Aim: Angiosarcoma of the breast is a rare, aggressive soft tissue neoplasm occurring as either a primary or secondary malignancy due to previous radiotherapy for breast carcinoma. There is an unmet medical need for targeted therapies for angiosarcoma.

Methods: Seventeen patients with angiosarcoma of the breast were identified (Caris Life Sciences) and profiled for biomarkers of drug response using multiplatform methodologies (Tumor DNA sequencing, gene copy number alterations, RNA/microarray and protein/IHC expression).

Results: Eight primary, 5 post-radiation and 4 mammary angiosarcomas of unknown etiology were identified in women (age 31-85 years), all exhibiting multiple biomarker alterations. Eight out of 17 cases (47%) harbored overexpression (mRNA and/or protein) of the genes [VEGFR2 (5/17), PDGFRA/PDGFRB (3/17), c-KIT (2/17)] that can be targeted by multikinase inhibitor Sunitinib. Based on the VEGFR2 overexpression, one patient with recurrent, refractory angiosarcoma was treated with Sunitinib resulting in a complete remission and is disease free at 14 months. Also, multiplatform molecular profiling revealed useful predictors of various other treatment modalities including anthracyclines (overexpression of topoisomerase 2α in 69%), topo 1 inhibitors (topoisomerase 1 overexpression in 44%), and fluoropyrimidines (low levels of thymidylate synthase in 29%). One case devoid of the Sunitinib-associated genetic alterations harbored a KRAS mutation indicating a potential benefit of MEK inhibitors.

Conclusions: A comprehensive molecular profiling of breast angiosarcomas enables identification of various molecular alterations that can be treated by both targeted and conventional treatment modalities.

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