DOI: https://doi.org/10.54393/pjhs.v5i06.1915

PAKISTAN JOURNAL OF HEALTH SCIENCES
https://thejas.com.pk/index.php/pjhs
ISSN (P): 2790-9352, (E): 2790-9344
Volume 5, Issue 6 (June 2024)

After 20 Years of Treatment with Aprepitant for Chemotherapy-Induced Nausea and Vomiting, Should the Therapeutic Indications for Aprepitant be Expanded?

Riffat Mehboob [1,2] and Miguel Muñoz[3*]

[1]Cell and Developmental Biology Center, National Heart, Lung and Blood Institute, National Institutes of Health, Bethesda, Maryland, United States of America
[2]Lahore Medical Research Center, Lahore, Pakistan
[3]Research Laboratory on Neuropeptides, Institute of Biomedicine Sevilla (IBIS), Sevilla, Spain
miguel.mmunoz@gmail.com

ARTICLE INFO

How to Cite:
Mehboob, R., & Munoz, M. (2024). After 20 Years of Treatment with Aprepitant for Chemotherapy-Induced Nausea and Vomiting, Should the Therapeutic Indications for Aprepitant be Expanded?. Pakistan Journal of Health Sciences, 5(06). https://doi.org/10.54393/pjhs.v5i06.1915

The drug aprepitant, a selective antagonist of the neurokinin-1 receptor (NK-1R), was approved in 2004 by the FDA for the treatment of CINV, blocking the activation of the receptor by substance P (SP). Oral aprepitant (day 1: 125 mg; days 2-3: 80 mg) (low doses) was coadministered with dexamethasone and a serotonin 5-HT3 receptor antagonist. The aprepitant triple regimen is effective for the prevention of CINV in patients being treated with moderately or highly emetogenic chemotherapy [1]. Furthermore, activation of the SP/NK-1R system has been reported to mediate also pruritus and cough. A study published on 17 patients with skin T-cell lymphomas (CTCL) with refractory pruritus was treated with aprepitant administered according to the standard of 125–80–80 mg either in a weekly or a biweekly repetition regimen. They show that aprepitant was safe, well tolerated and effective for the treatment of severe chronic pruritus in patients with CTCL [2]. In addition, two randomized clinical trials have clearly demonstrated that aprepitant (day 1: 125 mg; 2-7/2-3: 80 mg) suppresses treatment-refractory cough in patients with lung cancer [3,4]. Regarding safety, NK-1R antagonist aprepitant was safe and well tolerated. In a placebo-controlled trial in patients with moderate-to-severe major depression, a dose of 300 mg/day (moderate doses) of aprepitant was well tolerated and no statistically significant difference in the frequency of adverse events was observed as compared with placebo. Additionally, aprepitant was as antidepressant as paroxetine [5]. Furthermore, in the las 20 years has been reported many papers about the involvement of SP/NK-1R in cancer progression and the use of NK-1R antagonist aprepitant counteract all the pathophysiological functions of SP related to cancer. In fact, aprepitant is a broad-spectrum antitumor drug. Obviously, the concentrations or doses of aprepitant to have antitumor activity are higher (20-40 mg/kg/day) (high doses) [6].

In conclusion, based on the safety (low and moderate doses) and efficacy of aprepitant, its use in refractory pruritus with CTCL and treatment-refractory cough in patients with lung cancer should be approved. Regarding cancer treatment (high doses) we suggest the initiation of a Phase I clinical trial to see what safe doses are and Phase II clinical trials to evaluate the efficacy of aprepitant alone or in combination therapy with chemotherapy or radiotherapy at least in tumors with the poor prognosis.

REFERENCES

[1] Qiu T, Men P, Xu X, Zhai S, Cui X. Antiemetic regimen with aprepitant in the prevention of chemotherapy-induced nausea and vomiting: An updated systematic review and meta-analysis. Medicine (Baltimore). 2020 Aug; 99(33): e21559. doi: 10.1097/MD.0000000000021559.

[2] Maroñas-Jiménez L, Estrach T, Gallardo F, Pérez A, Andrés Borja H, Servitje O *et al.* Aprepitant improves refractory Pruritus in primary cutaneous T cell lymphomas: experience of the Spanish Working Group on Cutaneous Lymphomas.

DOI: https://doi.org/10.54393/pjhs.v5i06.1915

British Journal of Dermatology 2018; 178: e273–e274. doi: 10.1111/bjd.16128.

[3] Noronha V, Bhattacharjee A, Patil VM, Joshi A, Menon N, Shah S *et al.* Aprepitant for Cough Suppression in Advanced Lung Cancer: A Randomized Trial. Chest. 2020 Jun; 157: 1647-1655. doi: 10.1016/j.chest.2019.11.048.

[4] Smith JA, Harle A, Dockry R, Holt K, Russell P, Molassiotis A et al. Aprepitant for cough in lung cancer. A randomized placebo-controlled trial and mechanistic insights. American Journal of Respiratory and Critical Care Medicine. 2021; 203: 737-745. doi: 10.1164/rccm.202006-2359OC.

[5] Kramer MS, Cutler N, Feighner J, Shrivastava R, Carman J, Sramek JJ et al. Distinct mechanism for antidepressant activity by blockade of central substance P receptors. Science. 1998 Sep; 281(5383): 1640-5. doi: 10.1126/science.281.5383.1640.

[6] Muñoz M and Coveñas R. The Neurokinin-1 Receptor Antagonist Aprepitant: An Intelligent Bullet against Cancer? Cancers(Basel). 2020; 12:2682. doi: 10.3390/cancers12092682.