therapy using gene *E in vitro* using MCF-7 breast cancer cells forming MTS. In order to determine the effect of the combined therapy (gene therapy and citotoxics) transfected MCF-7 MTS were treated with gradient concentrations of the drug diluted in the culture medium: paclitaxel, docetaxel and doxorubicin. We studied the action mechanism of the combined therapy: study of apoptosis and cellular cycle, and the modulation of the volumes of the MTS of tumour cells.
Results: Our results showed that the use of doxorrubicin in MCF-7 breast cancer MTS transfected with *E* gene enhanced the chemotherapeutic effect of this drug. This inhibition was greater than that obtained using the gene therapy or chemotherapy alone.
Conclusions: The transfection of gene *E* in MCF-7 MTS is able to increase the chemotherapeutic effect of drugs and specially is able to enhance the anticancer effect of the doxorubicin in comparison to the growth inhibition obtained using the gene therapy or chemotherapy alone. These results indicate that this combined therapy may be of potential therapeutic value in breast cancer.

5201 POSTER

Guidelines in breast cancer – are they keeping up with the times?

S. Verma[1]. [1]*Sunnybrook Odette Cancer Centre, Division of Medical Oncology, Toronto, Canada*

Background: This study aimed to determine how quickly various pivotal clinical trial data in adjuvant treatment for breast cancer were adopted into local and international guidelines.
Materials and Methods: PubMed and conference Web sites were searched to identify representative trials of 3 key adjuvant advances in breast cancer: taxanes, trastuzumab, and aromatase inhibitors (AIs). The inclusion of these treatments in the following international guidelines was analyzed: American Society of Clinical Oncology (ASCO), National Comprehensive Cancer Network (NCCN), and St. Gallen consensus. Several regional guidelines were also reviewed: National Institute for Health and Clinical Excellence (NICE; UK), Danish Breast Cancer Cooperative Group (DBCG), and German Gynecological Oncology Working Group (AGO).
Results: Early studies on taxanes as adjuvant therapy were presented in 1998 and 2000, but adjuvant taxanes were not readily adopted into guidelines. In contrast, guidelines were quickly updated (1−2 y) to recommend adjuvant trastuzumab after data were presented in 2005. Following initial data on adjuvant AIs with the release of the ATAC findings, NCCN guidelines were updated within months. The ASCO technology assessment, St. Gallen consensus, and NICE guidelines were updated several years later, but upfront AIs were not recommended over tamoxifen. With the release of data indicating an emerging survival benefit with upfront letrozole for 5 years, guidelines are being revisited, and further updates are expected. In the 2009 St. Gallen consensus vote, the majority (70%) favored upfront use of AIs.

Treatment	Representative data		Adoption into guidelines	
	Trial	Date	Guideline	Date
Taxanes	CALGB 9344	1998	NCCN	2003
	NSABP B-28	2000	St. Gallen	2007
			NICE	2006 (paclitaxel not recommended)
Trastuzumab	HERA	May 2005	NCCN	2006
			St. Gallen	2006
			NICE	2006
			ASCO	2007
AIs	ATAC	Dec 2001	NCCN	Jan 2002
			ASCO	2005
			St. Gallen	2005
			NICE	2006
AIs	BIG 1−98	Dec 2008	St. Gallen	2009
			DBCG	2009
			AGO	2009

Conclusions: Of the 3 classes of adjuvant therapy investigated in this study, the inclusion of adjuvant trastuzumab into guidelines has generally been the most rapid, and the inclusion of adjuvant taxanes into guidelines has been the slowest. Clinicians have traditionally relied on guidelines to assist them in treatment decision-making. In the current era of rapid advances in oncology, the guideline process needs to be modified to help integrate emerging evidence in a timely manner.

5202 POSTER

Deletions of PTEN and FBXW7 in breast carcinomas investigated with array comparative hybridization (aCGH) are associated with reduced survival in a long term follow up clinical cohort

H. Vollan[1], E.U. Due[2], R. Kåresen[1], E. Schlichting[1], A.L. Børresen-Dale[2]. [1]*Ullevål University Hospital, Department of Breast And Endocrine Surgery, Oslo, Norway;* [2]*The Norwegian Radium Hospital, Department of Genetics, Oslo, Norway*

The protein mTOR (mammalian target of rapamycin) is a promising target of cancer therapy in human disease. mTOR is a key player in the PI3K-Akt pathway and the group of rapamyoid chemotherapeutic drugs seem to inhibit mTOR in a specific manner. In previous studies the *PTEN* (phosphatase and tensin homolog) and *FBXW7* (F-box and repeat domain containing 7) both seem to inhibit the mTOR level. Deletions in these tumor suppressor genes may thus be a marker for the response of rapamycin. There is evidence for a reciprocal relationship between deletions of these genes. The aim of this study was to investigate the frequency of deletions in PTEN and FBXW7 in a clinical cohort with long term follow up with a high resolution array comparative genomic hybridization platform (aCGH). Tumor tissues from a series of 212 primary breast cancer cases were sequentially collected at Ullevål University Hospital between 1990 and 94. Tissues were sampled at the time of primary surgery and snap frozen. We performed aCGH on 167 of these tumors. DNA was isolated using chloroform/phenol extraction, followed by ethanol precipitation. The aCGH-platform was the Agilent Human-Genome-CGH Microarray 244k. For detection of aberrations, we used an algorithm for segmentation of aCGH data called piecewise constant fit (PCF). The platform contained 10 oligonucleotide probes inside the PTEN gene and 26 probes withinin the FBXW7 gene, 4 in isoform 2, 7 in isoform 3 and 26 for isoform 1. Gene deletion was defined as a value of less than −0.3 of the segmented data on a log2-scale. Statistical analyses of clinical data and survival analyses were performed using SPSS 16.0.
Many significant genetic alterations were found, with a large heterogeneity between the different tumors. In our cohort we found 29 deletions of PTEN (17.4%) and 29 deletions of FBXW7 (17.4%). 12 of these samples (5.7%) harboured a combined loss of these tumor suppressor genes. The survival for patients with a loss in the FBXW7 gene had a significantly reduced survival compared with no loss with a p-value of 0.007. For a PTEN loss the same significant difference were seen ($p < 0.005$). The subset of samples with a combined loss shows evidence of reduced survival compared to loss of one gene and suggests an additive effect of this combinated deletions. The detailed aCGH profiles and clinical data will be presented.

Gastro-intestinal malignancies − Colorectal cancer

Oral presentations (Mon, 21 Sep, 11:00−12:45)

Gastro-intestinal malignancies − Colorectal cancer I

6000 ORAL

Aspirin prevents cancer in Lynch syndrome

J. Burn[1], A.M. Gerdes[1], J.P. Mecklin[2], F. Macrae[3], G. Moeslein[4], M.L. Bisgaard[5], R. Ramesar[6], D.T. Eccles[7], J.C. Mathers[8], D.T. Bishop[9]. [1]*University of Newcastle upon Tyne, Department of Human Genetics, Newcastle upon Tyne, United Kingdom;* [2]*Jyväskylä Central Hospital, Department of Surgery, Jyväskylä, Finland;* [3]*Royal Melbourne Hospital, Department of Colorectal Medicine and Genetics, Melbourne, Australia;* [4]*St. Josefs-Hospital Bochum-Linden, Department of General and Visceral Surgery, Bochum, Germany;* [5]*Panum Institute, Department of Medical Genetics, Copenhagen, Denmark;* [6]*University of Cape Town and Groote Schuur Hospital, Department of Surgery, Cape Town, South Africa;* [7]*Princess Anne Hospital, Wessex Clinical Genetics Service, Southampton, United Kingdom;* [8]*Institute for Ageing and Health, Human Nutrition Research Centre, Newcastle upon Tyne, United Kingdom;* [9]*Leeds Institute of Molecular Medicine, Section of Epidemiology and Biostatistics, Leeds, United Kingdom*

CAPP2 recruited 1009 eligible carriers of Lynch syndrome (HNPCC) to a randomised controlled trial of 600 mg aspirin and/or 30 g Novelose (resistant starch) in 43 centres worldwide. After a mean of 29 months (range