OMICS International
conferenceseries.com

Chemotherapy 2015, 4:2
http://dx.doi.org/10.4172/2167-7700.S1.003

International Conference on
Antimicrobial Agents and Chemotherapy
August 04-06, 2015 Valencia, Spain

Molecular characterization of irinotecan (SN-38) resistant human breast cancer cell lines

Jan Stenvang
University of Copenhagen, Denmark

Studies in taxane and/or anthracycline refractory metastatic breast cancer patients have shown approximately 30% response rates to irinotecan. Hence, a significant number of patients will experience irinotecan-induced side effects without obtaining any benefit. The aim of this study was to lay the groundwork for development of predictive biomarkers for irinotecan treatment in breast cancer. We established breast cancer cell lines with acquired or de novo resistance to SN-38 by exposing human breast cancer cell lines (MCF-7 and MDA-MB-231) to either stepwise increasing concentrations over six months or an initial high dose of SN-38 (the active metabolite of irinotecan). The resistant cell lines were analyzed for cross-resistance to other anti-cancer drugs, global gene expression, growth rates, TOP1 and TOP2A gene copy numbers, Top1 and Top2a protein expression, and inhibition of the ABCG2 encoded breast cancer resistance protein (BCRP) drug efflux pump. The resistant cell lines showed 7-100 fold increased resistance to SN-38 but remained sensitive to docetaxel and the non-camptothecin Top1 inhibitor LMP400. The resistant cell lines were characterized by Top1 down-regulation, changed isoelectric points of Top1 and reduced growth rates. The gene and protein expression of ABCG2/BCRP was up-regulated in the resistant sub-lines and functional assays revealed BCRP as a key mediator of SN-38 resistance. Based on our preclinical results, we suggest analyzing the predictive value of the BCRP in breast cancer patients scheduled for irinotecan treatment. Moreover, LMP400 should be tested in a clinical setting in breast cancer patients with resistance to irinotecan.

stenvang@sund.ku.dk

Protontherapy vs. carbon ion therapy: Advantages, disadvantages and similarities

Marcos d'Avila Nunes
University of Sao Paulo, Brazil

More than 100,000 patients have been treated with particle beams around the world, of which about 13% were treated with C-ion RT. In 1946, Wilson R proposed the use of proton for cancer therapy, and the first patient was treated at the Lawrence Berkeley National Laboratory in the USA (1954). In 1994, clinical trial on C-ion RT was launched at the National Institute of Radiological Sciences in Japan. Protons have a better dose distribution but a lower RBE (1.0-1.1) than carbon ions (1.5-3.4). However, RBE depends on radiation quality, LET, fraction size, and the biological aspects of the target. Higher RBE is good for tumor control, but it is bad for normal tissue toxicity. The biological benefits of C-ion RT have been demonstrated in inoperable cases with various types of sarcoma, adenocarcinoma, adenoid cystic carcinoma and malignant melanoma arising from various sites that are well known as photon-resistant tumors (and/or located close to critical structures). At HIT, Heidelberg, there is the Cleopatra and Pinocchio trial, both with a primary endpoint of toxicity. All studies on both proton and carbon ion therapy are small and therefore difficult to compare, also, assessment of the efficacy of protontherapy vs. C-ion RT is not feasible, mainly due to the dose fractionation differences. The use of C-ion RT is recommended, when the advantages of using carbon ions outweigh the therapeutic advantages that can already be obtained by fractionated photon RT.

marcosdavilanunes@gmail.com