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Basic science

1PD Breast cancer blood-derived exosomes: Characterisation of protein composition in search for new biomarkers

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Background: Exosomes are known to be involved in the signalling processes and cell-to-cell communication both in healthy organisms and during the development of various cancer types. However, the exact mechanisms of sorting and secreting as well as the circulation patterns and composition of exosomes are still unclear. The aim of our research is to identify protein content of blood-derived exosomes and determine potential biomarkers specific for breast cancer development. Since exosomes are naturally binding with the cells, we decided to extract them not only from blood plasma but also from blood cells surface in order to understand their percentage, properties and composition.

Methods: Exosomes from blood plasma and blood cell surface-bound exosomes were obtained using methods developed in our lab (RF Patent #2556825, #2571507). The resultant samples were characterized by transmission electron microscopy (TEM) and immunogold labeling to state the presence of characteristic exosome tetraspanins CD-9, CD-24 and CD-63. Proteins from exosome samples were separated by electrophoresis in gradient polyacrylamide gel and identified by MALDI-TOF analysis.

Results: Immunogold labeling confirmed the presence of antigens characteristic for exosomes: CD-9, CD-24 and CD-63. The evaluation of particle diameter of 14 950 exosomes has shown that the blood of breast cancer patients is mostly presented with exosomes diameter from 50 to 70 nm, the blood of healthy women - from 30 to 50 nm. We discovered that 61% of blood-derived exosomes are bound to the surface of blood cells. MALDI TOF/TOF identified more than 150 proteins in exosomes from the blood of healthy women ($n = 5$) and breast cancer patients ($n = 5$), the majority of which are found in exosomes for the first time (according Exocarta database at the summer of 2016).

Conclusions: Although it is still unclear what leads to differences in exosome size in plasma and on the surface of the blood cells the results suggest the importance of this exosome fraction and provides us with the new perspective in exosome research. Further analysis with expanded sample size may lead us to biomarker patterns as well as new insight into exosome structure.

Legal entity responsible for the study: Laboratory of Molecular Medicine, Institute of Chemical Biology and Fundamental Medicine of Siberian Branch of Russian Academy of Sciences

Funding: Russian Foundation for Fundamental Research grant

Disclosure: All authors have declared no conflicts of interest.

2P Novel cKIT kinase inhibitor, BPRCKJ001, as an advanced therapeutic candidate for GIST

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Background: During the past decade, first-line use of imatinib has benefited GIST patients. GIST patients develop imatinib-resistance due to secondary mutation in cKIT after 20-24 months of drug treatment. Although the 2nd line drugs such as, sunitinib is effective, activation loop mutations quickly overcame their potent inhibitory effects. Moreover, these drugs have numerous potential side-effects. Even with the newly launched sorafenib and nilotinib for advanced GIST, the long term clinical outcome was still not very promising for GIST patients, due to the rapid development of drug resistance on cKIT.

Methods: IBPR has identified a series of novel cKIT inhibitors, the BPRCKJ series, which exhibited potent cKIT kinase activity inhibition. To evaluate the potential of BPRCKJ compounds as novel cKIT inhibitors against GIST, eight different imatinib-resistant mutated cKITs were selected to examine the inhibitory activities of BPRCKJ series. The results showed that BPRCKJ series has a broad spectrum activity against various forms of imatinib-resistant mutant c-KITs. Most importantly, the ability to overcome imatinib- and sunitinib-resistant mutant cKITs is demonstrated.

Results: Through the comprehensive SAR study, we had identified BPRCKJ001 as a potential candidate, which was shown to strongly inhibit the enzymatic activities of several mutant c-KIT. BPRCKJ001 also effectively inhibited three GIST sensitive and resistant cell lines with IC_{50} values below 20 nM. It is interesting to note that BPRCKJ001 is 10-times and 400-times more potent than sunitinib in GIST430 cells and sunitinib-resistant cell lines (GIST48), respectively. The Western blot analyses also clearly showed that BPRCKJ001 can suppress the cKIT phosphorylation and downstream AKT phosphorylation more effectively than imatinib and sunitinib in GIST430 cells.

Conclusions: BPRCKJ001 had shown excellent in vitro effects, targeting against both imatinib- and sunitinib-resistant mutants in both enzymatic and cellular systems. More importantly, BPRCKJ001 also demonstrated in vivo efficacy by oral administration in GIST430 xenograft model. These results indicate that CKJBPR001 series has reasonable pharmaceutical properties to be developed as a potential cKIT inhibitor

Legal entity responsible for the study: Weir-Torn Jiaang

Funding: MOEA, Taiwan

Disclosure: All authors have declared no conflicts of interest.

3P Anti-VEGF and integrin-linked kinase knockdown inhibit angiogenesis in vitro and suppress vascular tumor growth in vivo

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Background: Angiogenesis is the process by which new blood vessels are formed. It is also a key feature in the growth and progression of several cancers. Studies have identified vascular endothelial factor (VEGF) as an important regulator of angiogenesis in both the physiological and pathological settings. In the context of cancer, VEGF signalling was shown to be impaired in several neoplasms. This discovery led to the development of therapies against VEGF. While antiangiogenic VEGF-targeted therapy has resulted in increased cancer patient survival, the development of resistance has necessitated the discovery of alternative or complimentary therapeutic strategies. Integrin-linked kinase (ILK) is an effector of integrin-mediated cell adhesion. It is also involved in the regulation of the PI3k/Akt pathway.

Methods: The effects of ILK knockdown and anti-VEGF were evaluated on endothelial cell proliferation using BRdU-labeling, and on migration and invasion using the xcelligence system. The effects of the combination treatment on vascular tumour growth were studied in C57BL/6 mice inoculated with sEnd.2 cells. The secretion of VEGF, platelet derived growth factor (PDGF) and basic fibroblast growth factor (bFGF) were measured employing ELISA.

Results: ILK knockdown with siRNA and anti-VEGF treatment with DMH4 resulted in a more pronounced decrease in cell survival, proliferation and migration when compared to the individual treatments, even following VEGF induction. The combination treatment was also more potent in inhibiting angiogenesis in vitro. Western blot analysis revealed the suppression of Akt phosphorylation. Also, results revealed a decrease in the expression of HIF1-α and nitric oxide (NO), as well as a decrease in proangiogenic factors, namely, VEGF, PDGF and bFGF. In vivo, there was a significant reduction in tumor diameter in vascular tumor-bearing mice treated with Cpd 22, an inhibitor of ILK and DMH4 ($n = 6$ per group; $P < 0.05$). Immunohistochemical evaluation revealed a reduction in microvessel density in treated mice.

Conclusions: Therefore, the combination approach may be useful in the elaboration of antiangiogenic therapy in vascular tumors, further studies are warranted.

Legal entity responsible for the study: Peace Mabeta

Funding: National Research Foundation; University of Pretoria

Disclosure: All authors have declared no conflicts of interest.

4P IGF-IR, but not EGFR, regulates DNA damage response in HeLa cells following irradiation

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Background: The roles of receptor tyrosine kinases in DNA damage response (DDR) are still largely unknown. In this study, we examined the possible involvement of insulin-like growth factor I receptor (IGF-IR) and epidermal growth factor receptor (EGFR) in the DNA damage response (DDR) following irradiation.

Methods: HeLa cells expressing the fluorescence ubiquitination-based cell cycle indicator (Fucci) probes (HeLa-Fucci cells) were used in this study. Kinetics of the Fucci fluorescence were detected by FACS and time-lapse imaging. NVP-AEW541, Tyrphostin AG1478, LY294002, PD98059, NU7026 were used as specific inhibitors for IGF-IR, EGFR, PI3-K, MEK, and DNA-PKcs, respectively. Phosphorylation of ERK1/2 and Akt was detected by western blotting. Double strand breaks (DSBs) were detected by immunofluorescence staining for 53BP1. Cells were irradiated using an RX-650 Cabinet X-radiator system (Faxitron).

Results: To investigate the possible involvement of EGFR and IGF-IR in G2 arrest, FACS analysis and time-lapse imaging of Fucci fluorescence were performed using specific inhibitors. Results showed that inhibition of IGF-IR, but not that of EGFR, prolonged G2 arrest, which was irrespective of cell cycle phases at irradiation, i.e., red (G1 phase) or green (S/G2 phases) phase in the Fucci system. Similarly, only inhibition of IGF-IR decreased the DSB repair activity. Hereafter, further analysis was focused on IGF-IR-associated events. We next attempted to identify the responsible IGF-IR-downstream signaling pathways. Irradiation phosphorylated both Akt and ERK; however, inhibition of IGF-IR abrogated activation of only Akt. Moreover, inhibition of PI3-K/Akt, but not that of MEK/ERK, prolonged G2 arrest, which mimicked that of IGF-IR. Inhibition of DNA-PKcs, a major factor of non-homologous end joining (NHEJ), also prolonged G2 arrest.

Conclusions: We conclude that irradiation is likely to preferentially activate the IGF-IR/PI3-K/Akt signaling pathway in HeLa-Fucci cells, which may enhance DSB repair, eventually contributing to reduction of G2 arrest in the DDR following irradiation.

Legal entity responsible for the study: Tokyo Medical and Dental University

Funding: Tokyo Medical and Dental University, MEXT Japan

Disclosure: All authors have declared no conflicts of interest.

5P Targeted degradation of anaplastic lymphoma kinase by target degraducer in non-small cell lung cancer

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Background: Recently, a new and powerful technology, called "proteolysis targeting chimeras" (PROTAC), has been highlighted in the drug discovery area. Treatment of PROTAC molecule, which contains a ligand for the targeted protein, a ligand for E3 ubiquitin ligase binding, and a linker for connection of two ligands, successfully induced targeted protein degradation, thereby inhibiting cancer growth in in vivo animal model study. Anaplastic lymphoma kinase (ALK) gene fused to various partner genes are observed in 3–7% of non-small cell lung cancer (NSCLC) in humans. The constitutively activated ALK fusions play an essential role in cancer growth and survival. In this study we aimed to identify novel ALK target degraders (TDs) by applying PROTAC technology.

Methods: LDK-378 (ceritinib) as an ALK ligand and VHL or CRBN as an E3 ubiquitin ligase were selected. Hydroxyproline analogs (HP-7) and pomalidomide were used for VHL and CRBN E3 ligase ligands, respectively. All TDs were evaluated in enzymatic- and cell-based assays. ALK degradation by TDs were confirmed by western blotting in SU-DHL-1 cell lines. In vivo antitumor activities were evaluated in xenograft mouse model with H3122 cell lines.

Results: A series of TDs were synthesized with various linkers. The TDs showed anti-ALK activities in both enzymatic and cell-based assays. The TDs exhibited ALK degradation through ubiquitination-proteasome process in cells. Finally, the TDs could inhibit tumor growth in xenograft study with H3122 cells.

Conclusions: These results suggest that the ALK-TDs, inducing ALK degradation, represents a promising strategy for the treatment of ALK-driven NSCLC.

Legal entity responsible for the study: Jong Yeon Hwang

Funding: Korea Research Institute of Chemical Technology

Disclosure: All authors have declared no conflicts of interest.

6P Quinazoline clubbed s-triazine derivatives as VEGFR2 kinase inhibitor: Design, synthesis, docking, antiproliferative and antiangiogenic activity on cancer-induced chick embryo

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Background: Angiogenesis is a fundamental and complex process of endothelial cells, pericytes and responsible for executing normal physiological responses like wound healing, embryonic development and bone remodelling etc. Judah Folkman and colleagues established the concept of angiogenic inhibition in tumour growth. The epidermal growth factor (EGF) receptor (EGFR) and vascular endothelial growth factor (VEGF) pathways play an important role in the growth, metastatic potential of tumours and their inhibition is a prime target for various therapeutic agents including quinazoline based compounds because it represents the most validated signalling pathway. Considering that we have developed quinazoline clubbed 1,3,5-s-triazine derivatives (QCTD) as a potential inhibitor of VEGFR2 kinase for anti-cancer activity.

Methods: Designing of (QCTD) was done on the basis of molecular field mapping and alignment studies with standard angiogenic inhibitor vandetanib. Further docking studies were performed by Autodock 4.2 for most promising similar designed derivatives and all screened (QCTD) were developed via cost-effective synthetic route. The synthesized derivatives were evaluated for their in-vitro anti-cancer activity on four different cell line HeLa (Human Cervical Carcinoma), MCF-7 (Breast Carcinoma), HL-60 (Human promyelocytic leukemia) and HepG2 (Human Hepatocellular carcinoma) and and also in-ovo angiogenic inhibition was performed on chick embryo.

Results: All the designed derivatives explored more than 50% similar pattern of field and atomic arrangement. Thiourea (8b), chloranilino(8d), hrdrazicarboxamide(8j) and methylamino(8m) substituted derivatives selected for docking calculations due to higher similarity value. Docking studies revealed significant result like standard drug vandetanib on protein VEGFR2 kinase (PDB ID: 3EWH). IC_{50} report clearly marked that derivatives have significant antiproliferative action against wide verity of cancer cell line and in-ovo result explored that derivatives are non-toxic to the normal cells.

Conclusions: We have developed a novel class of anticancer agents.

Legal entity responsible for the study: N/A

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7P Selenium-enriched polysacchride green tea extract alters the early stage hepatocellular carcinoma by angiogenesis hypoxia and metastatic inhibition

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Background: Targeting various pathways during progression and expansion of hepatocellular carcinoma (HCC) is one promising strategy to control the complications of liver cancer. The present investigation targeted the potential effect of selenium-enriched green tea polysaccharides on HOX, hypoxia-induced factor, Vascular Endothelium Growth Factor (VEGF), matrix metalloproteinase (MMP-2 and MMP-9), alpha fetoprotein (ALF) and CD31 in diethylnitrosamine induced HCC rats.

Methods: The extract was rich in uronic acid (3.2%), carbohydrate (91.2%) and 4.5 µg/g of selenium to represent SCP. This extract was evaluated for apoptosis mechanism against HCC cell lines viz., Hep-G2 and HuH-7. Invivo study, can be read as: Normal; NC + SCP (20 mg/kg); DEN treated; DEN + SCP (20 mg/kg). The treatment was initiated a week before the DEN administration and was carried for 22 weeks. HCC via DEN is known for significant alteration in biochemical, inflammatory, antioxidant parameters and liver histopathology. Furthermore we also estimated the HOX, HIF, VEGF, MMP-2 and MMP-9, ALF and CD31 parameters.

Results: In vitro studies confirmed the inhibition of the growth of Hep-G2 and HuH-7 cells in a dose-dependent manner via scavenging the cell at G2 phase of cells. Cell death was confirmed via enhanced caspase 3, 9 activity and Bax/Bcl2 ratio, suggesting the effect on the c-caspase pathway on apoptosis. The animal studies confirm the alteration in biochemical, antioxidant and inflammatory markers. Further to substantiate our claim SCP also inhibited the protein elevation of HIF-1a, VEGF, MMP-2, 9 and CD31 compared with DEN control group rats. The alteration in these parameters was sufficient to confirm the reduction of angiogenesis, hypoxia and metastasis and proved the potential effect of SCP at early expansion stage of disease.

Conclusions: Collectively, we can conclude that selenium-enriched polysaccharides of green tea reduced the progression and expansion of hepatocellular carcinoma via multiple mechanisms.

Legal entity responsible for the study: N/A

126P Assessment of EpCAM Intensity of Expression and Outcome in breast Carcinoma Neoadjuvant Chemotherapy Treated Patients

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Background: Back ground: The wide use of Neoadjuvant chemotherapy nowadays became so wide to the degree that it is more or less established as a standard regimen in management of breast neoplasia, in spite of different outcome results. Expression of epithelial cell adhesion molecule (EpCAM) is deregulated in epithelial malignancies. It is found that it acts as signaling molecule with tumor-promoting functions in addition to its role in cell adhesion. Aim of Work: It is aimed to assess the expression intensity of malignant mammary cells of EpCAM and its relation to the patient out come and their response to neoadjuvant chemotherapy.

Methods: 140 patients with breast carcinoma and undergone treatment with neoadjuvant chemotherapy were included in the study. Both Tru-cut tissue biopsy and radically-excised breast tissues; before and after neoadjuvant chemotherapy, were examined for intensity of staining by EpCAM.

Results: High intensity of EpCAM expression pattern is found correlated with lympho-vascular invasion status and higher nuclear grade ($P = 0.01$ and 0.008, respectively), and was associated with poor outcome ($P < 0.001$). We also found that patients with high EpCAM expression before and after neoadjuvant chemotherapy showed worse pathological and clinical outcome ($P = 0.008$ and <0.001, respectively) than the patients with high intensity before and low intensity after neoadjuvant chemotherapy. The overall survival rate of the first group is less than the second one ($P = 0.049$).

Conclusions: Strong EpCAM intensity in carcinoma of breast is correlated with bad response to neoadjuvant chemotherapy and subsequently with worse prognosis than in patients with negative or low staining intensity.

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127P Synergistic role of HIF-1α and Nav1.5 in potentiating breast cancer metastasis

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Background: Hypoxia, a condition of low oxygen concentration especially in locally advanced solid tumors has emerged as a pivotal factor in tumor prognostic since it can initiate tumor progression and resistance to therapy. Under this condition, transcription factor HIF-1α is the major regulator that induces activation or repression of particular homeostatic regulatory genes leading to cancer cell survival and metastasis. Additionally, ion channels such as voltage-gated sodium channels (VGSCs), have been reported to be elevated in various metastatic cancer cells in the past two decades. Several recent studies captured VGSCs in having a mechanistic role in promoting invasion and migration. Specifically in aggressive breast cancer cells, an isoform of VGSCs, Nav1.5 exhibited an increased in expression. Since both HIF-1α and Nav1.5 are highly expressed in aggressive breast cancer cells, this study is designed to investigate the synergic contribution of HIF-1α and Nav1.5 which may provide a better strategy-plan to combat metastatic disease.

Methods: Herein, HIF-1α was stabilized using cobalt chloride, $CoCl_2$ (hypoxia mimicking agent) in the less aggressive breast cancer, MCF-7 cells which lack of HIF-1α and Nav1.5. mRNA of Nav1.5 and CA9 (a common target gene of HIF-1α) was analyzed by relative real-time PCR. Nuclear protein for HIF-1α was measured using Western blotting. Growth, lateral motility and transwell migration assays were conducted to investigate metastatic properties of the cells.

Results: $CoCl_2$ successfully increased HIF-1α nuclear protein and mRNA expression of CA9. This was followed by increased Nav1.5 mRNA expression. Although $CoCl_2$ did not alter growth of MCF-7 cells, motility and migration were enhanced.

Conclusions: In conclusion, increased mRNA of HIF-1α leads to upregulation of Nav1.5 expression. In combination, both molecules promote breast cancer cell aggressiveness though possible interaction between the two needs further studies.

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128P The alteration of p53-pathway gene expression in advanced breast cancer after neoadjuvant chemo- and hormone therapy

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Background: Nowadays, neoadjuvant chemo- and hormone therapy has been widely used for locally advanced breast cancer patients to reduce tumor size. However, the effect of both neoadjuvant therapy (NAT) on metastatic breast cancer remains unknown, particularly in association with apoptotic-pathway. This study aimed to examine the expression alteration of p53-apoptotic pathways genes in advanced breast cancer patients after neoadjuvant chemo- and hormone therapy.

Methods: We collected stage IIIb and IV breast cancer tissues from 46 patients before and after neoadjuvant chemo- (5-fluorouracil, anthracyclines, cyclophosphamides) and hormone (tamoxifen or aromatase inhibitor) therapy. Patients were treated for 6 months prior to tumor resection. The expression profile of p53-pathway genes was investigated using Next- Generation Sequencing and Targeted RNA expression p53 panel comprising of 52 genes (TruSeq®, Illumina). The alteration of the p53-pathway gene expression after NAT was analyzed using dependent t-test and correlated with clinical characteristics and patients' overall survival.

Results: In this study, we found that the expression of 7 genes in p53 panel was significantly altered after NAT. Among these 7 genes, 3 apoptosis-inducing genes (ATM, CASP8 and CASP9) were overexpressed, whereas 1 anti-apoptosis genes BIRC5, as well as 2 proliferative genes (CDK1 and PCNA) were under-expressed. Surprisingly, the death-agonist BID gene was significantly underexpressed. No significant difference of these 7 gene expression profiles based on ER, PR and HER2 status, and NAT types. The ATM gene expression alteration was significantly different between stage IIIb and IV groups. Furthermore, we demonstrated that the alteration of PCNA gene expression was significantly correlated with the patients' 3-years survival.

Conclusions: Alteration of six p53-pathway gene expressions after NAT indicates the effectiveness of both chemo- and hormone therapy to suppress tumor proliferation and induce apoptosis in advanced breast cancer prior to mammosurgery. However, the overexpression of BID gene should be considered as an inducer of therapy resistance.

Clinical trial indentification: This study has been approved by The Ethics Comittee of Faculty of Medicine, Universitas Indonesia.

Legal entity responsible for the study: Faculty of Medicine, Universitas Indonesia

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Disclosure: All authors have declared no conflicts of interest.

129P Inhibition of breast cancer cell explosion rate by irinotecan loaded zinc oxide nanoparticles through E2F3/Akt signaling circuits: A milestone in cancer gene therapy

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Background: The E2F3 transcription factor claims its role in controlling cell cycle progression. Accordingly, the present investigation has been designed to assess to what extent E2F3 would be overexpressed in breast cancer. Although chemotherapeutic drugs are widely applied for clinic tumor treatment, severe toxicity restricts their therapeutic efficacy. The present study was to emphasize that the synthesis of stable SiRNA (E2F3) conjugated irinotecan loaded Zinc Oxide Nanoparticles (SiRNA-irinotecan-ZnONPs) and the elucidation of their mechanism of action in preventing the growth of breast tumors. Cell viability and expression of apoptotic markers (p58, Bax, and cytochrome c) were assessed and the level of E2F3 is increased in breast cancer and highlights the efficacy of siRNA targeted to E2F3.

Methods: We used the green-bio method to synthesize SiRNA-irinotecan-ZnO nano complex for its use as a cancer-targeted drug delivery system to achieve enhanced cellular uptake and anticancer efficacy. To investigate the expression level of E2F3/Akt/Mdm2/AR by RT-PCR and Western blotting analysis was carried out.

Results: Here, we prepared siRNA conjugated irinotecan-ZnONPs against E2F3 significantly blocked the expression of the E2F3 in breast cancer and investigated its inherent anticancer mechanisms. We found SiRNA-irinotecan-ZnONPs inhibit growth of breast LNCaP cancer cells through activate Akt kinase and Mdm2 regulated degradation through proteasome pathway, dramatically inhibited tumor growth and significantly promote cell apoptosis.

Conclusions: This in vitro and in vivo study demonstrates that E2F3 is a newly identified diagnostic and potential therapeutic target in breast cancer. Outcomes of this study affirm that SiRNA-irinotecan-ZnONPs for E2F3 facilitates the silencing of E2F3 overexpression and fights against breast cancer cells growth. These findings suggested that SiRNA-irinotecan-ZnONPs were deemed as a potential drug nanocarrier for cancer therapy and opens a new path for synergistic treating of cancer with higher efficacy and decreased side effects.

Clinical trial indentification: In this study were approved by the Institutional Animal Ethical Committee of the Sankaralingam Bhuvaneshwai College of Pharmacy (622/PO/c/02/CPCSEA/2014) in accordance with the policie established in the Guide to Care & Use of Experimental Animals prepared by the Committee.

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Disclosure: All authors have declared no conflicts of interest.

130P Locoregional treatment in de novo stage IV breast cancer: A retrospective study of Chinese population

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Background: The role of locoregional therapy of the primary in patients presenting with de novo stage IV breast cancer remains controversial. The aim of the present study was to evaluate the impact of locoregional resection and radiotherapy on survival of Chinese women with stage IV breast cancer.

Methods: The retrospective study included Chinese patients with de novo stage IV breast cancer in National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences between January 1st 2001 and November 30th 2015.Patients were identified as having local surgery if the date of breast-conserving surgery or mastectomy was within 1 year of initial breast cancer diagnosis date. All patients were treated with primary chemotherapy treatment. The target volume for locoregional radiotherapy was the chest wall and draining lymphatics and regimen delivered 50 Gy in 25 fractions. Kaplan-Meier curves were reported for overall survival (OS), and distant progression free survival (DPFS). Log-rank test was used to compare the difference in groups. Cox proportional models were fitted for multivariate analysis.

Results: Of the 157 patients who presented with stage IV breast cancer, 66 (42.0%) underwent surgery, 52 (33.1%) patients received locoregional radiotherapy. Median age was 58.0 years (range 28 to 83 years). Median follow up time was 44.5 months (range 5 to 180 months). Median OS and DPFS were 36 months and 21 months. Patients in the surgery group had longer OS and DPFS than non-surgery group (5-y OS 93.3% vs 60.4%, $P = 0.002$; 5-y DPFS 57.6% vs 26.4%, $P < 0.001$). DPFS was also significantly longer in patients who received radiotherapy ($P = 0.034$). Multivariate analysis showed that surgical treatment was the only factor associated with OS (HR = 0.41, CI = 0.18-0.95, $P = 0.04$), and response to systemic therapy (HR = 0.24, CI = 0.07-0.76, $P = 0.016$), surgery (HR = 0.43, CI = 0.24-0.78, $P = 0.005$) and PR status significantly influenced the DPFS (HR = 2.97, CI = 1.40-6.26, $P = 0.004$).

Conclusions: Locoregional surgical treatment and radiotherapy were associated with improved survival in Chinese patients with stage IV breast cancer. Response to systemic therapy and PR status may be impact factors for predicting prognosis.

Legal entity responsible for the study: Cancer Institute and Hospital, Chinese Academy of Medical Sciences (CAMS), Beijing, China

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Disclosure: All authors have declared no conflicts of interest.

131P Breast-specific gamma imaging (BSGI) as follow-up after breast cancer surgery: Comparison with ultrasound and mammography

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Background: To evaluate breast-specific gamma imaging (BSGI) for detection of locoregional recurrence after surgery in breast cancer patients and to compare it with ultrasound and mammography.

Methods: Our study included 165 breast cancer patients who had undergone post-operative BSGI between August 2010 and December 2013. The imaging findings (BSGI, ultrasound [US] and mammography) were retrospectively reviewed for recurrence. The standard reference was the pathologic result and follow-up BSGI or US conducted within the past two years. The sensitivities, specificities, accuracies, negative predictive values (NPV), and positive predictive values (PPV) of BSGI, US and mammography were calculated.

Results: Locoregional recurrence was confirmed in five patients. The recurrence sites were the contralateral breast (n = 1), ipsilateral breast (n = 1), ipsilateral axilla (n = 1), supraclavicular area (n = 1), and infraclavicular area (n = 1). The previous pathologic stagings were stage 1 (n = 1), 2 (n = 1), and 3 (n = 3). The sensitivities, specificities, PPV and NPV for recurrence were as follows: on BSGI, 40%, 88.1%, 9.5% and 97.9%; on US, 100%, 92.5%, 29.4% and 100%, and on mammography, 33.3%, 100%, 100% and 98.6%, respectively. The diagnostic accuracies of BSGI, US and mammography were 86.7%, 92.8%, and 98.6%.

Conclusions: The diagnostic accuracy of BSGI for detection of locoregional recurrence in breast cancer patients was 86.7%. BSGI was not superior to US or mammography in this regard. Therefore, BSGI should not be recommended for routine post-operative follow-up on breast cancer patients.

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Disclosure: All authors have declared no conflicts of interest.

132P Quality of life and psychosocial needs of metastatic breast cancer patients

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Background: Review prior literature and patient survey reports related to metastatic breast cancer (MBC) patients' quality of life (QoL) needs, and assess extent to which local organizations are meeting them.

Methods: (1) Research findings of > 150 published, peer-reviewed research articles including quantitative and qualitative studies of MBC patients and their families, were summarized around the realities of living with MBC. (2) 13 surveys of ~8,000 MBC patients were examined for common concerns. (3) Desk research analysis of leading nonprofits' patient advocacy, research, education and support (n = 16); and interviews with leadership about services for patients (n = 16).

Results: The extensive research base around MBC QoL issues was summarized into 6 categories: psychosocial distress; emotional support; information about the disease, its treatment, and resources; communication and decision making about care; relief of physical symptoms; and practical concerns. Sources of emotional support, individual and group psychotherapy, and counseling, as well as adequate information about the disease, its treatments, and methods to alleviate symptoms and side effects have been shown to be useful in helping patients cope with MBC. However, patients are typically not well informed in areas required for decision making about their care, and patient–clinician communication can be difficult. MBC symptoms and side effects of continuous treatment - fatigue, sleeping difficulties, and pain - and emotional distress interfere with daily life; supportive and palliative care is often insufficient. While the majority of the major local breast cancer advocate organizations focus on meeting the support needs of the breast cancer community, not enough attention is paid to the MBC patient population. Gaps in information include lack of detailed information on latest treatments, QoL, palliation, communication with health care providers, and advanced directives and end-of-life care.

Conclusions: While QoL issues for MBC patients/caregivers are well understood, the resources and commitment to address these issues are still lacking. Targeted information and support services addressing QoL needs are as necessary to patients as medical treatments.

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Disclosure: All authors have declared no conflicts of interest.

134P Safety and efficacy of eribulin and trastuzumab in anti-HER2 therapy pretreated patients with HER2-positive metastatic breast cancer: A Japanese multicenter phase 2 study (SBP-04 study)

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Background: The efficacy of eribulin for HER2 negative metastatic breast cancer (MBC) was confirmed by EMBRACE trial. However, there is no definitive Asian evidence about efficacy and safety of eribulin combined with trastuzumab (ET) for HER2 positive MBC.