Preclinical In Vitro Investigation of MDM2 Inhibition in Combination with Antiangiogenic Therapy for Breast Cancer Treatment	
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Abstract: Background: Combining antiangiogenic drugs with other chemotherapeutic drugs has been found to produce superior therapeutic outcomes and prevent drug resistance in a variety of cancers. Methods: Experimental assays such as the MTT assay, flow cytometry, western blotting, and qPCR have been used to evaluate the efficacy of combination therapy. Results: When compared to controls and monotherapies, the combination treatment of axitinib and idasanutlin demonstrated a substantial decrease in cell viability at lower doses, a significant decrease in migration, and a shift toward early and late apoptosis. This study examined major apoptotic, metastatic, and angiogenic factors, including MDM2, p21, BCL-2, BCL-XL, and MMP9, which have showed differential expressions at the protein and mRNA levels after combination. Axitinib and idasanutlin decreased tumorigenesis and migration in vitro in the MCF-7 cell line when compared to other chemotherapeutic medications. The suggested mechanisms of the antitumorigenic effect of the combination therapy may depend on its capacity to promote the production of apoptotic markers and reduce antiapoptotic markers. Conclusions: Treatments with axitinib and idasanutlin demonstrated effective therapeutic targeting of the primary angiogenic growth factor and, consequently, the pro-metastatic arbitrators. This will not only eliminate cancer cells but also stop other malignant processes and ultimately reduce the metastatic cascade.