

# Radiation therapy and delayed emesis

Richard J. Gralla

Jacobi Medical Center, Albert Einstein College of Medicine, Bronx, NY, USA

Correspondence to: Richard J. Gralla. Jacobi Medical Center, Albert Einstein College of Medicine, Bronx, NY, USA. Email: rgralla@gmail.com.

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Comment on: Ganesh V, Drost L, DeAngelis C, *et al.* A pilot study with palonosetron in the prophylaxis of radiation-induced nausea and vomiting. *Ann Palliat Med* 2018;7:211-20.

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Not all clinical trials need to be large randomized comparisons to add to our ability to care for patients. The study of Ganesh *et al.* in this issue (1), coupled with an earlier report by this group (2), provide useful findings advancing knowledge about radiation induced nausea and vomiting (RINV).

The authors correctly point out that there are far more trials investigating emesis caused by chemotherapy (CINV) than by radiation. Clearly there are unique factors influencing the incidence and control of emesis which differ between radiation and chemotherapy; but, at the same time there are lessons that apply to both modalities. The guidelines developed by MASCC (3) have provided a framework for the prevention emesis, and their detailed analysis concerning the prevention of RINV has become the worldwide standard (4). The multiple editions of these evidence-based guidelines have advised that radiation dosage and location are major risk predictors for emesis, as are female gender and younger age. The latter two factors are also found as key emesis risk factors in patients receiving chemotherapy.

The Ganesh trial and the Dennis study provide firm evidence concerning the risk and frequency of delayed emesis in patients receiving radiation therapy. Delayed emesis has been less well characterized in RINV than in emesis caused by chemotherapy. Delayed emesis, or that emesis beginning or persisting the day after the start of treatment, is less well controlled than acute emesis (emesis on the day of treatment) in patients given chemotherapy. Consistent reporting from the Ganesh and the Dennis trials confirms that with radiation delayed emesis not only is a problem, but that it is more difficult to control with this treatment modality than is acute emesis. Furthermore, these

authors demonstrate that delayed emesis is common with both single fraction and with multiple fraction treatment. These findings are important in educating patients, in planning emesis prevention and in designing future clinical research.

A prominent difference between the Ganesh and the Dennis papers is the choice of the serotonin type-3 receptor antagonist used in each trial (palonosetron in the former study, and ondansetron in the latter). Emetic control was reported to be higher in the study using palonosetron, and this was especially seen in the delayed emesis setting with this antiemetic which has a longer half-life and increased affinity for the serotonin type-3 receptor than does ondansetron. The authors acknowledge their comparison is a historical one, using their two reports, and that differences in patient and treatment characteristics may exist. Nonetheless, it is interesting to note that with chemotherapy, several prospective large randomized trials with chemotherapy have shown significantly better control of delayed emesis with palonosetron (5,6) when compared with other serotonin receptor antagonists, and these results have been bolstered by a large meta-analysis (7). To answer fully the question of which serotonin type-3 receptor antagonist is superior in RINV, a large randomized clinical trial would be required. One could ask, however, given the results of these two trials in RINV and the demonstration of efficacy differences in CINV, is such a large trial the best use of research resources? No toxicity differences have been observed between the two agents, other than less effect of palonosetron on electrocardiographic QTc intervals (8). Even modest reductions in nausea and vomiting, given the clear impact of emesis on quality of life and the ability

to perform normal activities are noteworthy; as such, the above observations may be sufficient for decision making. The main consideration then becomes the acquisition cost difference between the two agents versus the current clinical findings supporting better emetic control (1,2,7).

The Ganesh trial highlights the occurrence of delayed emesis in patients receiving RT, a fact that has not been sufficiently emphasized previously. Although the control rate is fairly good in this study, the delayed emesis problem still exceeds that of acute emesis, and this observation applies to both single and multiple fraction treatments. This paper carefully outlines the magnitude of the problem of delayed emesis and provides a good basis for further study.

Would the addition of an NK<sub>1</sub> receptor antagonist agent improve control of RINV delayed emesis, and if so, what schedule should be used and for which patients? This trial also illustrates that smaller, well-conducted studies can guide future research while influencing clinical awareness and practice. Additionally, this study demonstrates that there are many common supportive care problems in the practice of radiation therapy that could be improved by the findings of careful clinical trials.

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### Footnote

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