CHINESE CLINICAL ONCOLOGY

Peer Review File

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Reviewer A

Nausea and vomiting are frequent complications of chemotherapy. Setrons and NK1 receptor inhibitors have been a major advance in the prevention of acute vomiting and delayed nausea. For several years, MASCC has published recommendations for the management of nausea and emesis. For "highly emetogenic" chemotherapy (primarily cisplatin and anthracyclin), the MASCC recommendations are a combination of aprepitant, setrons and steroids.
The aim of this study is to monitor compliance with these recommendations and effectiveness in a real life population of 1000 people receiving chemotherapy considered as highly emetogenic.
the article is interesting, well-written and a real-life study on the follow-up of international recommendations is very useful.
Response: Thank you for your kind comment.

Nevertheless some points need to be improved or clarified
- the inclusion criteria were "highly emetogenic chemotherapy," 72% cisplatin and 18.6% anthracycline but 10% of patients had low emetogenic chemotherapy: exclude these patients? A clarification: were carboplatin-based chemotherapies excluded?
Response: Yes, in our inclusion criteria, enrolled patients were scheduled to receive highly emetogenic chemotherapy, so low emetogenic chemotherapy subjects should be excluded, but there are still 9 subjects (0.9%) took the chemotherapeutic drug were not high-risk emetogenic, who excluded from efficacy evaluation.

- the article is too long and needs to be shortened, especially the tables:
shorten table 1 (grouping lung tumour sites, breast sites, other) simplify tables 3 to 7 by reducing the number of lines that make the reading of the tables very complex. In my opinion, the additional tables are useless.
Response: The table 1 is shortened according to your suggestion. We added a new table 3, so tables 4 to 8 are simplified for reading by reducing the line spacing of the table. The supplementary table 1 is deleted.

The results of the study confirm the effectiveness of the MASCC recommendations. The role of chronic alcohol consumption, male sex are favourable factors, what is more curious is that a history of chemotherapy would be a protective factor.

Response: Thank you for your kind comment, yes, for this curious result of history of chemotherapy was a protective factor, which need to be confirmed in further study.

Reviewer B

The work is quite confusing in drafting and analyzing the results. The study population is very heterogeneous and the analysis of the results is difficult. Furthermore, even if confused, the data do not add any new information to what already exists in the literature, confirming that the triplet is better than single agent or other combinations. This is a phase IV study that should consider safety and efficacy. Safety data are insufficient and there is no reference to any drug interactions that can explain serious adverse events.

Response: Thank you for your suggestion. We added a new table 3 to explain the drug interaction related AE analysis results in text, but we found there were no clinically relevant unexpected drug interactions noted in this study.

Table 3 The safety profile of AEs, drug related AEs and SAEs for the subjects having clinically relevant unexpected drug interactions

Concomitant CYP3A4 or CYP2C9	Subjects Having Concomitant CYP3A4 or CYP2C9	Subjects with Adverse Events	Subjects with Drug-related Adverse Events
CYP3A4	11	6 (54.5%)	2 (18.2%)
Vincristine	11	6 (54.5%)	2 (18.2%)
CYP2C9	165	65 (39.4%)	1 (0.6%)
Celecoxib	5	4 (80.0%)	0
Cyclophosphamide	146	57 (39.0%)	1 (0.7%)
Glimepiride	1	1 (100.0%)	0
Ibuprofen	7	4 (57.1%)	0

Note: Each subject is counted at most once within each category. The subjects would be counted if one or more adverse events occurred after the start date of specific concomitant CYP3A4 or CYP2C9.