Assessing Oxygenation Response to Eribulin in a Patient with Recurrent Breast Cancer after Resistance to Endocrine Therapy

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Abstract

We present our initial experience with a novel method of functional hypoxia imaging. 18F-fluoromisonidazole-positron emission tomography/computed tomography and diffuse optical spectroscopic imaging were used to noninvasively evaluate the biological effects induced by eribulin monotherapy in a patient treated for recurrent breast cancer with acquired resistance to endocrine therapy. Eribulin monotherapy clearly induced reoxygenation, indicated by the markedly reduced 18F-fluoromisonidazole uptake and enhanced oxygen saturation levels in the lesion. These observations suggest that the reversal of hypoxia can be captured utilizing 18F-fluoromisonidazole positron emission tomography/computed tomography and diffuse optical spectroscopic imaging.

Eribulin mesylate (eribulin) is a first-in-class halichondrin B-based inhibitor of microtubule dynamics. In a randomized phase III clinical trial (EMBRACE) in patients with metastatic disease, eribulin yielded significant improvements in overall survival when compared to physician-selected treatment [1]. Consequently, it was approved as a monotherapeutic agent for patients with metastatic breast cancer and a history of treatment with anthracycline and taxane chemotherapy. Recently, basic and clinical studies have revealed that eribulin induces vascular remodeling and subsequent tissue reoxygenation, thus stabilizing the cancer microenvironment and reversing the epithelial–mesenchymal transition associated with malignancy. These responses lead to the suppression of cancer invasion and metastasis .

Endocrine therapy is the mainstay of treatment for patients with Hormone Receptor (HR)-positive breast cancer. However, the long-term effectiveness of endocrine therapy is limited by the development of endocrine resistance, which is strongly associated with hypoxia in the tumor microenvironment [6]. A noninvasive technology for quantifying tumor hypoxia is 18F-fluoromisonidazole (FMISO) positron emission tomography/computed tomography (PET/CT) imaging Investigators have reported FMISO uptake as a robust measure of intracellular hypoxia, and reduced hypoxic activity after endocrine therapy has been identified as a good predictive marker of clinical response in patients with HR-positive metastatic breast cancer Tissue hypoxia can also be noninvasively measured using Diffuse Optical Spectroscopic Imaging (DOSI) with near-infrared light, which can enhance the characterization of vascularity and tissue oxygenation.

A postsurgical pathological examination revealed a 3.6-cm tumor with an invasive ductal carcinoma component. Immunohistochemistry revealed estrogen receptor (ER) positivity (Allred score: 8), progesterone receptor positivity (Allred score: 3), and HER2 negativity (1+), as well as nodal involvement (pN 2/18). She received standard-of-care adjuvant chemotherapy, including epirubicin and cyclophosphamide followed by docetaxel, and breast irradiation.

Seventeen months after finishing adjuvant chemotherapy and while receiving adjuvant leuprorelin (L) plus tamoxifen therapy, she complained of chest pain; recurrence of breast cancer in the PLN was subsequently diagnosed by fine-needle biopsy. Dynamic-contrast enhanced magnetic resonance imaging (DCE-MRI) and a baseline 18F-fluorodeoxyglucose (FDG)-PET/CT revealed PLN metastasis and plural breast cancer dissemination, as well as increased glycolytic activity [maximal standardized uptake value (SUVmax): 11.3]. The patient wished to continue endocrine therapy, which had a minimal risk of side effects and minimal financial burden. Therefore, we suggested three cycles of eribulin monotherapy (1.4 mg/m2, day 1; 8 per 21-day cycle), followed by additional endocrine therapy

Here we present a case of a premenopausal woman with a recurrence of breast cancer in the Parasternal Lymph Node (PLN) after adjuvant endocrine therapy. Following eribulin monotherapy, we observed tissue reoxygenation in the recurrent PLN lesion via FMISO-PET/ CT and DOSI.

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