

min intravenously on days 1 and 8 of a 21-day cycle or TPC (cytotoxic, hormonal, or biologic monotherapy, or supportive care only). Exploratory OS sub-analysis was carried out.

Results: Of the 254 pts enrolled in the TPC arm, 156 received a class of agent they had not previously received, and 98 had been re-challenged with a therapy of the same type. Re-challenged pts were in the following TPC groups: taxanes (n=38/41; 92.7%), anthracyclines (n=24; 100%), vinorelbine (n=5/65; 7.7%), capecitabine (n=4/45; 8.9%), hormonal therapy (n=4/8; 50%), and other (n=23/25; 92.0%); no-one receiving gemcitabine (n=46) was re-challenged. When the re-challenged pts were excluded from the analysis, eribulin significantly improved OS vs TPC (HR 0.74; 95% CI 0.58, 0.94; nominal p=0.014) with median OS of 13.1 and 10.5 months, respectively. Analysis of eribulin vs the 98 re-challenged pts in the TPC arm showed median OS of 13.1 vs 10.7 months, respectively (HR 0.92; 95% CI 0.68, 1.23; nominal p=0.556).

Conclusions: Eribulin demonstrated OS improvement for pts with locally recurrent or MBC, even when re-challenged pts were removed from the TPC arm.

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ORAL

The MicroRNAs-30 Family Interferes With the Formation of Breast Cancer Bone Metastases by Targeting Osteomimetic Genes

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MicroRNAs (miRNAs), a class of endogenous small non coding RNAs have been involved in tumorigenesis and metastatic dissemination through their activity as negative regulators of gene expression. Alterations of miRNA expression have been reported in the different steps of initiation, progression and dissemination of breast tumours. Breast cancer cells preferentially invade and grow as secondary tumours in bone. To adapt and thrive in this environment metastatic breast cancer cells express genes normally expressed by the osteoblasts and acquire a bone cell pseudo-phenotype named osteomimicry.

To investigate if miRNAs interfere with this specific steps of bone metastasis formation, we compared the expression profiles of the human breast cancer cell line MDA-MB-231 with that of a subpopulation (MDA-BO2) that metastasize to bone with high efficiency, using TaqMan Low Density Array analysis. Then, target genes of the differentially expressed miRNAs within the two cell lines were predicted by looking at sequence complementarities of the 5' seed regions of the miRNAs within the 3' UTR of the genes using miRanda, PicTar and TargetScan softwares. By doing so, it appeared that the miRNAs-30 family which is composed of 5 members: miRNA-30a, 30b, 30c, 30d and 30e, was substantially downregulated in MDA-BO2 cells. Therefore, the expression of these miRNAs-30 in MDA-BO2 cells were restored through retroviral transduction using the pmiR-Vec plasmid vector to perform functional studies. The mRNA expression of connective tissue growth factor (CTGF), connexin 43, integrin $\beta 3$ and transcription factor runx2, which all harbor phylogenetically conserved miRNAs-30 binding sites in their 3' UTR, was decreased in MDA-BO2 overexpressing miRNAs-30 (miRNAs-30-BO2), when compared to pmiR-Vec-BO2 clones. The expression of cadherin-11, for which we found a perfect base pairing of the miRNAs-30 "seed region" in the coding sequence, was also decreased. MDA-BO2 modified clones were inoculated into the tail vein of nude mice and bone metastases were radiographically detected and enumerated. A 50% decrease in the extent of osteolytic lesions was observed in animals bearing miRNAs-30-BO2 tumours versus mice inoculated with pmiR-Vec-BO2 clones or with MDA-BO2 wild-type clones.

These results strongly suggest that miRNAs-30 act as a regulator of breast cancer bone metastases formation.

Oral Presentations (Sat, 24 Sep, 11:15–13:20) Breast Cancer – Early Disease

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ORAL

Long Term Results of Video-assisted Breast Surgery (VABS)

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Background: The breast conserving surgery and the sentinel node (SN) biopsy became to be recognized as the standard treatment for early breast cancers. We have reported about cosmetic effectiveness and lower

infestation of the video-assisted breast surgery (VABS) for the breast diseases. We devised the trans-axillary retro-mammary (TARM) approach of VABS. It needs only one skin incision in the axilla and can treat any tumour even in the medial or lower side of the breast without making any injuries on the breast skin. And it can preserve skin touch sensation. We evaluated the aesthetic results and the curability of this surgical method.

Methods: We have performed VABS on 300 patients since December, 2001. The newly devised trans-axillary retromammary-route approach (TARM) was performed on 120 patients of early breast cancer, stage I and II. After endoscopic sentinel node biopsy, we elongated the axillary skin incision to 2.5 cm. We marked the surgical margin 2 cm apart from the tumour edge by injecting blue dye into subcutaneous and retromammary. We dissected major pectoral muscle fascia to detach retromammary tissue under the tumour. The working space was made by lifting traction sutures through the gland. We cut the proximal side of the gland vertically at dye marking points, and dissect skin flap over the tumour by tunnel method. Then we cut each sides of the gland vertically and removed it through the axillary port by using the tumour collection bag. The breast reconstruction was done by filling absorbable fiber cotton. The postoperative aesthetic results were evaluated by our original score system, ABNSW.

Results: Breast conserving surgery was performed on 286 patients (26 after preoperative chemotherapy) and skin-sparing total mastectomy on 14. We do not use the special disposable apparatus. The operative cost is very low as the conventional one. There was no significant difference in operational infestation. There was no serious complication after surgery. Surgical margin was minimally positive in 2 patients. The original shapes of the breast were preserved well. All patients expressed great satisfaction. The follow-up time is 112 months at maximum and 72 months on average. There is two locoregional recurrence and 12 distant metastases (brain: 4 with 2 cancer deaths, lung: 3, liver: 3, bone: 5). 5-year survival rate is 97.3%. With regard to TARM, The skin incision was made only in the axilla without any wound on the breast. It could be applied for any tumour existing in the medial or caudal side of the breast (A and B regions). The reconstruction by filling absorbable fiber cotton need no excessive detachment of the skin beyond the surgical margin of the mammary gland. The postoperative esthetic results were excellent and good. The sensory disturbance was minimal, observed only in the detached area within the surgical margin.

Conclusions: VABS can be considered as a surgical procedure with good locoregional control and can provide aesthetic advantages for patients with breast disease.

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ORAL

Near-infrared Fluorescence Sentinel Lymph Node Detection in Breast Cancer Patients – the GREEN LIGHT Studies

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Introduction: Detection of the sentinel lymph node is important in the staging and treatment of breast cancer. Near-infrared (NIR) fluorescence imaging is a technique that can be used to visualize lymph nodes during surgery, several centimeters into the living tissue, in real-time. Currently, indocyanine green (ICG) is the only clinical approved NIR fluorescent contrast agent. Premixing of ICG with human serum albumin (HSA) improved the fluorescence and sentinel lymph node retention in preclinical experiments. The current studies focus on optimizing the use of NIR fluorescence imaging for the sentinel lymph node procedure in 3 clinical trials with a total of 64 patients.

Material and Methods: In all studies, the Mini-FLARE intraoperative imaging system (Frangioni Lab, Boston, USA) was used. First (study 1), the optimal dose of ICG:HSA was studied in 24 consecutive patients. These patients received the standard of care sentinel lymph node procedure (blue dye and ^{99m}Tc-nanocolloid) and were injected with 1.6 mL of ICG:HSA (dose groups 50 to 1000 μ M).

The potential advantage of premixing of ICG with HSA was then studied in a randomized, double-blind study (study 2), with 18 consecutive patients. Patients were injected with 1.6 mL of 500 μ M ICG alone or ICG:HSA. Subsequently, sentinel lymph node mapping was performed using 500 μ M ICG in 24 patients, with randomization between the use or omission of patent blue (study 3).

Results: The sentinel lymph node was successfully detected in all patients. In the dose finding study (study 1), a total of 35 lymph nodes were detected (average 1.45), all of which were radioactive, 30 nodes were blue. The optimal dose was between 400 and 800 μ M.

No differences were observed when premixing ICG with HSA (study 2), in the number of sentinel lymph nodes identified (average of 1.4 per patient), nor in fluorescence intensity (P=0.18). No difference in fluorescence was