Session 2: Breast cancer symposium

OCPS 14: Next-generation therapeutics for metastatic breast cancer and perspectives on clinical translation

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Metastatic breast cancer (MBC) is prevalent and a leading cause of cancer-related death among women; this trend is projected to continue for the next decades (World Cancer Report 2014, edited by Bernard W. Stewart and Christopher P. Wild, IARC-WHO Publications, 2014). At present there is no “gold standard” therapeutics for MBC and systemic chemotherapy, combined in specific cases with targeted agents, remains the cornerstone therapeutics. However, this therapeutic modality has an unpredictable clinical outcome, often disappointing, and inevitably many patients experience recurrence and progress to life threatening disseminated forms. Search for alternative therapeutics for MBC is at the forefront of drug discovery research. With the advent of molecular medicine heralded by the Human Genome Project and the remarkable progress in high-throughput genomic technologies, our ability to interrogate breast cancer genome and epigenome at the molecular levels has expanded. Breast cancer is now recognized as a highly heterogeneous disease that encompasses diverse molecular subtypes with distinct biological and clinical implications, in particular in relation to metastasis incidence and prognosis. Within breast cancer subtypes associated with aggressive behavior, e.g. basal type/ triple-negative and Her2+, new concepts for metastasis development have emerged (e.g. stem cell and/or epithelial-mesenchymal transition concepts, metabolomics, tumor dormancy,...) and opened-up new avenues for discovery of innovative therapeutic targets for MBC. As well, we have begun to realize the extent to which it is critical to target signaling cross talks between cancer cells and their tissue microenvironment; these are critical determinants for cancer cells to evade primary sites and metastasize and survive in distant organs. Tumor cell dependence on several of these mechanisms also creates, under specific circumstances, vulnerabilities that can be exploited to identify innovative therapeutics for incurable MBC. In this context, the focus of this presentation is to overview the current status of newly developed therapeutic agents undergoing clinical trials, as well as new generation of experimental therapeutics under development, including from this investigator’s team, and targeting drivers of metastasis such as regulators of stem cell and epithelial-mesenchymal signaling, immune response, tumor dormancy, and metabolomics. The translational potential of these emerging therapeutics in relation to personalized care tailored to specific subtypes of MBC disease will be discussed.