Intravenous Fosaprepitant for the prevention of chemotherapy induced vomiting in children: a double blind placebo controlled, phase III randomized trial

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Faculty Disclosure

Nothing to Disclose

Background

- Chemotherapy induced vomiting (CIV) affects as many as 60% of children with present standard of care (ondansetron and dexamethasone).
- Fosaprepitant is a Neurokinin-1 (NK-1) receptor antagonist and prodrug of aprepitant which is approved for use in children.
- Approved in adults for the prevention of CIV moderately or highly emetogenic chemotherapy (MEC or HEC).
- Efficacy and safety of fosaprepitant in children is unknown.

Aim of Study

- To study the efficacy and safety of intravenous fosprepitant, neurokinin 1 (NK-1) receptor inhibitor, for the prevention of chemotherapy-induced vomiting (CIV) in pediatric patients, receiving moderate to highly emetogenic chemotherapy.

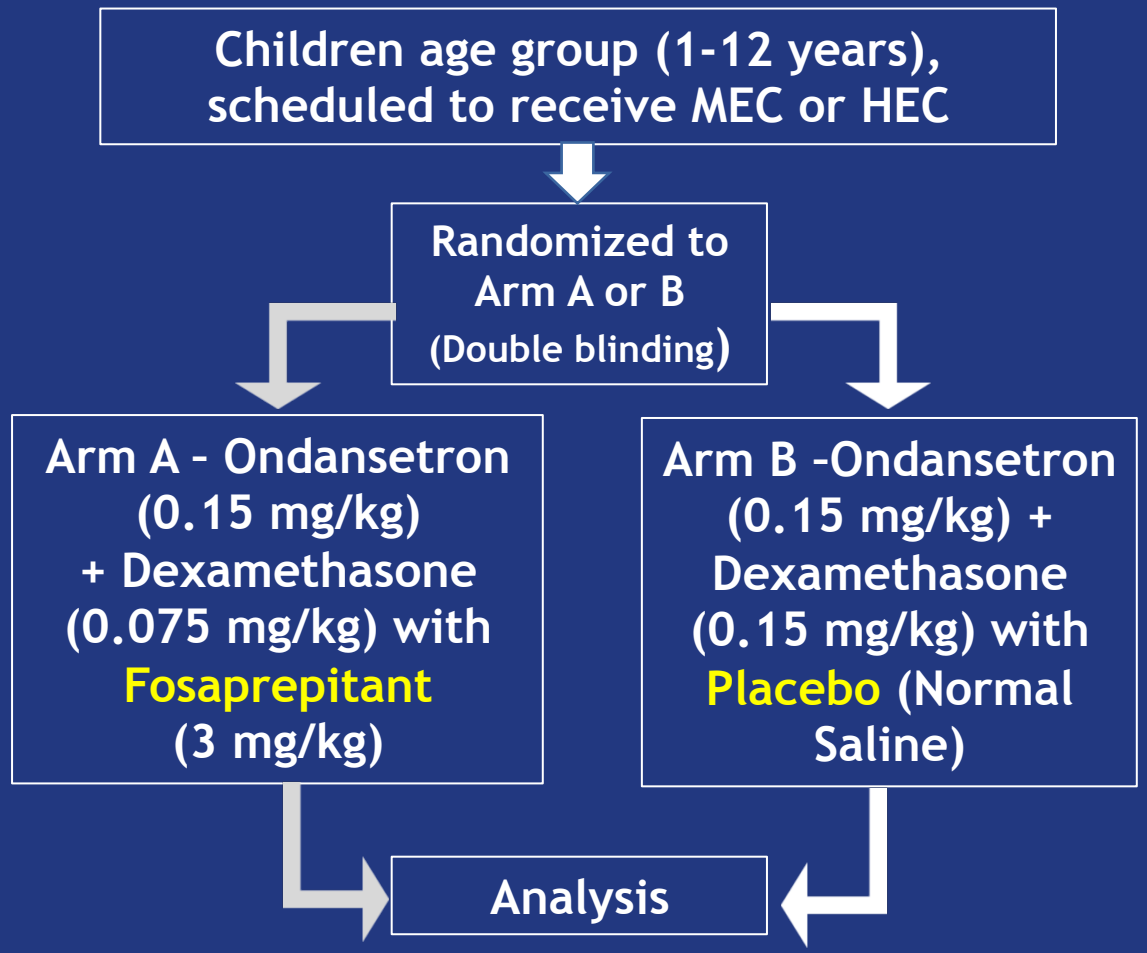
Rationale of Study

- Single dose intravenous fosaprepitant versus 3 day course of oral aprepitant. Shorter duration is better for compliance.
- Fosaprepitant will be useful for patients who cannot take or swallow oral aprepitant due to young age or vomiting.
- Oral suspension of aprepitant for children is not available in many countries.
- Fosaprepitant is less costly than aprepitant (320$ vs 705$).

Study Design

- Approved by institute ethical committee
- Study design
  - Phase-III, Randomized, Superiority design, Placebo controlled, Double blind
  - Allocation : Computer generated table of random numbers: concealed
- Study Population
  - Children less between 1-12 years receiving moderate or highly emetogenic chemotherapy
- Study Duration: March 2017 – Jan 2018
- Sample Size: 68 in each arm (90% power, alpha 0.05) to show 25% improvement in CIV with fosaprepitant.

Methods



- **Primary end-point** - proportion of patients who achieved a complete response (defined as no vomiting, no retching) during the 25–120 hours (delayed phase)

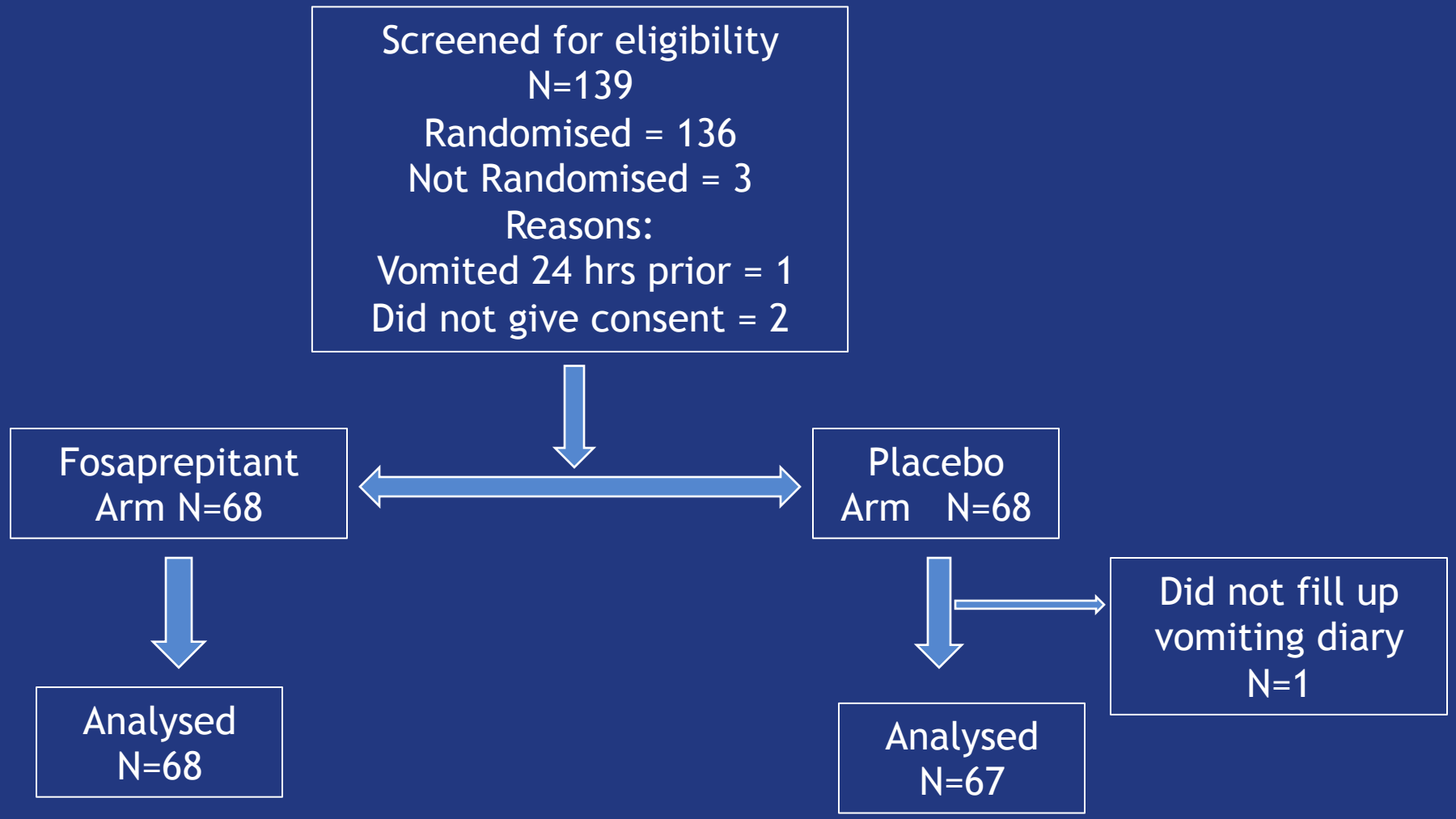
- **Secondary end-points** - proportion of patients who achieved complete response during the acute (0–24 hours) and overall phases.

Assessment of vomiting

All the events were prospectively recorded in vomiting diary

Grade	Severity of vomiting
0 (Nil)	No vomiting
1 (Mild)	1–2 episodes in 24 h
2 (Moderate)	3–5 episodes in 24 h
3 (Severe)	≥6 episodes in 24 h; tube feeding, TPN, or hospitalisation
4 (Very severe)	Life-threatening consequences; urgent intervention indicated
5	Death

Results - Consort diagram



Baseline characteristics

	Fosaprepitant Arm	Placebo Arm
No. of patients	68	68
Median Age (years)	6 (1-12)	6 (1-12)
Male	41	43
Female	27	25
Ratio	1.5:1	1.7:1
Median Weight (kgs)	17 (8-45)	18.75 (8-44)
Prior exposure to chemo	52	52
Prior exposure to Aprepitant/Fosaprepitant	12	7

Diagnosis

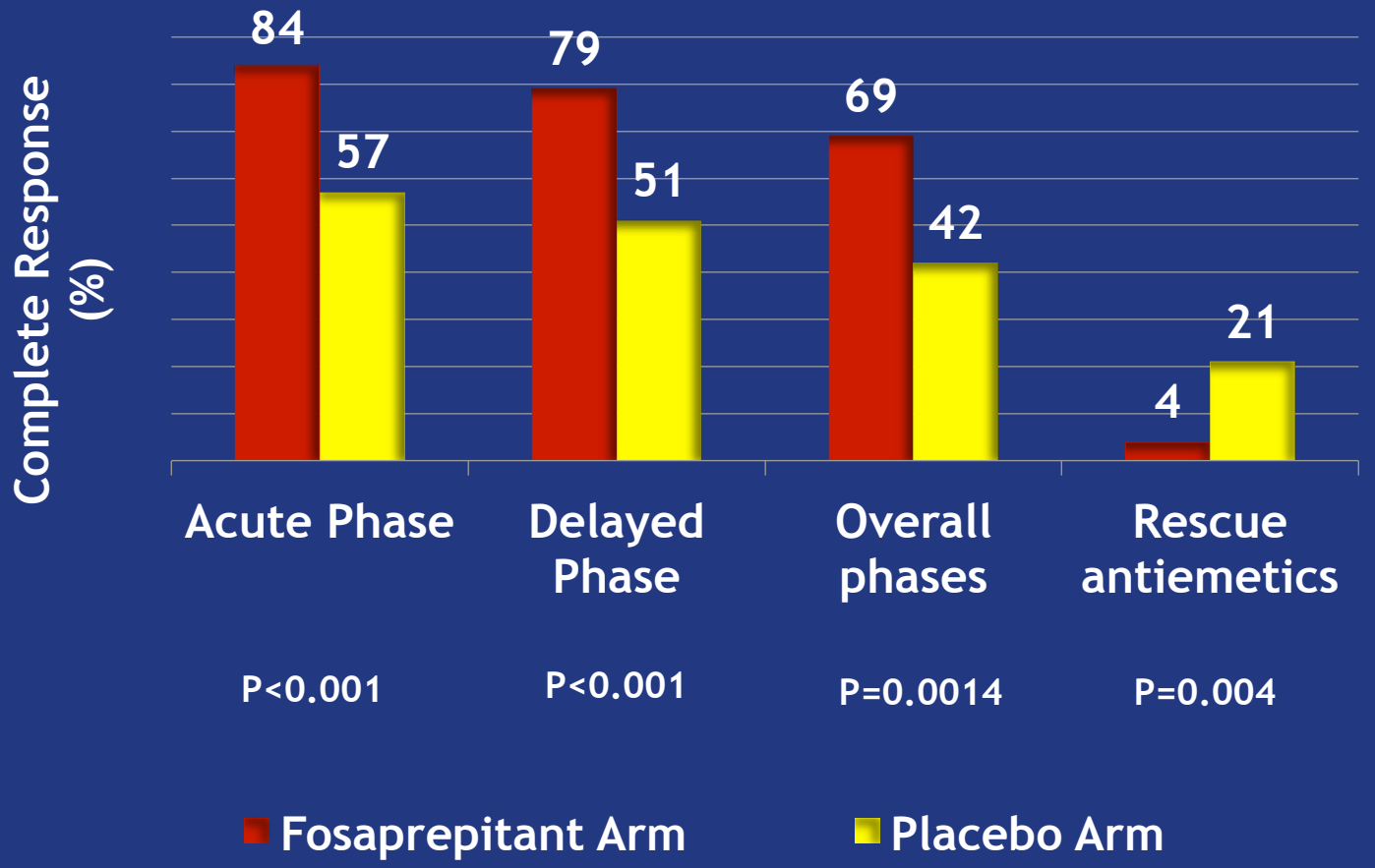
Diagnosis	Fosaprepitant (n=68)	Placebo (n=68)
ALL	28	30
NHL	4	4
HL	7	8
Osteosarcoma	5	3
Ewing's Sarcoma	10	7
Wilm's tumor	3	1
NB	3	5
RMS	2	2
Others	6	8

Chemotherapy

Regimens	Fosaprepitant (n=68)	Placebo (n=68)
AVD/ABVD	7	8
Cyclophosphamide 1gm/m^2	19	25
CCG-3891	2	4
HDMTX	12	6
VAC/IE	9	7
IA/IAP	5	4
VAdC	2	2
Others	12	10

Results

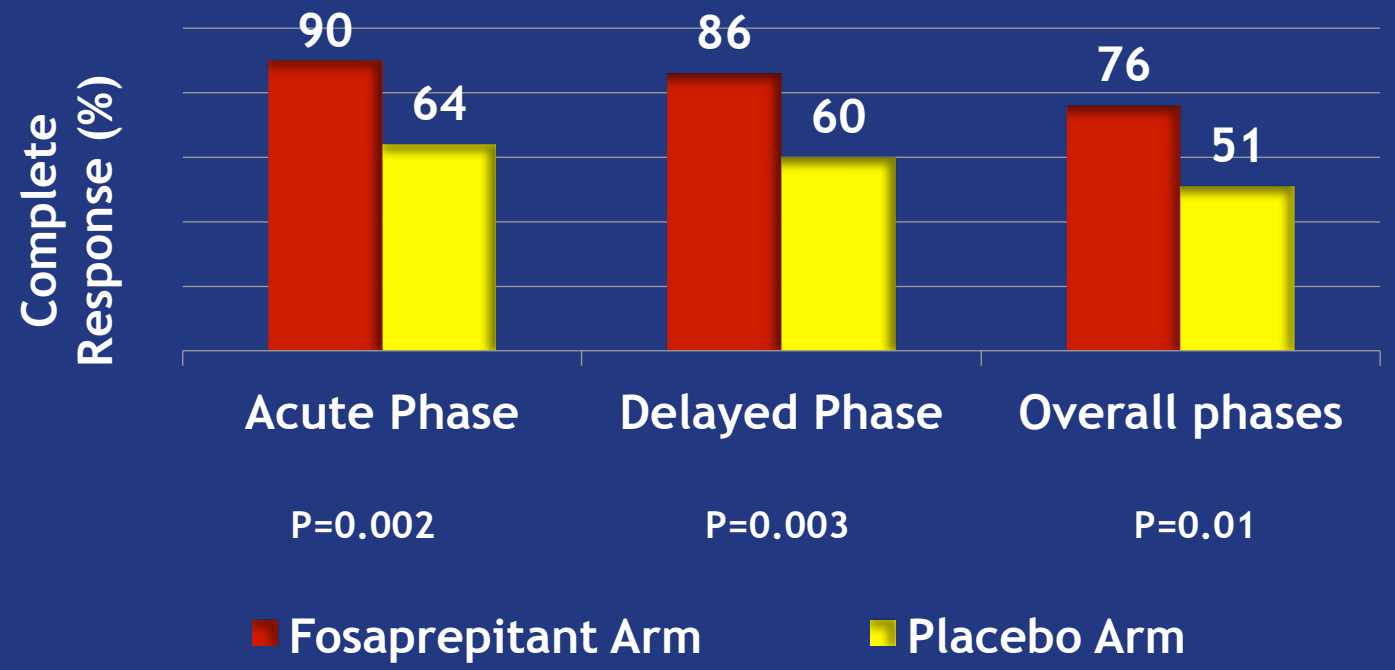
- 135 patients were analyzed
- 68 in fosaprepitant arm
- 67 in placebo arm
- Complete response rates were significantly higher in fosaprepitant arm in all the phases



No fosaprepitant related grade 3-4 adverse events were observed

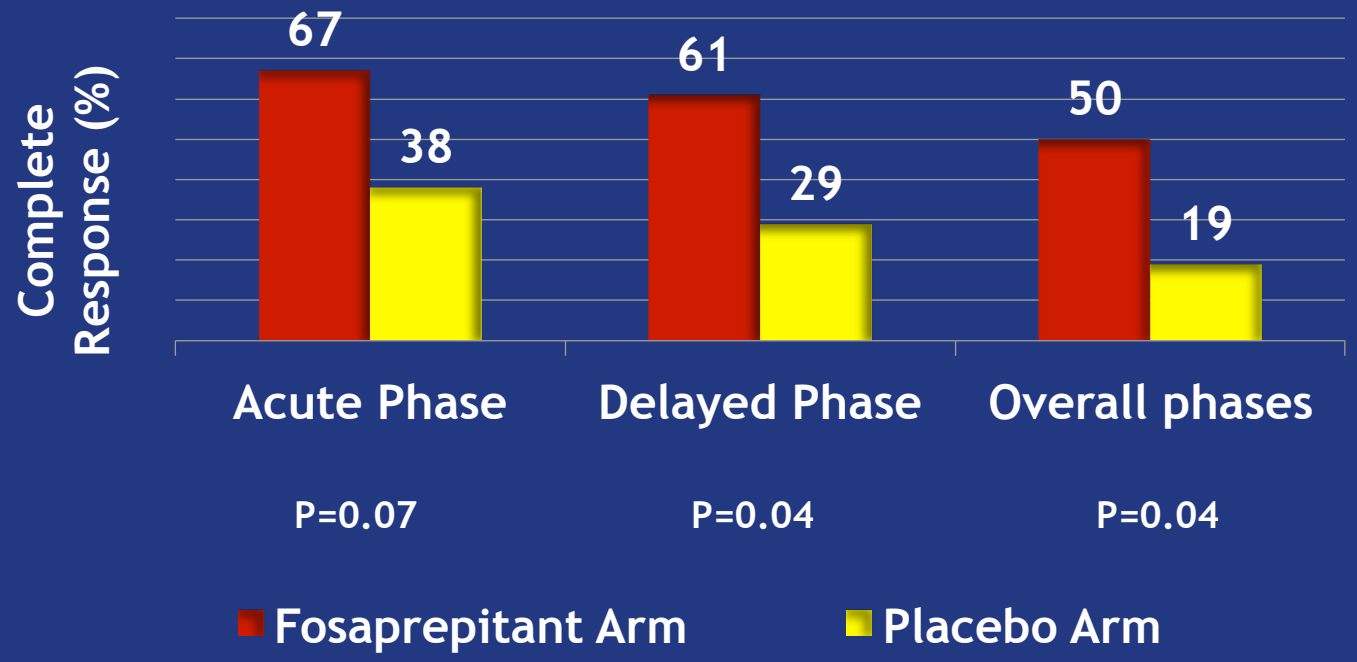
MEC

Complete Response	Fosaprepitant Arm (n=50)	Placebo Arm (n=47)	P value
Acute Phase	45 (90%)	30 (64%)	0.002
Delayed Phase	43 (86%)	28 (60%)	0.003
Overall Phase	38 (76%)	24 (51%)	0.01



HEC

Complete Response	Fosaprepitant Arm (n=18)	Placebo Arm (n=21)	P value
Acute Phase	12 (67%)	8 (38%)	0.07
Delayed Phase	11 (61%)	6 (29%)	0.04
Overall Phase	9 (50%)	4 (19%)	0.04



Discussion

- Complete response rates were significantly higher in fosaprepitant arm across all the phases – acute, delayed and overall
- It is effective in both the subgroups (MEC and HEC)

Conclusion

- Addition of fosaprepitant to ondansetron with dexamethasone is safe and effective for the prevention of chemotherapy induced vomiting in children being treated with moderately or highly emetogenic chemotherapy.

THANK YOU