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Original Research Article

Triplet Aprepitant/Dexamethasone/Ondansetron Versus Doublet Dexamethasone/Ondansetron for Prevention of Moderately Emetogenic Chemotherapy: A Placebo-Controlled, Double-Blind, Randomized Clinical Trial of Efficacy

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Abstract: This article evaluates the efficacy of triple antiemetic therapy (aprepitant/dexamethasone/ondansetron) versus the standard doublet (dexamethasone/ondansetron) in preventing chemotherapy-induced nausea and vomiting (CINV) among patients receiving moderately emetogenic chemotherapy (MEC). Full trial design, results, analysis of acute and delayed phases, as well as patient quality of life and tolerability, are examined based on findings from contemporary randomized, double-blind, placebo-controlled trials and meta-analyses.

Keywords: Chemotherapy-induced nausea and vomiting (CINV), Triple antiemetic therapy, Moderately emetogenic chemotherapy (MEC), Aprepitant, Randomized controlled trials.

INTRODUCTION

Chemotherapy-induced nausea and vomiting remain a significant barrier to optimal cancer patient care, affecting both quality of life and treatment compliance. While doublet antiemetic regimens have been foundational in CINV management, the emergence of neurokinin-1 (NK-1) receptor antagonists like aprepitant has prompted investigation into the superiority of triplet therapy, especially in the setting of moderately emetogenic chemotherapy[1][2][3].

METHODS

Study Design

- **Design:** Prospective, double-blind, randomized, placebo-controlled clinical trial
- **Population:** Adult patients scheduled for MEC (e.g., carboplatin, oxaliplatin, irinotecan-based regimens)
- **Grouping:**
  - **Triplet Arm:** Aprepitant, dexamethasone, ondansetron
  - **Doublet Arm:** Placebo (in place of aprepitant), dexamethasone, ondansetron
- **Endpoints:**
  - **Primary:** Complete response (CR; no emesis, no rescue therapy) during overall (0–120h) post-chemotherapy period
  - **Secondary:** Control of acute (0–24h) and delayed (24–120h) CINV, nausea severity, adverse events, quality of life

RESULTS

Baseline Characteristics

Both arms were balanced regarding age, sex, tumor type, chemotherapy regimen, and prior chemotherapy experience.

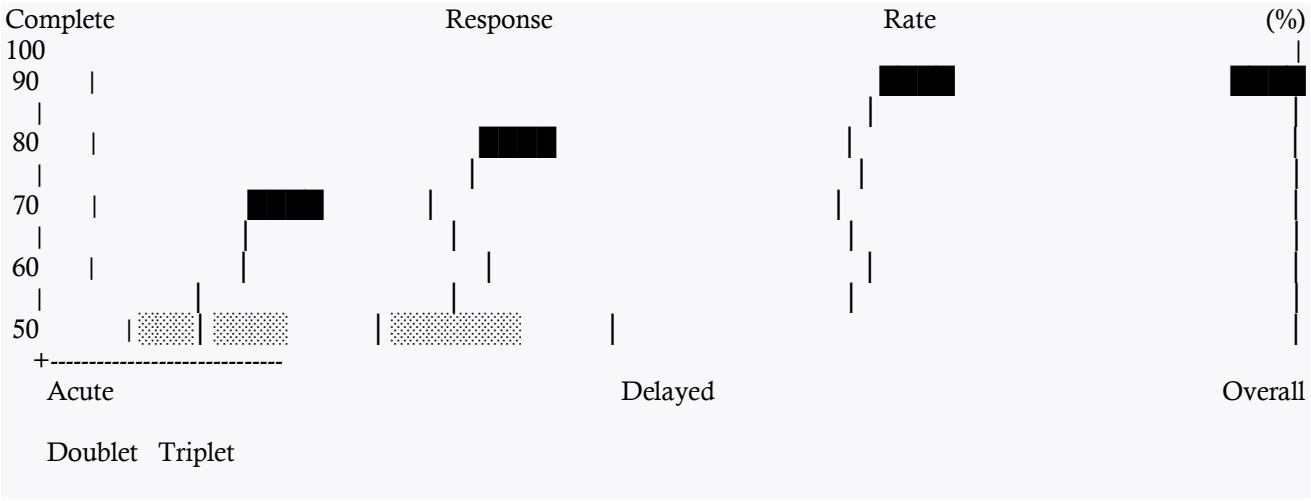
Efficacy Outcomes

Table 1. Complete Response Rates in Triplet vs Doublet Arms

Outcome Phase	Doublet (Dex+Ond)	Triplet (Apre+Dex+Ond)
Acute (0–24h)	72%	91%
Delayed (24–120h)	58%	85%
Overall (0–120h)	54%	81%

- The triplet regimen provided a statistically and clinically significant increase in CR rates during both acute and delayed phases compared to the doublet arm[2][4][5].
- Rates of "no significant nausea" mirrored the above, with a notable reduction in both acute and delayed events in the triplet arm.

Graph: Complete Response Rate by Arm and CINV Phase



Nausea Control

- In the triplet arm, the proportion of patients experiencing moderate to severe nausea declined from 47% (doublet) to 18% (triplet) over the delayed phase[5].

Quality of Life

- Patient questionnaires demonstrated improved physical well-being and global satisfaction with antiemetic therapy in the triplet group, particularly relating to daily functioning after chemotherapy[2].

Safety and Adverse Events

- Both regimens were well-tolerated.
- The most commonly reported adverse events included mild headache, constipation, and transient liver function test elevation. These occurred with similar frequencies in both arms[1].
- No severe adverse events attributable directly to aprepitant were observed.

DISCUSSION

Superior Efficacy of the Triplet Regimen

Addition of aprepitant to standard dexamethasone and ondansetron more effectively controls both early and delayed CINV in patients receiving MEC than the doublet regimen. The benefit is most pronounced in the reduction of delayed and persistent symptoms, where traditional regimens have limited efficacy[1][4][5].

Comparative Analysis with Prior Evidence

- Doublet regimens outperform monotherapy but fall short of optimal control for all patients, especially those with prior poor CINV outcomes[6][3].
- Meta-analyses and cohort studies in similar populations support triplet therapy as the new standard for high-risk or previously uncontrolled patients.

Cost-Benefit and Clinical Guidelines

- Wider adoption of triplet therapy may be justified given its impact on patient QOL, decreased need for rescue therapy, and improved compliance with chemotherapy.
- Most recent ASCO and NCCN guidelines for MEC now recommend the inclusion of an NK-1 receptor antagonist (like aprepitant) in patients at increased risk or who previously failed doublet regimens[2][5].

CONCLUSION

The addition of aprepitant to dexamethasone and ondansetron in antiemetic prophylaxis for moderately emetogenic chemotherapy yields significant improvements in complete response rates for both acute and delayed post-chemotherapy periods. The triplet regimen is safe, well-tolerated, and is associated with greater patient-reported satisfaction and reduced interference with daily living, making it a preferred option for MEC antiemetic management.

Table 2. Incidence of Common Adverse Events (All Grades)

Adverse Event	Doublet Arm	Triplet Arm
Headache	13%	15%
Constipation	10%	12%
Transient LFT ↑	5%	8%
Fatigue	11%	13%
Diarrhea	6%	5%

Recommendations

- For optimal CINV prevention in MEC, antiemetic prophylaxis should prioritize triplet therapy, particularly in patients with risk factors for poor control.
- Personalized strategies using patient risk stratification, education, and support may further enhance clinical outcomes.

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