Nelfinavir exerts antineoplastic effects in a number of other systemic malignancies besides breast carcinomas. For instance, similar effects are seen in non–small cell lung carcinomas. Nelfinavir causes caspase-dependent apoptosis as well as caspase-independent apoptosis within the pulmonary malignancies. Nelfinavir administration leads to augmentation of C/EBP homologous protein levels (2). Simultaneous accentuation of activating transcription factor 3 levels is also seen (3). As a result, there is a marked increase in intratumoral apoptosis. Nelfinavir also attenuates the activation of Akt. In fact, recent studies in humans suggest that nelfinavir when used in conjunction with chemoradiotherapy demonstrates an overall response of 100% in stage IIIA/IIIB non–small cell lung carcinomas (4). The maximum tolerated dose in this study was 2500 mg administered in two divided doses. (2) In fact, nelfinavir synergistically augments the cytotoxicity of other chemotherapeutic agents such as bortezomib in pulmonary malignancies (5). Similarly, nelfinavir attenuates tumor growth in ovarian carcinomas. It mediates this role by increasing the expression of BiP (GRP78). It also causes augmentation of eIF2α phosphorylation (6). Simultaneous downregulation of cyclin D3 is also seen. These metabolic changes result in accentuated induction of the unfolded protein response (2). As a result, intratumoral apoptosis is markedly augmented within ovarian tumors (6). Nelfinavir administration also increases the expression of DR5 (7). As a result, it augments the proapoptotic effects of tumor necrosis factor–related apoptosis–including ligand receptor antibody.

It is clearly evident from the preceding examples that nelfinavir has significant antineoplastic properties. Further studies in humans are needed to fully evaluate its anticarcinogenic role.


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correspondence@jnci.org