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An update on methods for cryopreservation and thawing of hemopoietic stem cells

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This presentation will focus on a number of variables related to stem cells cryopreservation procedures of minimally manipulated products containing allogeneic or autologous hemopoietic progenitor cells (HPC) used for transplantation. The issues includes: regulations and standards, processing, process validation and qualification, volume reduction, cell concentration, volume, freezing, storage, cooling rate, warming events, quarantine, cross contamination during storage and thawing. New approaches of processing were developed such as automatic devices for volume reduction and high cell concentration in the frozen product. DMSO at 10% final concentration is still the most used cryo-protectant for HPC cryopreservation. Although controlled rate freezing is the recommended method for HPC cryopreservation, alternative methods may be used. Last generation vapor storage vessels ensure temperature stability better than older tanks and may reduce risks of cross-contamination. Finally, advantages and disadvantages of thawing procedures carried out at patient's bedside or in the laboratory will be discussed.

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DCIS in *BRCA1* and *BRCA2* mutation carriers: Prevalence, phenotype and expression of oncodrivers C-MET and HER3

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Background: Studies report conflicting evidence regarding the existence of a (ductal carcinoma in situ) DCIS-associated premalignant pathway in BRCA mutation carriers. We aimed to examine the prevalence, phenotype and expression of oncodrivers in pure DCIS (pDCIS) and invasive breast cancer with concurrent DCIS (IBC+DCIS) in mutation carriers.

Methods: A cohort of *BRCA1* and *BRCA2* mutation carriers >18 years old who underwent surgery for breast cancer at an academic hospital (1992-2011) and had pathology available for review were included for study. Invasive breast cancer (IBC) and DCIS were stained for ER, PR, HER1, HER2, and HER3, and C-MET. DCIS prevalence was evaluated. Correlation of IBC and DCIS phenotypes was evaluated in patients with IBC+DCIS. DCIS and IBC expression of tumor markers were examined by BRCA mutation.

Results: We identified 114 breast tumors. Of all *BRCA1*-associated tumors, 21.1% were pDCIS and 63.4% were IBC+DCIS. Of all BRCA2-associated tumors, 23.3% were pDCIS and 60.5% were IBC+DCIS. In *BRCA1* and BRCA2 mutation carriers with IBC+DCIS, there was a significant correlation in ER, PR, and HER3 expression between the DCIS and IBC components. Most *BRCA1*-associated DCIS did not express ER, PR or HER2, while most BRCA2-associated DCIS expressed ER and PR. *BRCA1*- as well as BRCA2-associated DCIS had expression of HER3 and C-MET.

Conclusions: The majority of BRCA-associated tumors had DCIS present. Concordance of DCIS and IBC phenotypes was high, arguing for the existence of a DCIS-associated premalignant pathway. Oncodrivers HER3 and C-MET were expressed in the DCIS of mutation carriers, suggesting an opportunity for prevention strategies.

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