Why you should read this article:

- To recognise the potential negative effects of chemotherapy-induced nausea and vomiting (CINV) on people with cancer
- To learn about the findings of a service evaluation that assessed the effectiveness, safety and acceptability of NEPA (netupitant and palonosetron) in the prevention of CINV in patients undergoing multiple cycles of chemotherapy
- To enhance your awareness of the available treatments that can be used to prevent and relieve CINV

Patient-reported effectiveness and safety of NEPA in preventing chemotherapy-induced nausea and vomiting: a UK online service evaluation

Elaine Tomlins, Simona Aganovic and Elisaveta Parry

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Correspondence
Elaine.Tomlins@rmh.nhs.uk
@lennae13

Conflict of interest
Elaine Tomlins is a consultant for Chugai Pharma UK Ltd and is now employed by the Royal Marsden Hospital. Simona Aganovic was employed by Chugai Pharma UK Ltd as a medical manager at the time of writing and is now employed by Novartis Pharmaceuticals UK Ltd. Elisaveta Parry has no conflicts of interest to declare

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Abstract

Background Chemotherapy-induced nausea and vomiting (CINV) is one of the most feared and difficult side effects of chemotherapy. In clinical trials, the oral fixed-combination drug NEPA (netupitant and palonosetron) has been shown to prevent acute and delayed CINV and to be well-tolerated by patients. However, there is limited real-world UK data concerning the effectiveness, acceptability and potential benefits of a single dose of NEPA per cycle of chemotherapy among patients receiving highly emetogenic chemotherapy (HEC) or moderately emetogenic chemotherapy (MEC).

Aim To assess the effectiveness, safety and patients' acceptability of NEPA in the prevention of CINV in patients undergoing multiple cycles of chemotherapy (HEC, including anthracycline and cyclophosphamide combination (AC) and cisplatin, or MEC) in a real-world setting.

Method This service evaluation recruited patients from two UK centres who were scheduled for at least three HEC, including AC and cisplatin, or MEC chemotherapy cycles, and taking NEPA as per the UK licence before each cycle. A web-based app was used to register patients, record their baseline characteristics and collect data. Patients used the app to rate their nausea and vomiting, report adverse events and rate their satisfaction with the effectiveness and convenience of NEPA for five days post-chemotherapy.

Results Of the 37 recruited patients, the majority reported 'no significant nausea' (nausea score <3 on a numerical rating scale from 0 to 10) (89.1%) and no episodes of vomiting (97.1%) across the three chemotherapy cycles. Patients' satisfaction with NEPA was high.

Conclusion The results of this service evaluation support the effectiveness and acceptability of NEPA. Healthcare professionals should feel able to reassure patients that there are effective, tolerable and easy-to-use treatments available to prevent and relieve CINV.

Author details

Elaine Tomlins, consultant nurse, University Hospital Southampton NHS Foundation Trust, Southampton, England (at the time of writing); Simona Aganovic, medical manager – haematology/oncology, Chugai Pharma UK Ltd, London, England (at the time of writing); Elisaveta Parry, lead oncology pharmacist, East Kent Hospitals University NHS Foundation Trust, Kent, England

Keywords

adverse reactions, cancer, cancer treatments, chemotherapy, clinical, medicines, nausea, nursing care, oncology, pharmacology, professional, signs and symptoms, vomiting

Background

Chemotherapy-induced nausea and vomiting (CINV) is distressing for people with cancer and is one of the most feared and difficult side effects of chemotherapy (Vidall et al 2011, Lorusso et al 2017), despite progress in the range and availability of prophylactic treatments for it. CINV can occur within 24 hours of receiving chemotherapy (acute onset) or between two and five days afterwards (delayed onset) (Grunberg et al 2004, Hernandez Torres et al 2015).

In five prospective studies conducted between 2008 and 2015, more than 40% of people with cancer experienced ≥grade 2 CINV (acute or delayed onset) (Dranitsaris et al 2017). In one prospective observational study, oncology specialists greatly underestimated the incidence of delayed-onset CINV, which highlights the difficulty of monitoring CINV once patients have left the hospital setting (Grunberg et al 2004). In previous reports, patients have indicated that they 'tried to be strong by not complaining about nausea or vomiting' and that CINV 'meant the treatment was working' (Salsman et al 2012). The under-reporting of CINV by patients may be a potential barrier to its management by healthcare professionals (Salsman et al 2012).

Achieving complete control of CINV (no significant nausea and no vomiting) continues to be a clear unmet need in this population, particularly in terms of nausea, which has been reported to be one of the worst side effects of chemotherapy. Complete CINV control would substantially improve patients' quality of life and their ability to undertake activities of daily living (Bloechl-Daum et al 2006, Hernandez Torres et al 2015, Aapro 2018). It would also reduce the need to delay treatment, reduce doses, admit patients to hospital and discontinue chemotherapy early (Dranitsaris et al 2017).

Chemotherapy-associated nausea has substantial negative effects on patients' lives. In Farrell et al (2013), a greater proportion of patients who experienced acute and delayed chemotherapy-associated nausea were found to have malnutrition and impaired physical quality of life compared with patients without nausea, with a similar trend noted for psychological distress. In Molassiotis et al (2012), the negative effect of chemotherapy-associated nausea on patients' physical quality of life and nutritional status was greater among those who experienced ≥2 additional symptoms alongside nausea, such as loss of appetite, pain, dry mouth and lack of energy.

Risk factors associated with CINV include having experienced nausea or vomiting in previous chemotherapy cycles, being ≤55 years of age, anticipatory nausea or vomiting, history of morning sickness and the cycle of chemotherapy, while CINV has been shown to be reduced in patients with high alcohol consumption (Vidall et al 2011, Sekine et al 2013, Young et al 2013, Dranitsaris et al 2017). The prediction of patients' risk of CINV may assist healthcare providers in their choice of antiemetic therapy and may help to prevent anticipatory nausea and vomiting (Molassiotis et al 2016, Dranitsaris et al 2017).

Guidelines from the Multinational Association of Supportive Care in Cancer/European Society for Medical Oncology (MASCC/ESMO) (Roila et al 2016), the American Society of Clinical Oncology (ASCO) (Hesketh et al 2016) and the National Comprehensive Cancer Network (NCCN) (Ettinger et al 2018) provide recommendations on the most appropriate antiemetic treatments for patients receiving chemotherapy.

These recommendations are based on the emetogenic potential of the antineoplastic agent (its potential to cause nausea and vomiting). For patients receiving moderately emetogenic chemotherapy (MEC) or highly emetogenic chemotherapy (HEC), a combination of antiemetics is recommended to minimise acute and delayed CINV. For patients receiving MEC (excluding carboplatin-based MEC), the guidelines recommend a prophylactic combination of a 5-hydroxytryptamine type 3 (5-HT_3) receptor antagonist and dexamethasone, while for patients receiving HEC, a neurokinin-1 (NK_1) receptor antagonist should be administered as well. The MASCC/ESMO (Roila et al 2016) and NCCN (Ettinger et al 2018) guidelines also recommend the addition of an NK_1 receptor antagonist for patients receiving carboplatin-MEC, which is considered a high-risk MEC. Similarly, the NCCN guidelines (Ettinger et al 2018) recommend the addition of an NK_1 receptor antagonist for patients with additional risk factors or those in whom previous therapy with corticosteroids and 5-HT_3 antagonists alone has failed. Awareness of, and adherence to, guideline recommendations have been shown to be generally low among European oncology nurses responding to a survey of antiemetic practices (Dielenseger et al 2019).

NEPA (netupitant and palonosetron)

NEPA is an oral fixed-combination drug containing 300mg netupitant (NETU), an NK_1 receptor antagonist, and 0.50mg

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palonosetron (PALO), a second-generation 5-HT_3 receptor antagonist that has molecular characteristics different from the first-generation 5-HT_3 receptor antagonist class, which includes ondansetron and granisetron (Rojas and Slusher 2012, Thomas et al 2014, Schilling et al 2020). Netupitant has been shown to have longevity in its effect (half-life of ≈3.75 days) due to its inhibition of substance P (Aapro et al 2014, Thomas et al 2014). PALO has a longer half-life (≈2 days) than the first-generation 5-HT_3 receptor antagonists, inhibits the 5-HT_3 receptor with high affinity binding, and leads to prolonged internalisation of the PALO-5-HT_3 receptor complex into the cell. Therefore, PALO produces long-lasting inhibition of the 5-HT_3 receptor. As a result, NEPA, with its fixed combination of NETU and PALO, provides prevention against acute and delayed CINV, especially during the delayed phase (Zhang et al 2018).

Three pivotal trials of NEPA have demonstrated that one NEPA dose per cycle of chemotherapy plus 12mg dexamethasone before treatment prevented CINV during the acute and delayed phase and was well-tolerated by patients (Aapro et al 2014, Gralla et al 2014, Hesketh et al 2014). Since clinical trials have stringent criteria regarding the patients recruited and are often conducted in specialised settings, it can be difficult to make generalisations from their results (Sherman et al 2016). Therefore, real-world evidence is essential to understand whether the results of rigorously controlled clinical trials are replicated in everyday clinical practice.

In the UK, NEPA is licensed in adults for the prevention of acute and delayed CINV associated with cisplatin-HEC or MEC (Chugai Pharma UK Ltd 2020). However, real-world UK data concerning the effectiveness, acceptability and potential benefits of a single oral dose of NEPA per cycle of chemotherapy among patients receiving HEC or MEC are limited. The authors of this article conducted a service evaluation – an assessment of the current care of patients, without randomisation or allocation to an intervention (Health Research Authority 2017) – in two UK centres to assess patient-reported effectiveness, safety and satisfaction with NEPA in preventing CINV in multiple cycles of chemotherapy (HEC, including anthracycline and cyclophosphamide combination (AC) and cisplatin, or MEC). This article reports data for patients taking NEPA to prevent CINV in up to three cycles of chemotherapy.

Aim

To assess the effectiveness, safety and patients' acceptability of NEPA in the prevention of CINV in patients undergoing multiple cycles of chemotherapy (HEC, including AC and cisplatin, or MEC) in a real-world setting.

Method

Participating centres

Two centres participated in this service evaluation: Southampton General Hospital and Kent and Canterbury Hospital. To be eligible, centres were required to have NEPA on their NHS trust formulary or to have made a decision to add it to their formulary before the start of the service evaluation. Centres were also required to have had NEPA as a treatment option for oncology patients receiving cisplatin-HEC and some MEC regimens and to have decided to make NEPA the standard of care for these regimens before, and independently of, the initial contact regarding their involvement in the service evaluation. The protocol was approved as a service evaluation by each of the NHS trusts and was reviewed by the appropriate personnel at each site, ensuring adherence to all necessary governance standards. A patient information leaflet, developed by Chugai Pharma UK Ltd, was approved for use in both centres.

Patient recruitment

Patients were recruited prior to their first chemotherapy cycle by a consultant nurse, an advanced nurse practitioner or a lead oncology pharmacist. To be eligible, patients had to:

- Be ≥18 years of age.
- Be scheduled to receive one or two days of either cisplatin-HEC, AC, or MEC for a minimum of three cycles.
- Have been prescribed NEPA as specified in the UK licence – one capsule combining NETU (300mg) and PALO hydrochloride equivalent to 0.5mg of PALO, one hour before the start of each chemotherapy cycle (Chugai Pharma UK Ltd 2020, Joint Formulary Committee 2020).

As this was a service evaluation, patients' treatment had been determined by their healthcare professional prior to their participation and there were no requirements for treatments to be changed. The service evaluation was designed to evaluate patients' current care without reference to a standard (Health Research Authority 2017).

Patients were excluded if they were pregnant; had received any drugs with potential antiemetic efficacy within 24 hours, or any systemic corticosteroids within

72 hours, of Day 1 of the chemotherapy cycle; and/or had a history of serious cardiovascular disease or a predisposition to cardiac conduction abnormalities (with the exception of incomplete right bundle branch block), a brain tumour or symptomatic brain metastases. Patients were also excluded if they had experienced vomiting, retching or anything more than mild nausea within 24 hours of Day 1 of the first chemotherapy cycle.

All potential patients were given a patient information leaflet before recruitment to help them decide whether to participate in the service evaluation. The leaflet explained the purpose of the service evaluation, what data would be collected via a web-based app designed for the evaluation, how personal data would be collected and anonymised (all data entered in the online diaries were encrypted, so no personal information was visible in the data outputs), how to complete the daily online diary and how to report side effects of NEPA. The leaflet also included the contact details of the patient's nurse or pharmacist if they needed to ask questions about how to complete the online diary.

Patient registration

Chugai Pharma UK Ltd developed a web-based app to facilitate consent, recruitment, documentation of baseline characteristics and data collection. Patients provided informed consent at the time of recruitment, which was captured by the recruiting healthcare professional by checking a tick box within the app in the presence of the patient.

Once consent had been obtained and captured, the recruiting healthcare professional recorded baseline characteristics including gender, cancer diagnosis and/or tumour type and stage, performance status (Oken et al 1982), previous chemotherapy exposure, previous antiemetic treatments and scheduled chemotherapy regimen. Baseline characteristics also included whether the patient had any of the following risk factors for CINV: <55 years of age, history of nausea and vomiting (including during pregnancy), history of motion sickness and low alcohol intake (<14 units of alcohol per week).

As part of the registration process, the recruiting healthcare professional asked the patient whether they had experienced nausea and/or vomiting (yes/no) in the preceding 24 hours. Based on their clinical judgement and using version 4 of the Common Terminology Criteria for Adverse Events grades (National Cancer Institute 2009), the healthcare professional then recorded the patient's baseline levels of nausea and vomiting. If a patient had experienced anything more than mild nausea and/or vomiting in the preceding 24 hours, they were not eligible for inclusion.

Completion of online diary

Patients were asked to use the app to complete a daily online diary from Day 1 to the morning of Day 5 of each cycle of chemotherapy. At 10am on Days 1-5 of each cycle, patients received an automated daily reminder to complete the diary in the form of a text message. Diary entries were reviewed by the patient with their nurse or pharmacist at the next chemotherapy appointment, any data gaps were discussed and entries were completed if necessary. This article reports data from diaries kept by patients for up to three cycles of chemotherapy.

Effectiveness, safety and satisfaction measures

To assess the effectiveness of NEPA in preventing CINV, patients were asked, on Days 1-5 of each cycle, to:

- Rate the degree of nausea they experienced on a numerical rating scale from 0 to 10.
- Indicate the number of vomiting episodes from 0 to 10+.
- Indicate whether they had required any hospital admissions related to nausea and vomiting (yes/no; and if yes, the duration of the hospital stay).

'No significant nausea' was defined as a patient-rated degree of nausea <3. This is consistent with the measurements in the three pivotal trials of NEPA mentioned above, which used a visual analogue scale that ranged from 0mm to 100mm (Aapro et al 2014, Gralla et al 2014, Hesketh et al 2014). The proportion of patients reporting nausea was calculated among patients with and without risk factors for CINV, who had completed one cycle of chemotherapy.

Patients were asked to report any adverse events they experienced as soon as they occurred (yes/no; and if yes, patients could provide more detail in a free-text box). When an adverse event was reported via the app, an automated text message was immediately sent to the nurse or pharmacist to prompt them to review the adverse event. At the next chemotherapy visit, the nurse or pharmacist ensured that the adverse event had been correctly reported by the patient and confirmed, based on their clinical judgement, whether the adverse event was related to NEPA and not to chemotherapy.

Key points

- The results of a UK service evaluation suggest that the oral fixed-combination drug NEPA (netupitant and palonosetron) is a simple and effective treatment for preventing chemotherapy-induced nausea and vomiting (CINV)
- Simplifying treatment regimens by using combination drugs such as NEPA may reduce polypharmacy
- Nurses should aim to tailor antiemetic regimens for patients undergoing chemotherapy so that these are individualised, rather than relying on a 'one-size-fits-all' approach
- Nurses need to work with the multidisciplinary team to achieve better control of CINV for people with cancer

All adverse events were reported to Chugai Pharma UK Ltd's pharmacovigilance department within 24 hours of the healthcare professional becoming aware of them.

To evaluate patients' satisfaction with the effectiveness and convenience of NEPA, the diary included the questions from the Treatment Satisfaction Questionnaire for Medication (Atkinson et al 2005) on Day 5 of each cycle. This gave patients the option to rate their satisfaction on a seven-point Likert scale as 'extremely dissatisfied', 'very dissatisfied', 'dissatisfied', 'somewhat satisfied', 'satisfied', 'very satisfied' or 'extremely satisfied'.

Table 1. Baseline patient characteristics (*n*=37)

Patient characteristic		%	*n*
Gender	Female	75.7	28
	Male	24.3	9
Tumour type	Breast	24.3	9
	Colon	2.7	1
	Head and neck	13.5	5
	Lung	27.0	10
	Ovarian	13.5	5
	Other	18.9	7
Performance status	0 = fully active, able to carry on all pre-disease activities without restriction	51.4	19
	1 = restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature – for example, light housework, office work	40.5	15
	2 = ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours	5.4	2
	3 = capable of only limited self-care; confined to bed or chair more than 50% of waking hours	2.7	1
Previous chemotherapy	No	78.4	29
	Yes	21.6	8
Scheduled chemotherapy regimen	Highly emetogenic chemotherapy (HEC): » Cisplatin » Anthracycline and cyclophosphamide combination (AC)	81.1 56.8 24.3	30 21 9
	Moderately emetogenic chemotherapy (MEC)	18.9	7
Risk factors for chemotherapy-induced nausea and vomiting (CINV)	<55 years of age	48.6	18
	Low alcohol intake (<14 units per week)	70.3	26
	History of motion sickness	29.7	11
	History of nausea and vomiting (including in pregnancy)	45.9	17
	None	10.8	4

Results

Baseline patient characteristics

Between 5 March 2018 and 11 February 2019, 37 patients were recruited to take part in the service evaluation and registered on the app. Among those 37 patients:

- Thirty (81.1%) were scheduled to receive HEC, comprising 21 (56.8%) scheduled to receive cisplatin-HEC and nine (24.3%) scheduled to receive AC/EC.
- Seven (18.9%) were scheduled to receive MEC.

Baseline patient characteristics are summarised in Table 1. Among the recruited patients, almost three quarters were female; the most common tumour types were breast and lung tumours; there were high levels of functioning (performance status of 0 or 1); and the most common risk factors for CINV were low alcohol intake, being <55 years of age and having a history of nausea and vomiting (including during pregnancy). Previously used antiemetic drugs were metoclopramide hydrochloride (*n*=2), ondansetron (*n*=3), cyclizine (*n*=1), aprepitant (*n*=1) and domperidone (*n*=1).

Number of diary entries and reasons for withdrawal

Thirty-one (83.8%) of the 37 recruited patients received oral NEPA and at least one cycle of their scheduled chemotherapy. Among these 37 patients, 24 (64.9%) provided a complete online diary (five days of diary entries) after receiving their first cycle of chemotherapy (Cycle 1); 14 (37.8%) provided a complete online diary of their second cycle (Cycle 2); 7 (18.9%) provided a complete online diary after receiving their third cycle (Cycle 3). In total, 238 daily diary entries were recorded from 60 chemotherapy cycles.

Reasons for withdrawal from the service evaluation included general non-compliance with the diary entry (*n*=8, 21.6% of recruited patients) and treatment change and/or discontinuation (*n*=16, 43.2% of recruited patients). General non-compliance included difficulties accessing or using the app. Treatment change and/or discontinuation included patients who received rescue medication (antiemetics other than NEPA) or changed and/or discontinued their chemotherapy treatment. Figure 1 shows a patient disposition flow chart summarising this information in visual form.

Patient-reported effectiveness

All patients had 'no significant nausea' (nausea <grade 3) at baseline, as rated by the recruiting healthcare professional using the Common Terminology Criteria for Adverse Events grades. Figure 2 shows daily patient reports of the degree of nausea experienced. In all three cycles of chemotherapy, substantial proportions of patients experienced 'no nausea' (nausea score = 0) across all five days of each cycle.

Figure 3 shows daily patient reports of 'no significant nausea' (nausea score <3) and 'no vomiting' (0 episodes of vomiting reported). Across all five days of the three cycles, the vast majority of patients reported 'no significant nausea' (89.1%) and 'no vomiting' (97.1%). In Cycles 1 and 2, the proportions of patients reporting 'no significant nausea' and 'no vomiting' tended to be higher during the delayed phase (Days 2-5). In Cycle 3, all patients reported 'no significant nausea' and 'no vomiting'.

Table 2 shows the proportion of patients with and without significant nausea among those with and without risk factors for CINV (<55 years, low alcohol intake, history of motion sickness, and history of nausea and vomiting) who completed Cycle 1. The majority of patients with a history of nausea and vomiting experienced significant nausea (nausea score ≥3) in Cycle 1.

Patient-reported adverse events

Nine out of the 31 treated patients (29.0%) reported at least one adverse event in 39 diary entries. The most commonly reported adverse events were:

- 'Constipation' – mentioned in 17 diary entries by four (12.9%) patients.
- 'Acid reflux', 'heartburn' or 'indigestion' – mentioned in 13 diary entries by three (9.7%) patients.
- 'Bloating' or 'wind' – mentioned in six diary entries by two (6.5%) patients.

Two (6.5%) of the treated patients reported more than one episode of vomiting within one day and were hospitalised, one of whom had low sodium levels that were deemed to be related to chemotherapy by the clinical team.

Patient-reported satisfaction

In total, 46 responses to the Treatment Satisfaction Questionnaire for Medication were provided. Almost all patients were 'satisfied', 'very satisfied' or 'extremely satisfied' with:

- The ability of NEPA to prevent CINV (*n*=44).
- The ability of NEPA to relieve symptoms (*n*=41).
- How easy NEPA was to take (*n*=45).
- How frequently they were expected to take it (*n*=45).

Throughout the service evaluation, few patients were 'dissatisfied' or 'somewhat satisfied' with the ability of NEPA to prevent CINV (*n*=2) or with the way NEPA relieved symptoms (*n*=3). However, these patients reported no episodes of vomiting throughout the service evaluation and only one of them reported experiencing significant nausea (nausea score ≥3) more than once.

No patients replied that they were 'extremely dissatisfied' or 'very dissatisfied' in response to any of the questions in the Treatment Satisfaction Questionnaire for Medication.

Discussion

Real-world patient-reported data from this UK service evaluation of the effectiveness of oral NEPA in preventing CINV after up to three cycles of HEC (AC or cisplatin) or MEC suggest that NEPA is effective in preventing both acute and delayed CINV. The degree of nausea reported by patients in Cycle 1 appeared to be lower on Days 4 and 5 than on the first three days, suggesting

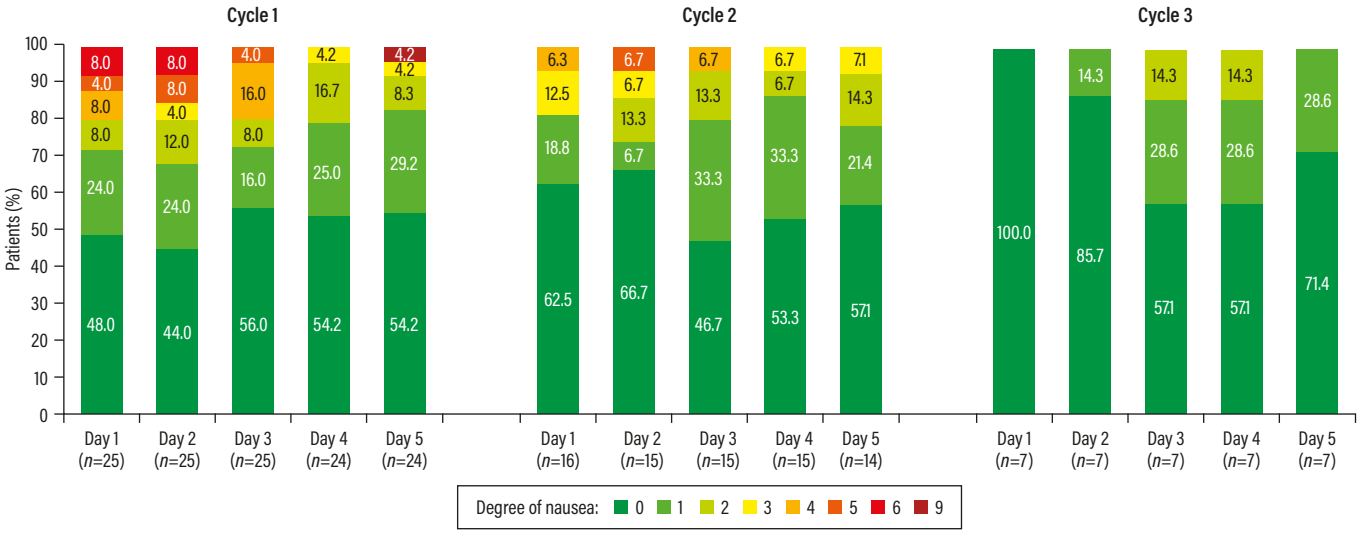
Figure 1. Patient disposition flow chart

* Treatment change/discontinuation included patients who received rescue medication (antiemetics other than NEPA (netupitant and palonosetron)) or changed and/or discontinued their chemotherapy treatment. General non-compliance included access difficulties when using the app. Completed = a full 5 days of diary entries. One patient was unable to swallow NEPA tablets due to radiotherapy

better effectiveness during the delayed phase. In patients who received more than one chemotherapy cycle, the degree of nausea decreased between Cycles 1 and 2 and between Cycles 2 and 3, which suggests that the effectiveness of NEPA is maintained and increases over multiple cycles of chemotherapy. However, a substantial proportion of patients did not complete their diaries at Cycles 2 and 3 and were therefore withdrawn from the service evaluation, so these data should be interpreted with caution. Despite patient withdrawals, the findings are in line with a real-world evidence study of NEPA in Germany, which showed that NEPA was highly effective in preventing CINV in patients receiving HEC or MEC (Schilling et al 2020), with positive effects on quality of life (Karthaus et al 2020).

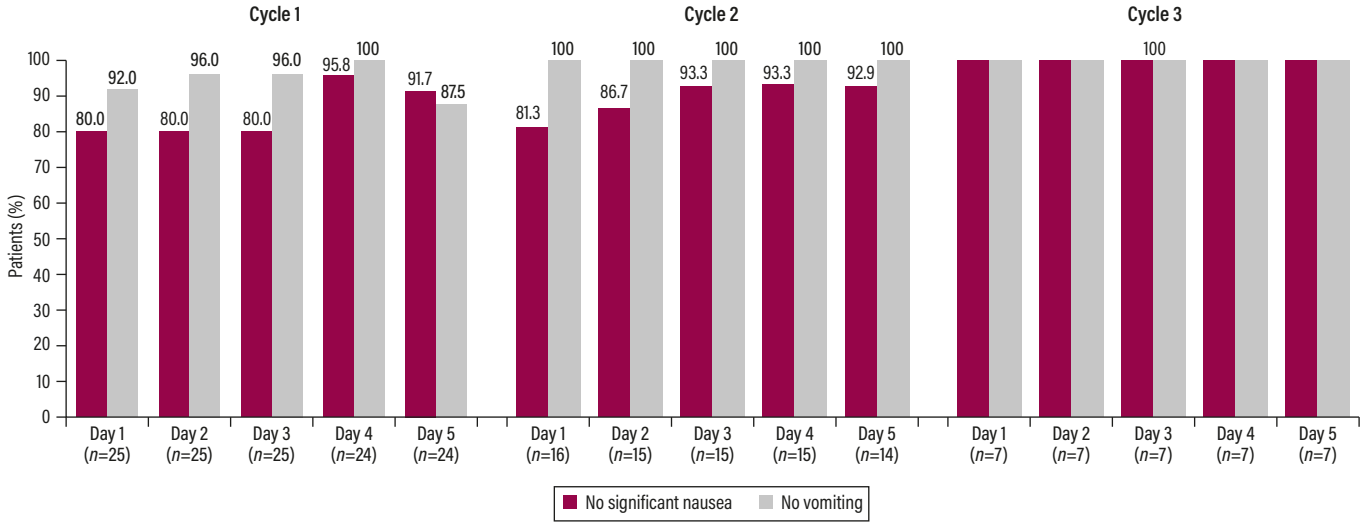
The use of daily online diaries in this service evaluation enabled real-time patient reporting of symptoms and adverse events. Patients typically experience CINV at home, so usually their healthcare professional would not see these symptoms (Young et al 2013). This is important, since a lack of control of CINV can lead to treatment disruption and

Figure 2. Daily patient reports of the degree of nausea experienced*



*Data shown for patients who provided at least one diary entry. Patients rated the degree of nausea experienced on a numerical rating scale from 0 to 10. 'No significant nausea' was defined as a score of <3. No patients rated their nausea 7, 8 or 10, so these scores are not included in the figure

Figure 3. Daily patient reports of 'no significant nausea' and 'no vomiting'*



* Data shown for patients who provided at least one diary entry. 'No significant nausea' was defined as a score of <3 on a numerical rating scale from 0 to 10

discontinuation, so if healthcare professionals are made aware of persistent CINV they can intervene early to avoid potential disruption or discontinuation of treatment. One of the reasons for patient withdrawal from this service evaluation was general non-compliance with the online diary entries, whereby patients received chemotherapy and NEPA but did not complete the diary. It is likely that the patients' general condition, in addition to the plethora of information received, may have adversely affected their overall compliance with the diary entries. Online data collection tools such as the web-based app used in this service evaluation have the potential to improve the accuracy of reporting, as they remove recall bias and reduce the likelihood of patients forgetting to report symptoms and adverse events. There is a need to optimise such online data collection tools to ensure that it is easy for patients to record and track symptoms and adverse events following chemotherapy, so further optimisation of data entry methodologies and technology is required, to this end.

Patients reported high levels of satisfaction with the effectiveness and convenience of NEPA, and the adverse events they reported are in line with safety data collected from clinical trials (Gralla et al 2014), which indicates that NEPA is well accepted and well tolerated by patients in the real world. The adverse events commonly reported in this service evaluation (constipation, acid reflux/heartburn/indigestion, and bloating/wind) are known side effects of NEPA and other agents of the same class, along with headaches, loss of appetite, diarrhoea, asthenia, dizziness and insomnia (Joint Formulary Committee 2020).

The use of NEPA in clinical practice appears to have beneficial implications for patients and the healthcare system. A high number of patients reported that they experienced complete control of CINV (no significant nausea and no vomiting); a single oral dose of NEPA per chemotherapy cycle was easy to take and convenient; and the degree of CINV control (acute and delayed) was acceptable. As NEPA is a combination prophylactic treatment, patients only require one prescription to control their CINV. This reduces polypharmacy, which has been associated with grade 3 and 4 CINV and increases the risk of adverse events (Woopen et al 2017). Reductions in costs and in the use of healthcare resources may also be seen with the use of NEPA, since better control of CINV may result in fewer hospital admissions (for example for dehydration) and reduced pharmacy dispensing costs.

Limitations

One limitation of this service evaluation was the small sample of patients throughout the cycles, which should be considered when interpreting these data. The number of patients who did not comply with diary completion was another limitation. The overall attrition limits the extrapolation of the results to other patient groups and the data should be interpreted with caution.

Using self-reporting of adverse events is appropriate for a real-world service evaluation, since subjective symptoms such as pain and nausea may be best described by the patient. However, these data should only be considered in the real-world context and cannot be

Table 2. Nausea among patients with and without risk factors for chemotherapy-induced nausea and vomiting who completed Cycle 1 (*n*=24)

	Risk factors								No risk factors
	Age		Alcohol intake		Motion sickness		Nausea and vomiting		
	<55 years of age (*n*=10)	≥55 years of age (*n*=14)	Low alcohol intake (<14 units per week) (*n*=17)	High alcohol intake (>14 units per week) (*n*=7)	History of motion sickness (*n*=8)	No history of motion sickness (*n*=16)	History of nausea and vomiting (including during pregnancy) (*n*=10)	No history of nausea and vomiting (including during pregnancy) (*n*=14)	(*n*=3)
% (*n*) of patients with significant nausea (nausea score ≥3)	30.0 (3)	50.0 (7)	47.1 (8)	28.6 (2)	37.5 (3)	43.8 (7)	60.0 (6)	28.6 (4)	66.7 (2)
% (*n*) of patients with no significant nausea (nausea score <3)	70.0 (7)	50.0 (7)	52.9 (9)	71.4 (5)	62.5 (5)	56.3 (9)	40.0 (4)	71.4 (10)	33.3 (1)

directly compared with the rigorously defined adverse events reported in clinical trials.

Conclusion

This service evaluation conducted in two centres in the UK provides real-world data supporting the effectiveness and acceptability of NEPA. Patients were satisfied with the effectiveness and usability of a single oral dose of NEPA per chemotherapy cycle to prevent and relieve acute and delayed CINV associated with HEC (cisplatin or AC) or MEC. Healthcare professionals should therefore feel able to reassure patients that there are effective, tolerable and easy-to-use treatments available to prevent and relieve CINV.

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