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The Antiemetic Drug Aprepitant as a Broad-Spectrum Anticancer Drug?

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Is it possible for a drug to exert the same antitumor effect against many different types of cancer? Bioactive peptides promote and counteract the development of tumors [1, 2]. Some endogenous peptides (galanin) promote or block tumor development, while others (substance P (SP)) generally favor its development. Thus, it is possible to inhibit the development of the tumor by blocking with antagonists the neurokinin-1 receptor (NK-1R) that facilitates the oncogenic signal mediated by SP, because the SP/NK-1R system promotes tumor development (tumor cell proliferation/migration, anti-apoptotic effect, angiogenesis) [1]. This occurs in many types of cancer where the overexpression of the NK-1R occurs, something that does not occur in normal cells. Therefore, many different tumors could be treated by applying the same therapeutic strategy: the administration of NK-1R antagonists.

Aprepitant (Emend, MK-869, L-754,030) a non-peptide NK-1R antagonist is administered orally as antiemetic drug to treat chemotherapy-induced nausea and vomiting and it is safe; it binds specifically to the human NK-1R, crosses the blood-brain barrier, and exerts antitumor effects (inhibits proliferation, promotes apoptosis, blocks migration/invasion, anti-angiogenic) against different types of human cancer cells as many as twenty-one [1, 3, 4]. That is, all the opposite effects that SP performs on cancer cells. If aprepitant is used in clinical practice as an antiemetic, why has an antitumor effect not been observed then? It seems that this is due to the dose administered in clinical practice (125 mg (day 1), 80 mg (days 2 and 3)); to observe an antitumor effect, the dose and the days of treatment with aprepitant would have to be increased (20-40 mg/kg/day; administered daily until a response to the treatment was observed) compared to the dose/days of treatment as an antiemetic. This dose must be increased since there is an overexpression of the NK-1R in tumors and hence the right dose to be administered is absolutely associated to such overexpression and to the size of the tumor (larger size, higher dose) [1]. The use of aprepitant as an antitumor drug alone or in combination therapy with chemotherapy or radiotherapy is a possibility that should be tested as soon as possible. And even more so when it is known that the combination of aprepitant with chemotherapy or radiotherapy favored a synergic anticancer effect, promoted chemosensitization and radiosensitization, and decreased the side-effects (cardiotoxicity, hepatotoxicity, nephrotoxicity) induced by both therapies [5]. Is there any drug on the market that can potentially act against so many different types of cancer? Aprepitant perfectly meets this requirement. Its repositioning is urgent, its use as an antitumor drug would open new promising and unsuspected doors to fight cancer, and its administration is independent of the tumor biology, clinical stage, location, and tumor type. The SP/NK-1R system opens the door to new tumor research avenues, cancer diagnosis, tumor predictive factors, and anticancer strategies.

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