

## INTRODUCTORY REMARKS

### Navoban® (tropisetron): reducing the distress of the first-time chemotherapy patient

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Nausea and vomiting are the two most distressing symptoms among those reported by patients undergoing chemotherapy.

The quantitative importance of the symptom of vomiting is confirmed by the fact that antiemetic agents can be classified in three groups according to their potential to induce vomiting: low, moderate and high emetogenic activity.

Emesis is defined as acute when it occurs within 24 hours of antiemetic treatment and delayed when it occurs after this time limit. The pathophysiological mechanisms of the emesis-inducing action of antiemetic drugs are not fully known but seem to be caused by impulses of a differing nature which stimulate the vomiting centre (situated in the lateral reticular formation in the floor of the fourth ventricle) to organise and coordinate the emetic response.

The impulses arriving in the vomiting centre come from the following areas:

- chemoreceptor trigger zone in the posterior part of the fourth ventricle, stimulated by chemical mediators circulating in the blood and in the cerebrospinal fluid
- gastrointestinal tract through vagal and sympathetic pathways
- upper cortical centres
- vestibular apparatus.

Even though a complete picture of the neurotransmitters involved in the complex network of vomiting has not yet been defined, it has been clear since high-dose metoclopramide was first used in antiemetic therapy that part of its antiemetic effect was due to an antagonistic action on 5-HT<sub>3</sub>-receptors for serotonin. These

receptors have been identified both peripherally in the gastrointestinal mucosa and centrally in the area postrema.

Thanks to an adjusted cost-benefit ratio, the development of drugs which act as selective antagonists of 5-HT<sub>3</sub>-receptors, without interfering with dopaminergic 5-HT<sub>1</sub>- or 5-HT<sub>2</sub>-receptors, has led to a much improved efficacy together with a reduced toxicity.

While numerous 5-HT<sub>3</sub>-antagonists are still in Phase 1 and 2, only a few have proven to be clinically effective on a large scale. Of these, Navoban® (tropisetron) has some extremely interesting qualities:

- extreme selectivity
- high efficacy
- long-lasting action, with the possibility of mono-administration in a 24-hour period
- reduced incidence of side effects, which are not usually high-grade.

These characteristics have led to the drug being taken up into clinical oncological practice.

In order to improve the quality of life of patients undergoing chemotherapy, more research needs to be done, especially regarding a possible increase in antiemetic action through the association of Navoban® with other compounds against antiemetic regimens with high emetogenic potential.

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