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RESEARCH ARTICLE

A Prospective Non-Randomized Observational Study assessing efficacy of Netupitant and Palonosetron (NEPA) Versus Fosaprepitant and Palonosetron for Chemotherapy Induced Nausea and Vomiting Prevention in Autologous Stem Cell Transplantation at a South Indian Tertiary Cancer Centre

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ABSTRACT

Background: Chemotherapy-induced nausea and vomiting remain a significant problem during autologous stem cell transplantation, particularly during the delayed period of conditioning regimen chemotherapy. NEPA (netupitant+palonosetron) offers dual NK1/5-HT3 blockade in a single dose, but comparative evidence versus fosaprepitant+palonosetron in Autologous stem cell transplantation is limited.

Methods: We conducted a prospective, observational, non-randomized study at a tertiary cancer centre (September 2022–January 2025). Consecutive Transplant recipients received either BEAM (lymphoma) or melphalan (myeloma) conditioning. Antiemetic prophylaxis was NEPA (netupitant 300mg + palonosetron 0.5 mg) or fosaprepitant 150mg + palonosetron 0.25 mg. Vomiting episodes and CTCAE v4 grades were recorded daily. Acute (0–24 h), delayed (24–120 h), and overall (0–120 h) outcomes were analysed using Mann–Whitney and Chi-square tests.

Results: Sixty-five patients were included in the study (median age 42 years, with range 16–65; 60% male). Myeloma accounted for 34 (52.3%) and lymphoma 31 (47.7%). Antiemetic allocation was fosaprepitant+palonosetron in 43 (66.2%) and NEPA in 22 (33.8%), driven by affordability and availability.

Conditioning comparison: Acute outcomes were similar for BEAM versus melphalan (episodes 0.61 ± 1.54 versus 0.44 ± 0.93, p=0.828). In the delayed phase, BEAM showed a trend toward higher emesis (episodes 4.23 ± 4.30 versus 2.94 ± 4.57, p=0.105), with significantly higher vomiting grade on day 3 (p=0.042).

Antiemetic comparison: Acute, delayed, and overall summaries did not differ significantly between NEPA and fosaprepitant+palonosetron. On delayed day 5, NEPA was superior, with fewer episodes (0.32 ± 0.65 versus 0.88 ± 1.12; p=0.040) and lower vomiting grade (0.23 ± 0.43 versus 0.56 ± 0.67; p=0.047). No other day-wise differences were significant.

Conclusions: In this real-world Autologous stem cell transplantation cohort, NEPA and fosaprepitant+palonosetron achieved comparable overall control. NEPA conferred a distinct late delayed (day 5) benefit, while BEAM conditioning was associated with higher delayed vomiting grades than melphalan. NEPA may be preferred when late-phase control is critical. Larger randomized trials stratified by conditioning regimen are warranted.

Keywords: Autologous stem cell transplantation, Chemotherapy-induced nausea and vomiting NEPA, Fosaprepitant + palonosetron, Conditioning regimen

Introduction

Chemotherapy induced nausea and vomiting represents a clinically significant issue for most patients receiving Highly Emetogenic Chemotherapy (HEC) drugs. This unpleasant and distressing experience hinders patient confidence in taking subsequent chemotherapy and it can indirectly affect their nutritional intake. This can directly affect the patient outcomes. This problem is exacerbated in the patients receiving Conditioning regimens in Hematopoietic stem cell transplantation, where a poorly controlled nausea and inadequately controlled emesis can lead to electrolyte imbalance, dehydration as well as malnutrition.[1]

Since 1990, many efforts have been made in understanding the mechanism behind Chemotherapy Induced Nausea and Vomiting (CINV) and this has led to the invention of newer molecules to target the mechanisms. Acute period (0-24h) of chemotherapy is predominantly controlled by 5HT3 neurotransmitters and Delayed period(24-120h) post chemotherapy is mainly dependent on NK1 pathways[2].

NCCN and ESMO/MASCC guidelines suggest use of Three drug regimen combining NK1 receptor antagonist, dexamethasone and 5HT3 receptor antagonist as an effective standard antiemesis prophylaxis strategy in patients receiving HECs[3,4]. NEPA which is an oral fixed-dose formulation of netupitant and palonosetron, simultaneously blocks both NK1 and 5-HT3 receptors pathways in a single administration and has shown superior convenience and efficacy in solid-tumour chemotherapy.[5]

However, there is scarcity of prior direct comparative trials comparing NEPA with fosaprepitant-based regimens specifically in the context of Autologous Stem cell Transplantation (ASCT). To our knowledge, no prospective study from India or other low- and middle-income countries has directly evaluated these two approaches in the transplant setting.

In this context, to explore this we performed a non-randomized, prospective, real-world observational study at a tertiary cancer centre in South India, comparing fosaprepitant + 5-HT3 antagonist (palonosetron) with NEPA (netupitant + palonosetron) for prevention of acute and delayed CINV during ASCT conditioning. In routine care at our centre, the antiemetic regimen is influenced primarily by patient affordability and drug availability; in keeping with this real-world practice, patients who could afford NEPA generally received NEPA, whereas those who could not were managed with fosaprepitant + palonosetron. We prospectively followed outcomes to compare effectiveness across the two strategies.

Aims:

To compare the efficacy of NEPA versus Fosaprepitant combined with 5-HT3 antagonist (palonosetron) in preventing CINV among Autologous Stem Cell Transplantation patients.

Objectives:

1. To quantify the day-wise vomiting burden—number of episodes and vomiting grade—during the acute, delayed, and overall phases.
2. To compare CINV outcomes across conditioning regimens (BEAM versus melphalan).
3. To compare the antiemetic efficacy between two antiemetic arms—NEPA versus Fosaprepitant + palonosetron—among patients.

Materials And Methods:

STUDY DESIGN:

This is a real-world, non-randomized, prospectively conducted observational study carried out in the patients undergoing Autologous Stem cell transplantation in the Department of Medical-Oncology department in our hospital between September 2022 and January 2025. The trial protocol was approved by ethics committee and study aligned with the of Declarations of Helsinki and proper informed consent was taken before enrolling into the study.

PATIENTS:

Inclusion Criteria:

All patients who underwent Autologous stem cell transplantation for Lymphoma or myeloma disease in the Department of Adult Medical oncology at Kidwai Memorial Institute of Oncology were prospectively recruited into the study.

Exclusion Criteria:

All the patients who have not given consent to be the part of study.

Methedology:

TREATMENT:

Patients received one of the either two antiemetic regimens- Fosaprepitant (150mg) combined with 5HT3 antagonist (palonosetron-0.25mg) or NEPA (Netupitant 300mg and Palonosetron 0.5mg). This is a non-randomized allocation, and this is influenced primarily by patient affordability and drug availability.

Lymphoma patients received BEAM protocol (Multi-Day HECs) and Myeloma patients received Melphalan protocol (Single Day HECs). In BEAM protocol, NEPA or Fosaprepitant +palonosetron accordingly was repeated on day of Melphalan[6]. In both conditioning regimens steroid[7] was not used. Both these approaches are as a part Antiemesis protocol as per institutional policy. Metoclopramide was used as break through antiemetic agent.

ASSESSMENTS:

Acute Emesis period is considered till 24hrs post chemotherapy and Delayed emesis period is considered up to 120h[6]. Same definitions were applied across Both Multi-Day and Single Day HEC conditioning regimens.

Each day number of vomiting episodes were recorded, and the severity was graded as per CTCAEv4 in both arms. Comparison was done which is the better antiemetic in acute, delayed and over all periods.

STATISTICAL ANALYSIS:
The data set was analysed, and frequency of the subset were calculated. Number of vomiting episodes and grades of vomiting were expressed as mean ± standard deviation as well as median with ranges (Minimum and Maximum values). Chi-square test is used to differentiate between two conditioning regimens and between two Antiemetic arms. Mann- Whitney test is used to analyse between two antiemetics and to compare between the antiemetic control between two conditioning regimens.

Results:

BASELINE CHARACTERISTICS:
A total of 65 patients were included in the analysis. The median age wa 42 years (range 16–65) and the cohort consists of 60% male (39/65) and 40% female (26/65). Of these total 65 cases, 34 (52.30%) had myeloma, while 31 (47.69%) had lymphoma. Myeloma patients received melphalan protocol 34 (52.30%) and lymphoma patients received BEAM protocol 31 (47.69%). (Table 1)

Table 1: Base Line Characteristics

Parameters	n (%)
Total number of patients	**65(100)**
Gender Distribution	
Male	**39(60)**
Female	**26(40)**
Median age(Min-Max)y	**42(16-65)**
Disease Type	
Lymphoma	**31(47.69)**
Myeloma	**34(52.30)**
Conditioning Regimen	
BEAM protocol	**31(47.69)**
Melphalan protocol	**34(52.30)**

DISTRIBUTION OF ANTIEMETIC ARMS BY CONDITIONING REGIMEN:
Among 65 patients (BEAM 31; Melphalan 34), distribution of antiemetic arms was as follows: fosaprepitant+ palonosetron 43/65 (66.2%)—BEAM 20 (46.5%), Melphalan 23 (53.5%); NEPA 22/65 (33.8%)—BEAM 11 (50.0%), Melphalan 11 (50.0%). Chi-square p=0.498, indicating no significant association between conditioning regimen and antiemetic arm. (Table 2)

Table 2: Distribution of Antiemetic Arms by Conditioning Regimen

			Group		Total	p-value
			BEAM	MELPHALAN		
Antiemetic Prophylaxis Arm	Fosaprepitant+ Palonosetron	Count	20	23	43	0.498
		%	46.5%	53.5%	100.0%	
	NEPA	Count	11	11	22	
		%	50.0%	50.0%	100.0%	
Total		Count	31	34	65	
		%	47.7%	52.3%	100.0%	

Chi square test

COMPARATIVE CINV OUTCOMES BY CONDITIONING REGIMEN (BEAM VERSUS MELPHALAN):
Acute period outcomes were similar between BEAM (n=31) and melphalan (n=34): mean number of episodes 0.6129 ± 1.5422 versus 0.4412 ± 0.9274 (p=0.828), with median 0 in both groups (range 0–8 versus 0–4); acute period vomiting grade 0.2903 ± 0.5287 versus 0.2647 ± 0.5110 (p=0.833), median 0 in both (range 0–2). In the delayed period, mean episodes were 4.2258 ± 4.3028 versus 2.9412 ± 4.5656 (p=0.105), with median 3 versus 1 and maximum episodes 14 versus 21; delayed vomiting grade was 1.1935 ± 0.9099 versus 0.7941 ± 0.7699 (p=0.063), median 1 in both (range 0–3). Over the overall period, mean episodes were 4.8387 ± 5.2351 versus 3.3824 ± 4.7864 (p=0.200), with median 3 versus 2 and maximum episodes 21 in both; overall period vomiting grade was 1.1935 ± 0.9099 versus 0.8824 ± 0.7693 (p=0.148), median 1 in both (range 0–3). (Table 3)

Table 3: CINV outcomes by conditioning regimen (BEAM versus melphalan)

Parameter	BEAM (N=31)	MELPHALAN (N=34)	p-value
Acute Period Number of episodes	0.6129 ± 1.5422	0.4412 ± 0.9274	0.828
	Median: 0 (0-8)	Median: 0 (0-4)	
Acute Period Vomiting Grade	0.2903 ± 0.5287	0.2647 ± 0.5110	0.833
	Median: 0 (0-2)	Median: 0 (0-2)	
Delayed Period Number of episodes	4.2258 ± 4.3028	2.9412 ± 4.5656	0.105
	Median: 3 (0-14)	Median: 1 (0-21)	
Delayed Period Vomiting Grade	1.1935 ± 0.9099	0.7941 ± 0.7699	0.063
	Median: 1 (0-3)	Median: 1 (0-3)	
Overall Period Number of episodes	4.8387 ± 5.2351	3.3824 ± 4.7864	0.2
	Median: 3 (0-21)	Median: 2 (0-21)	
Overall Period Vomiting Grade	1.1935 ± 0.9099	0.8824 ± 0.7693	0.148
	Median: 1 (0-3)	Median: 1 (0-3)	

DELAYED-PHASE, DAY-WISE CINV: BEAM VERSUS MELPHALAN:

BEAM had a significantly higher vomiting grade on day 2 (0.6452 ± 0.8386 versus 0.2941 ± 0.7190; p=0.039; significant) and day 3 (0.7419 ± 0.8932 versus 0.3529 ± 0.6458; p=0.042; significant). Day 2 number (1.1613 ± 1.7146 versus 0.4706 ± 1.3081; p=0.050; medians 0 versus 0; maximum 5 versus 6) and day 3 number (1.2581 ± 1.7121 versus 0.6765 ± 1.3645; p=0.060; medians 1 versus 0; maximum 6 versus 5) were not significant; all other daily comparisons were not significant. (Table 4)

Table 4: Delayed-phase, day-wise CINV outcomes: BEAM versus Melphalan:

Parameter	BEAM (N=31)	MELPHALAN (N=34)	p-value
D1 Number of episodes	**0.3871 ± 0.8437**	**0.5294 ± 1.0220**	**0.358**
	Median: 0 (0-3)	**Median: 0 (0-5)**	
D1 Vomiting Grade	**0.2258 ± 0.4973**	**0.3529 ± 0.5440**	**0.257**
	Median: 0 (0-2)	**Median: 0 (0-2)**	
D2 Number of episodes	**1.1613 ± 1.7146**	**0.4706 ± 1.3081**	**0.05**
	Median: 0 (0-5)	**Median: 0 (0-6)**	
D2 Vomiting Grade	**0.6452 ± 0.8386**	**0.2941 ± 0.7190**	**0.039***
	Median: 0 (0-2)	**Median: 0 (0-3)**	
D3 Number of episodes	**1.2581 ± 1.7121**	**0.6765 ± 1.3645**	**0.06**
	Median: 1 (0-6)	**Median: 0 (0-5)**	
D3 Vomiting Grade	**0.7419 ± 0.8932**	**0.3529 ± 0.6458**	**0.042***
	Median: 1 (0-3)	**Median: 0 (0-2)**	
D4 Number of episodes	**0.8065 ± 0.9459**	**0.5000 ± 0.8961**	**0.1**
	Median: 1 (0-3)	**Median: 0 (0-3)**	
D4 Vomiting Grade	**0.5806 ± 0.6204**	**0.3529 ± 0.5971**	**0.091**
	Median: 1 (0-2)	**Median: 0 (0-2)**	
D5 Number of episodes	**0.6129 ± 0.9549**	**0.7647 ± 1.0748**	**0.592**
	Median: 0 (0-3)	**Median: 0 (0-4)**	
D5 Vomiting Grade	**0.4194 ± 0.6204**	**0.4706 ± 0.6147**	**0.679**
	Median: 0 (0-2)	**Median: 0 (0-2)**	

CINV OUTCOMES: FOSAPREPITANT+PALONOSETRON VERSUS NEPA:

In the acute period, mean episodes were 0.5581 ± 1.4360 versus 0.4545 ± 0.8004 (p=0.755), with medians 0 versus 0 and maximum 8 versus 2; acute vomiting grade was 0.2791 ± 0.5488 versus 0.2727 ± 0.4558 (p=0.810), median 0 in both (ranges 0–2 versus 0–1). In the delayed period, mean episodes were 4.0698 ± 4.8912 versus 2.5455 ± 3.3199 (p=0.299), with medians 2 versus 2 and maximum 21 versus 13; delayed vomiting grade was 1.0698 ± 0.9101 versus 0.8182 ± 0.7327 (p=0.331), median 1 versus 1 (ranges 0–3 versus 0–2). Over the overall period, mean episodes were 4.6279 ± 5.4599 versus 3.0000 ± 3.9158 (p=0.242), with medians 3 versus 2 and maximum 21 versus 15; overall vomiting grade was 1.1395 ± 0.8886 versus 0.8182 ± 0.7327 (p=0.179), median 1 versus 1 (ranges 0–3 versus 0–2). (Table 5)

Table 5: CINV outcomes: Fosaprepitant+palonosetron versus NEPA

Parameter	FOSA+PA LENO (N=43)	NEPA (N=22)	p-value
Acute period Number of episodes	0.5581 ± 1.4360	0.4545 ± 0.8004	0.755
	Median: 0 (0-8)	Median: 0 (0-2)	
Acute period Vomiting Grade	0.2791 ± 0.5488	0.2727 ± 0.4558	0.81
	Median: 0 (0-2)	Median: 0 (0-1)	
Delayed period Number of episodes	4.0698 ± 4.8912	2.5455 ± 3.3199	0.299
	Median: 2 (0-21)	Median: 2 (0-13)	
Delayed period Vomiting Grade	1.0698 ± 0.9101	0.8182 ± 0.7327	0.331
	Median: 1 (0-3)	Median: 1 (0-2)	
Overall period Number of episodes	4.6279 ± 5.4599	3.0000 ± 3.9158	0.242
	Median: 3 (0-21)	Median: 2 (0-15)	
Overall period Vomiting Grade	1.1395 ± 0.8886	0.8182 ± 0.7327	0.179
	Median: 1 (0-3)	Median: 1 (0-2)	

DELAYED-PHASE, DAY-WISE CINV: NEPA VERSUS FOSAPREPITANT+PALONOSETRON:

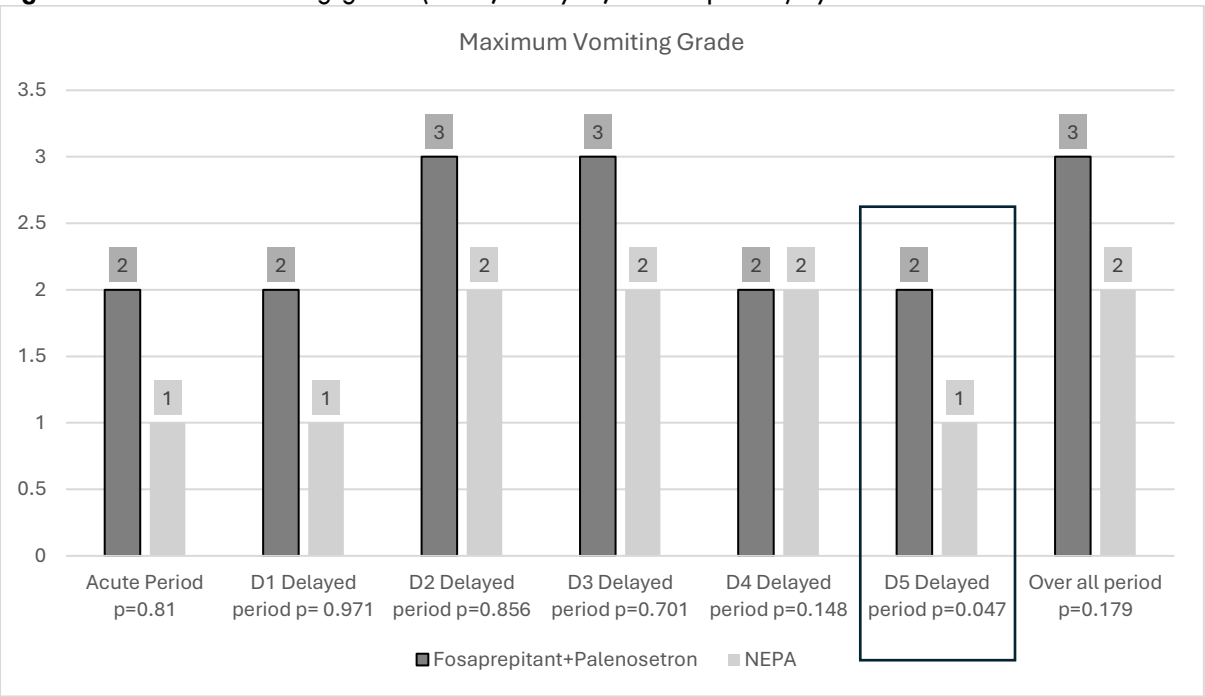
On day 5, NEPA was associated with significantly fewer vomiting episodes than fosaprepitant+palonosetron (0.3182 ± 0.6463 versus 0.8837 ± 1.1172; p = 0.040; median 0 versus 0; maximum 2 versus 4) and a significantly lower vomiting grade (0.2273 ± 0.4289 versus 0.5581 ± 0.6656; p = 0.047; median 0 versus 1; maximum 1 versus 2). Across the acute period and delayed days 1–4, between-arm differences in maximum vomiting grade were not significant. For the overall period, the maximum grade was numerically higher with fosaprepitant+palonosetron (3) than with NEPA (2), but the difference did not meet statistical significance (p = 0.179). (Table 6, Figure 1)

Table 6: Delayed-phase, day-wise CINV: NEPA versus fosaprepitant+palonosetron

Parameter	FOSA+PA LENO (N=43)	NEPA (N=22)	p-value
D1 Number of episodes	0.4884 ± 1.0322	0.4091 ± 0.7341	0.95
	Median: 0 (0-5)	Median: 0 (0-2)	
D1 Vomiting Grade	0.3023 ± 0.5578	0.2727 ± 0.4558	0.971
	Median: 0 (0-2)	Median: 0 (0-1)	
D2 Number of episodes	0.8837 ± 1.6933	0.6364 ± 1.2168	0.812
	Median: 0 (0-6)	Median: 0 (0-4)	
D2 Vomiting Grade	0.4651 ± 0.8266	0.4545 ± 0.7386	0.856
	Median: 0 (0-3)	Median: 0 (0-2)	
D3 Number of episodes	1.0465 ± 1.6468	0.7727 ± 1.3778	0.606
	Median: 0 (0-6)	Median: 0 (0-5)	
D3 Vomiting Grade	0.5814 ± 0.8517	0.4545 ± 0.6710	0.701
	Median: 0 (0-3)	Median: 0 (0-2)	
D4 Number of episodes	0.7674 ± 0.9719	0.4091 ± 0.7964	0.118
	Median: 0 (0-3)	Median: 0 (0-3)	
D4 Vomiting Grade	0.5349 ± 0.6305	0.3182 ± 0.5679	0.148
	Median: 0 (0-2)	Median: 0 (0-2)	
D5 Number of episodes	0.8837 ± 1.1172	0.3182 ± 0.6463	0.04
	Median: 0 (0-4)	Median: 0 (0-2)	
D5 Vomiting Grade	0.5581 ± 0.6656	0.2273 ± 0.4289	0.047
	Median: 0 (0-2)	Median: 0 (0-1)	

The data presented in the table is simplified and shown in the bar charts for comparison. Only the maximum grade of vomiting across acute, delayed and overall period. In the delayed period day wise data is shown. In Day 5 Maximum grade of vomiting is seen in Fosaprepitant and palonosetron group when compared to the NEPA group ,with the difference having statistical significance($p<0.05$)

Figure 1: Maximum vomiting grade (acute, delayed, overall period) by antiemetic arm.



Discussion:

In this prospective, non-randomized cohort of patients undergoing autologous stem cell transplantation (ASCT), acute, delayed, and overall chemotherapy-induced nausea and vomiting (CINV) outcomes were comparable between BEAM and melphalan conditioning, as well as between the two antiemetic regimens (NEPA versus fosaprepitant plus palonosetron). BEAM conditioning was associated with significantly higher vomiting grades on day 3, while NEPA demonstrated a distinct advantage on day 5 of the delayed phase, with fewer episodes and lower vomiting severity.

The pathophysiology of CINV in multiday conditioning regimens is complex, as the timing and sequence of individual chemotherapy agents influence both acute and delayed emetogenic risk. Optimal antiemetic selection should therefore be tailored to the emetogenic potential of each regimen.[8]

Large phase III trials have established NEPA as an effective antiemetic option in both moderately and highly emetogenic chemotherapy.

Aapro et al[5] within a large phase III clinical trial of patients on moderately emetogenic chemotherapy agents, single-dose NEPA + dexamethasone achieved better complete response than palonosetron + dexamethasone in the delayed vomiting period (76.9% versus 69.5%; p=0.001), in the overall vomiting period (74.3% versus 66.6%; p=0.001) and also in acute vomiting period (88.4% versus 85.0%; p=0.047) . Secondary endpoints (no significant nausea, no emesis, complete protection) similarly favoured NEPA in delayed/overall phases, with comparable safety. This emphasizes importance of NEPA combination drug in effective anti-emesis.

Zelek et al[9] in their pragmatic, multicentre randomized study of MEC patients, single dose NEPA was administered on day 1 achieved higher better complete response (no vomiting episodes and no rescue therapy required) over the 144-hour assessment window than a 3-day course of aprepitant with ondansetron (total MEC: 77.1% versus 57.8%, p=0.003). These data support NEPA's sustained efficacy and simpler dosing beyond 120 h, reinforcing its suitability as a backbone antiemetic in regimens where delayed-phase control is critical.

Gralla et al[10] in a randomized, multicentre phase III, double-blind study across 1961 cycles (Highly Emetogenic Chemotherapy /Moderately Emetogenic Chemotherapy), single-dose NEPA (netupitant 300 mg + palonosetron 0.5 mg day 1 + dexamethasone) was safe and well tolerated over repeated cycles. Antiemetic efficacy was high and maintained across cycles; in cycle 1, overall CR (0–120 h) was 81% with NEPA versus 76% with aprepitant + palonosetron, with a consistent numerical advantage for NEPA sustained in later cycles. This complements our finding of NEPA's superiority on day 5, as NEPA provides prolonged NK1 and 5-HT3 receptor coverage with a simplified single-dose approach.

Additional evidence supports the importance of sustained NK1 receptor blockade for delayed-phase control. In a phase II trial, Di Renzo et al.[11] evaluated alternate-day NEPA in patients receiving BEAM or FEAM conditioning for relapsed or refractory aggressive lymphoma, reporting high complete response rates in acute (88.6%), delayed (98.6%), and overall (87.1%) phases.

Evidence from a randomized, open-label HEC trial by Gao et al[12] shows that repeat fosaprepitant dosing (150 mg on days 1 and 3) and dexamethasone administered on days 1 to 3 with palonosetron day 1 reduced delayed CINV versus a day-1–only fosaprepitant schedule: delayed nausea 6.17% versus 12.66% (p=0.0056), with a trend toward less grade-1 vomiting (1.62% versus 3.80%, p=0.0953). These data underscore the value of sustained NK1 blockade for late delayed control and

complement our finding of a day-5 advantage with NEPA; where fosaprepitant is used, multi-day NK1 coverage may help mitigate late emesis.

Real-world data highlight gaps in current practice. A post-marketing surveillance study from China reported that only 43% of patients receiving aprepitant were free of delayed-phase nausea[13]. Another pragmatic study found that palonosetron with aprepitant or fosaprepitant plus dexamethasone was suboptimal, particularly for delayed nausea[14].

Similarly, Dranitsaris et al.[15] reported poor adherence to guideline-based prophylaxis, with only 12% of patients in highly emetogenic chemotherapy settings receiving the recommended triplet of 5-HT3 receptor antagonist, NK1 receptor antagonist, and dexamethasone.

The basic pharmacokinetics explains the predominant NEPA action in delayed phase. PET-CT data demonstrate that netupitant is a highly selective NK1RA that achieves ≥90% central NK1 receptor occupancy at Cmax across most brain regions, with prolonged occupancy over the 100–450 mg dose range. Pharmacokinetic–pharmacodynamic modelling identified a plasma threshold ~225 µg/mL to secure ~90% striatal occupancy. Oral 300 mg is the lowest dose that reliably reaches this target, providing a clear dose–selection rationale.[16]

In addition to this, an invitro study showed that combination of Netupitant and palonosetron enhances the substance P inhibition, compared with the situations when the drugs were used alone. This synergistic action demonstrated invitro along with the long duration of action can drive the NEPA combination a better clinical advantage[18].

Palonosetron is a 5HT3 receptor antagonist with distinctly differs from other drugs by a longer half-life. Another distinct property is palonosetron demonstrates allosteric receptor interactions, favourable cooperative binding, and sustained receptor blockade. It also promotes internalization of receptors and blocks cross-communication between NK_1 receptors and $5\text{-}HT_3$. Recent laboratory investigations have demonstrated that the combination of netupitant along with palonosetron act synergistically to blunt substance P–driven NK1 signalling, and they produce an additive increase in NK1 receptor internalization. Given their extended half-lives (netupitant ~96 h, palonosetron >40 h), the combination plausibly sustains antiemetic activity through the delayed phase, spanning 24–120 hours post- chemotherapy.[17-19]

The above pharmaco-kinetic advantage explains the probable delayed period effective anti-emesis. Our study aligns with other contemporary studies done in solid malignancies, where NEPA has a better antiemetic role specially in delayed phase. An effective anti-emesis has direct relation with the quality of outcome during the transplant course by avoiding malnutrition, electrolyte imbalance and reluctant to further doses in multi-day conditioning regimens[1,20].

Practical feasibility is another strength of NEPA. The complexity of multi-day NK1 receptor antagonist dosing schedules often leads to inconsistent prescribing and poor adherence in real-world practice. By contrast, NEPA provides a simplified single-dose regimen, improving compliance and ease of implementation[21-23].

Taken together, our findings, supported by prior trials and real-world data, suggest that NEPA is an effective and pragmatic option for controlling delayed-phase emesis in ASCT, particularly in multi-day conditioning regimens. Improved emetic control has direct implications for transplant outcomes and patient quality of life. Larger randomized studies, stratified by conditioning regimen, are warranted to confirm these findings.

STRENGTH:
Prospective daily data capture with CTCAEv4 grading, inclusion of both multi-day (BEAM) and single-day (melphalan) conditioning, and a real-world, pragmatic allocation reflecting affordability and availability increases external validity for LMIC settings. The day-wise analysis adds details on every day antiemesis control. These adds weight to our study.

LIMITATIONS:
Allocation was non-randomized and affordability-driven, introducing potential selection bias and unmeasured confounding despite similar baseline distributions. The sample size (NEPA n=22; fosaprepitant+palonosetron n=43) limits power to detect modest differences. Nausea was not accounted in the study. Administration of rescue antiemetics was not quantified in the study. These forms the potential limitations of the study.

FUTURE DIRECTIONS:
A randomized study trial stratified by conditioning regimen (BEAM versus melphalan), with larger sample size is warranted for further definitive evidence in this clinical context.

Conclusion:

Our study concludes that NEPA has no significant benefit in acute and overall phases, however Day 5 of delayed emesis showed better antiemetic control by NEPA. Between two conditioning regimen, BEAM protocol had higher vomiting grades on Day 3. Better emetic control contributes to improved transplant outcomes. These findings support considering NEPA when late delayed control is clinically critical and highlight the need for adequately powered randomized studies in the transplant setting.

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