

Phase III Double-Blind Placebo-Controlled Crossover Study Evaluating a 5HT₃ Receptor Antagonist + Dexamethasone +/- Aprepitant in Germ Cell Tumor Patients Receiving 5 Day Cisplatin Combination Chemotherapy

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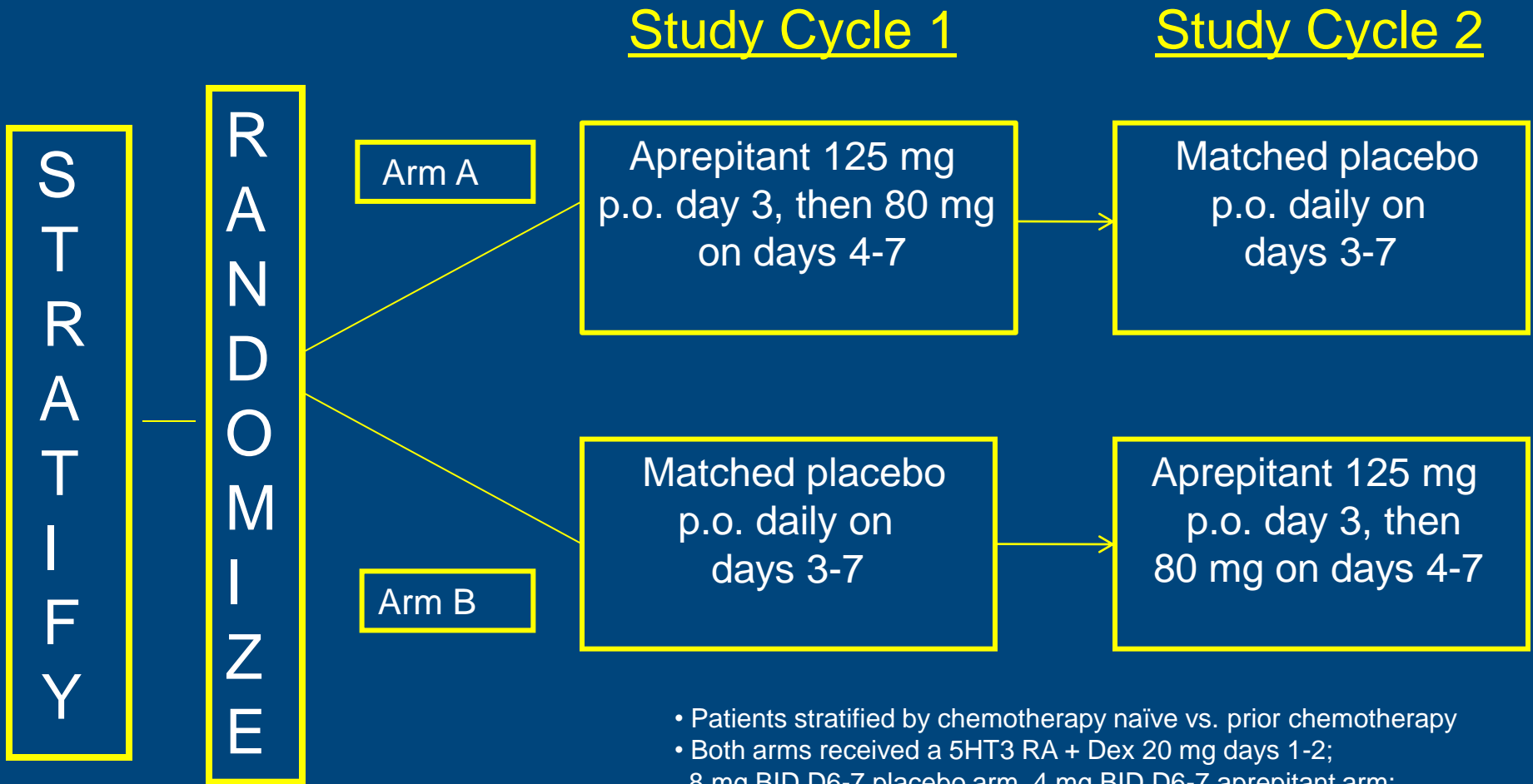


Annual '11
Meeting

INTRODUCTION

- Standard prophylaxis for 1 day highly emetogenic chemotherapy
- No data for multiple day cisplatin regimens
- 5 day cisplatin-based regimens for germ cell tumors

SCHEMA



- Patients stratified by chemotherapy naïve vs. prior chemotherapy
- Both arms received a 5HT3 RA + Dex 20 mg days 1-2; 8 mg BID D6-7 placebo arm, 4 mg BID D6-7 aprepitant arm; both arms 4 mg BID day 8
- Patients served as their own control

PRIMARY OBJECTIVE

- Determine whether the addition of aprepitant to a 5HT3 RA + dexamethasone can increase the complete response rate in patients receiving 5 day courses of cisplatin combination chemotherapy
 - C.R. definition

SECONDARY ENDPOINTS

- Emetic episodes (acute and delayed)
- VAS measurement for nausea
- Patient preference

PARAMETERS MEASURED

- Vomiting or retching log: days 1-8 of each cycle
- Rescue medication log: days 1-8 of each cycle
- VAS: days 1-8 each cycle
- Patient preference

ELIGIBILITY

- Male germ cell tumor patients receiving 5-day cisplatin-based chemotherapy
- No N/V 24 hrs. prior to study entry
- No antiemetics 72 hrs. prior to study entry
- Serum creatinine < 2 mg/dl and LFTs $< 3x$ ULN
- No known CNS metastases

INEVALUABLE (N = 9)

REASONS FOR WITHDRAWAL	APREPITANT	PLACEBO
Prior to study start		1
Prior to study drug	1	1
Nausea/vomiting	2	4

PATIENT POPULATION

	<u>Placebo</u>	<u>Aprepitant</u>
Median age	34	30
Chemonaive	29 (cycle 1)	28 (cycle 1)
BEP chemotherapy	30	32

NO EMESIS OR RETCHING (N = 60)

	<u>Aprepitant</u>	<u>Placebo</u>	<u>p value</u>
Days 1-5	50 (80%)	31 (52%)	< 0.0001
Days 6-8	55 (92%)	47 (78%)	0.0047

NO RESCUE MEDICATION (N = 60)

	<u>Aprepitant</u>	<u>Placebo</u>	<u>p value</u>
Days 1-5	33 (55%)	23 (38%)	0.0412
Days 6-8	43 (72%)	31 (52%)	0.0143

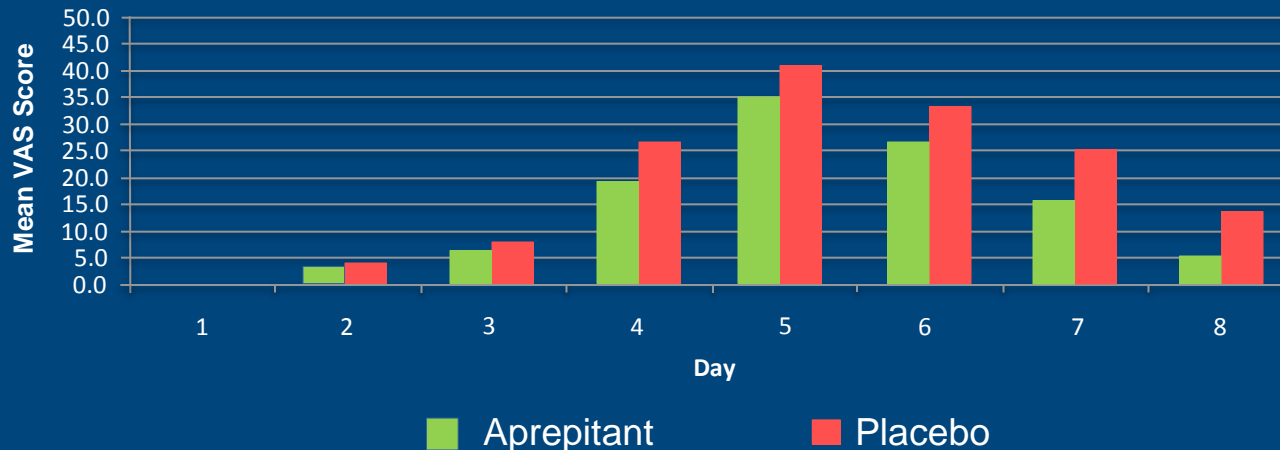
COMPLETE RESPONSE (N = 60)

	<u>Aprepitant</u>	<u>Placebo</u>	<u>p value</u>
Days 1-5	28 (47%)	9 (15%)	< 0.0001
Days 6-8	38 (63%)	21 (35%)	0.0004
Overall (days 1-8)	25 (42%)	8 (13%)	< 0.0001

Mean (SE) VAS Score by Aprepitant/Placebo and Day



Median VAS Score By Aprepitant/Placebo and Day



PREFERENCE (N = 60)

Aprepitant	38	(63%)
Placebo	11	(18%)
No preference	11	(18%)

$p < 0.0001$

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