therefore aimed to identify potential target genes associated with ART sensitivity using gene expression microarray, and to determine the selectivity of ART against a panel of BC cell lines representing the various known intrinsic subtypes.
Material and Methods: Cell growth inhibition of ART was measured using sulforhodamine B protein staining to determine sensitivity to ART of 31 different BC cell lines with known molecular subtypes. The half maximal inhibitory concentration (IC50) values of these cell lines were associated with their morphological properties and intrinsic subtypes. Also, differentially expressed genes (Affymetrix U133A array) between the 7 most sensitive versus the 10 most resistant cell lines were identified. Finally, to identify possibly involved networks and pathways, a pathway analysis involving the most significant differentially expressed genes (with $p < 0.01$) was carried out using Ingenuity.
Results: IC50 values of ART showed that this molecule had activity against all the 31 cell lines but had a significant preference to target spindle-shaped ($p = 0.044$), and also triple negative BC (TNBC) cell lines ($p = 0.025$) which lack expression of estrogen receptor, progesterone receptor and human epidermal growth factor receptor 2. We identified 119 differentially expressed probes, associated with 105 unique genes, between the 7 ART-sensitive and the 10 ART-resistant cell lines. Pathway analysis revealed that the top interaction network (25 out of 35 involved genes were differentially expressed) was associated with functions related to "cell-mediated immune response, cellular development, cellular function and maintenance", while the most significantly involved canonical pathway was "role of IL-17F in allergic inflammatory airway diseases" ($p = 0.002$).
Conclusions: Our studies showed the selectivity of ART against TNBC cell lines and identified a putative gene profile related to sensitivity to ART. Further studies will focus on confirming the differential expressed genes at protein level and functionally verifying the discovered pathway in differential ART sensitivity of BC cell lines.