Sergio Aguggini, J Cancer Sci Ther 2016, 8:10(Suppl)
http://dx.doi.org/10.4172/1948-5956.C1.088

Hypoxia-related biological markers as predictors of epirubicin-based treatment responsiveness and resistance in locally advanced breast cancer

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Because hypoxia mediates resistance to anthracyclines *in vitro*, we aimed to identify hypoxia-related biological markers involved in the response and resistance to epirubicin in patients with locally advanced breast cancer. 176 women with T2-4 N0-1 breast tumors were randomly assigned to receive epirubicin 120 mg/m2/1-21 (EPI ARM), epirubicin 120 mg/m2/1-21+erythropoietin 10.000 IU sc 3 times weekly (EPI-EPO ARM) and epirubicin 40 mg/m^2/w-q21 (EPI-W ARM). 16 tumor proteins involved in cell survival, hypoxia, angiogenesis and growth factor, were assessed by immunohistochemistry in pre-treatment samples and a multivariate generalized linear regression approach was applied using a penalized least-square minimization to perform variable selection and regularization. Ten-fold cross-validation and iterative leave-one-out were employed to validate and test the model, respectively. High VEGF and GLUT-1 and low ER were significant factors for complete clinical response to treatment in all leave-one-out iterations. EPO expression was positively correlated with pCR. High HB levels, bcl-2 and HIF-1 expression were significantly negatively correlated with pCR, HB baseline level and HIF-1 alpha nuclear expression were significantly positively associated with a higher risk of relapse and with overall survival.

Biography

Sergio Aguggini is a Breast Surgeon at Breast Cancer Unit-Women's Centre. He has completed his MD and PhD at the University of Milano. He is in charge of the screening program of the Unit. He has published more than 25 papers in reputed journals.

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