Sessione 2 - Tossicità gastrointestinale

Nausea e vomito: Linee Guida AIOM/ESMO

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Negrar (VR), 7 Luglio 2015

Disclosures

- Advisory Boards/Honoraria/Consultant for:
  - Celgene, Astra-Zeneca, Helsinn, Eli-Lilly, BMS, Novartis

- Research Support / Grants from:
  - A.I.R.C. (Associazione Italiana Ricerca sul Cancro)
  - I.A.S.L.C. (International Association for the Study of Lung Cancer)

AIRC

IASLC
International Association for the Study of Lung Cancer

THE MULTIPLE ROLES FOR 'SUPPORTIVE CARE' IN CANCER

- **Reduce or eliminate associated symptoms and side-effects**
- **Preserve or improve quality of life**
- **Permit safe out-patient treatment**
- **Enhance the use of the most effective anti-neoplastic agents**

MASCC
MULTINATIONAL ASSOCIATION OF SUPPORTIVE CARE IN CANCER

Modified - Courtesy of Gralla R, 2009

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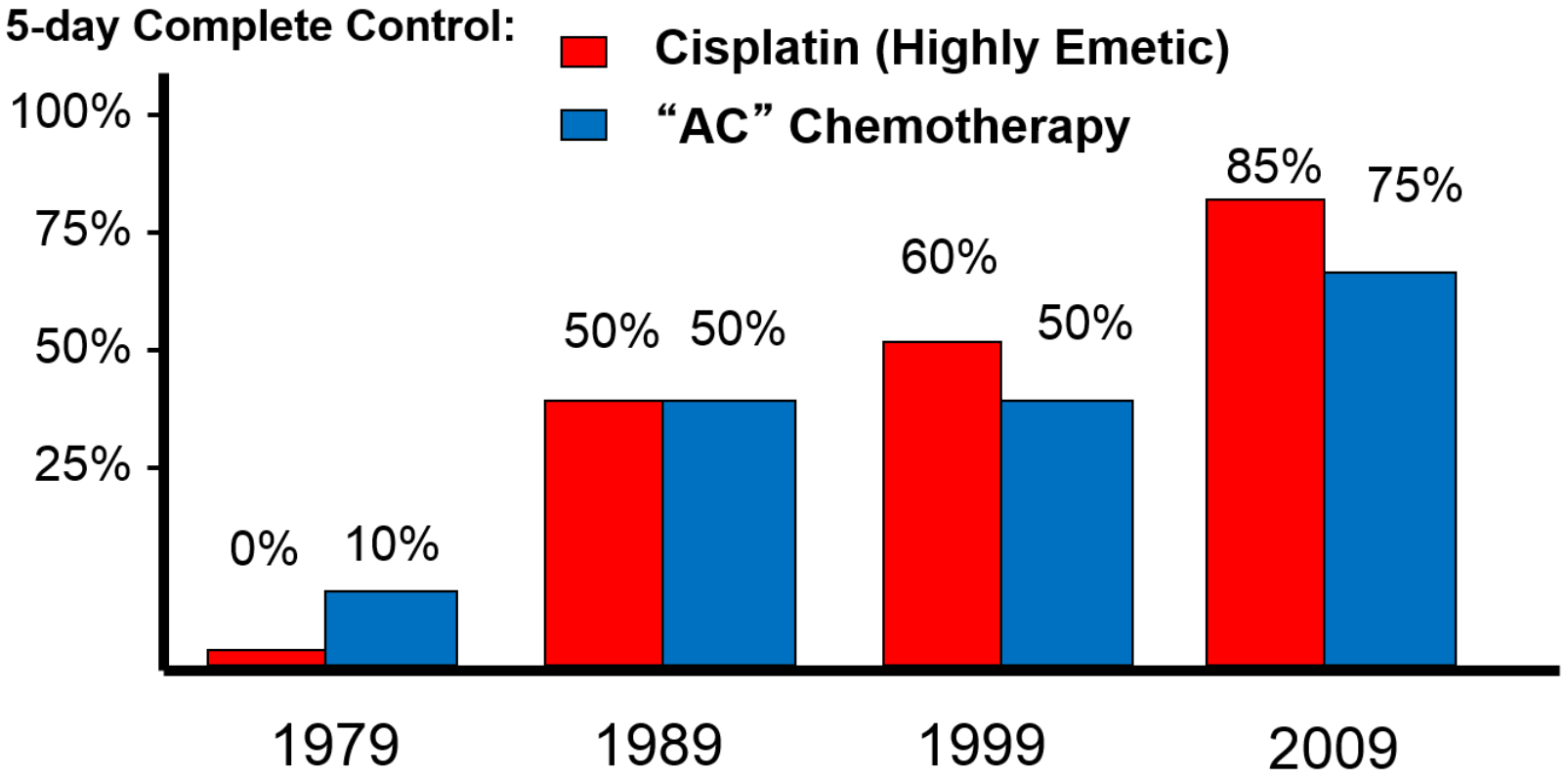
Modified - Courtesy of Gralla R, 2009

CONTROLLING CHEMOTHERAPY-INDUCED EMESIS: PROGRESS OVER THE PAST 30 YEARS: EFFICACY



HIGH	Risk in nearly all patients (> 90%)
MODERATE	Risk in 30% to 90% of patients
LOW	Risk in 10% to 30% of patients
MINIMAL	Fewer than 10% at risk

Modified by Gralla R, 2009

Nausea and Vomiting are Among Patients' Top Concerns

Ranking	1983 [1]	1993 [2]	1995 [3]	1999 [4]	2003 [5]
1	**Vomiting**	**Nausea**	**Nausea**	**Nausea**	Fatigue
2	**Nausea**	Fatigue	Hair Loss	Hair Loss	**Nausea**
3	Hair Loss	Hair Loss	**Vomiting**	Fatigue	Sleep Problems
4	Anxiety	Family Issues	Fatigue	**Vomiting**	Weight Loss
5	Treatment duration	**Vomiting**	Injection Fear	Taste Issues	Hair Loss

1. Coates *Eur J Cancer* 1983
2. Griffin, *Ann Oncol* 1996
3. de Boer-Dennert M, *Br J Cancer* 1997
4. Lindley *Cancer Pract 1999*
5. Hofman M, *Cancer 2004*

Modified by Di Maio M (2010) & Kris M (2012)

Issues for *CINV*

- Do we **reliably measure** that?
- Do we **use** agents **optimally**?
- Are **guidelines useful** for clinical practice?
- What is **new** for CINV in 2015?
- Are we **missing something**?

Issues for *CINV*

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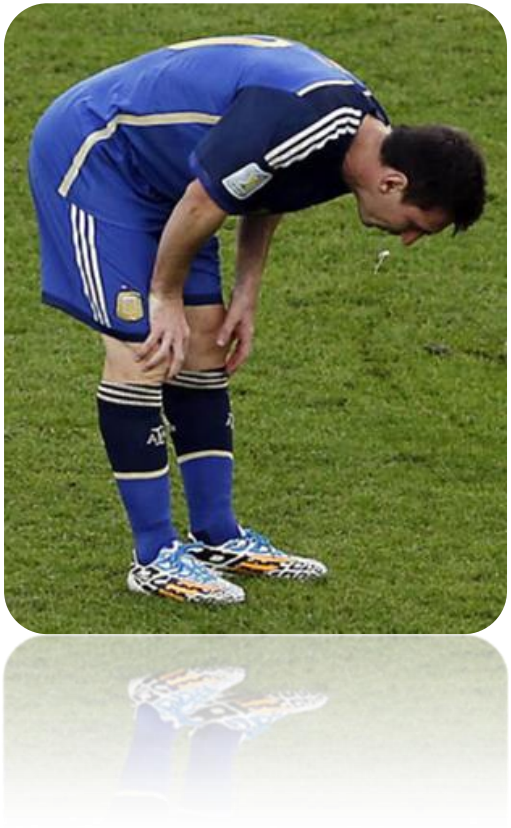


PERCEPTIONS AND REALITY

Underestimation of Emesis with Chemotherapy

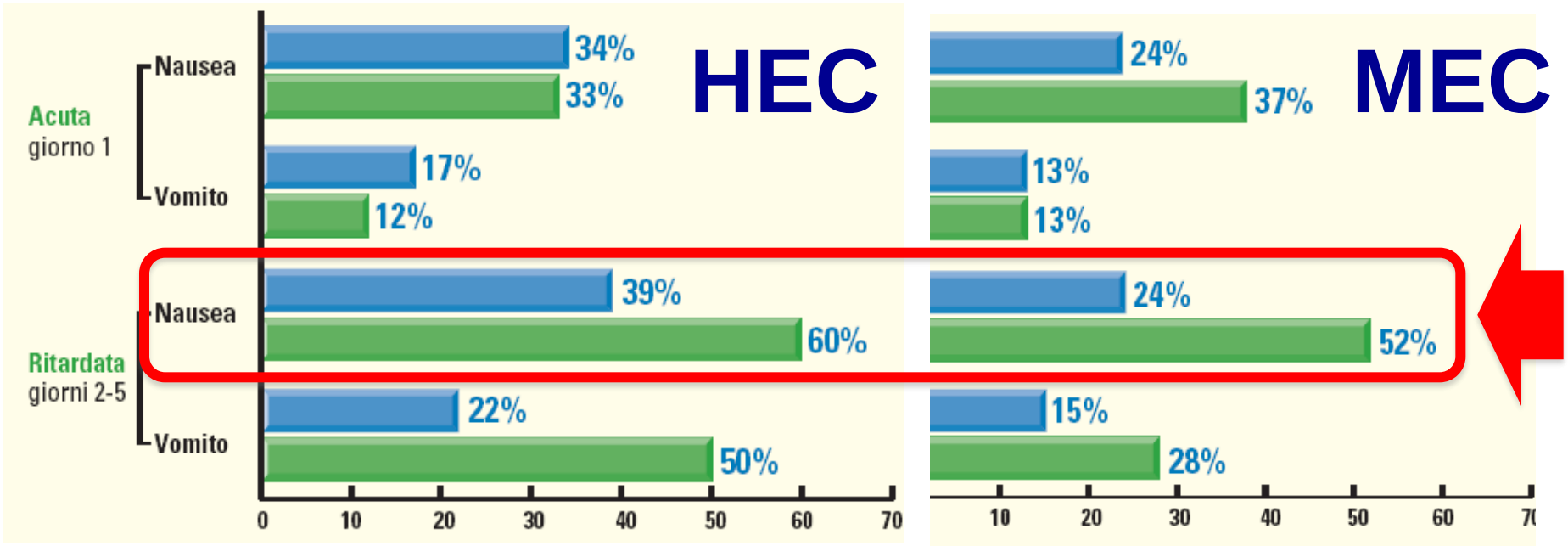
Physicians and nurses from 14 oncology practices in 6 countries

Patients [N=298]

75% women; 78% Mod emetic chemo; 50% breast cancer; 18% lung cancer

Grunberg S et al., Cancer 2004; 100: 2261-8

The 'ANCHOR' Study:
Prediction *vs* Observed



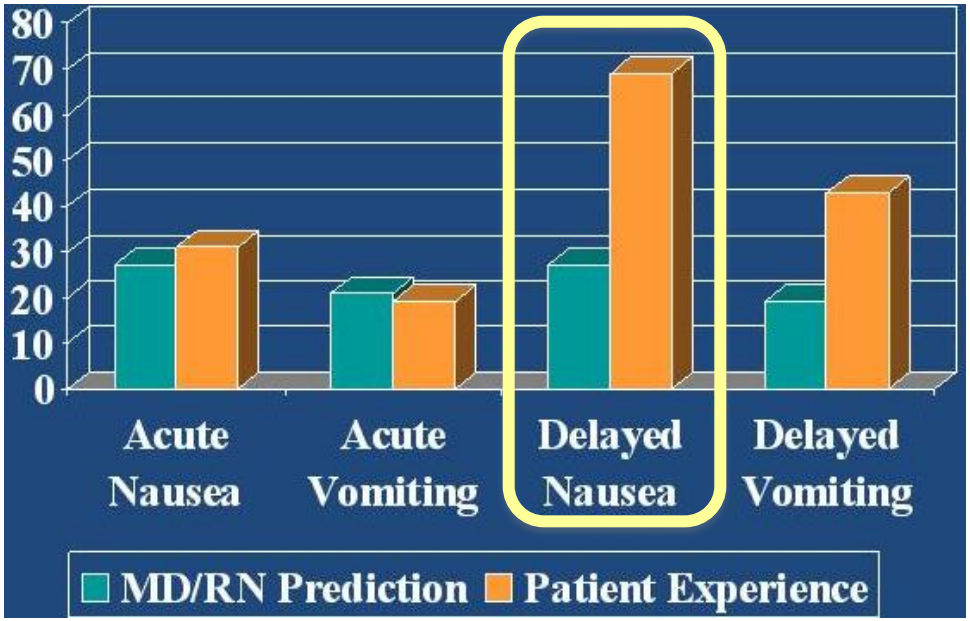
Grunberg S et al., Cancer 2004; 100: 2261-8

PERCEPTIONS AND REALITY

ASCO Annual '12 Meeting

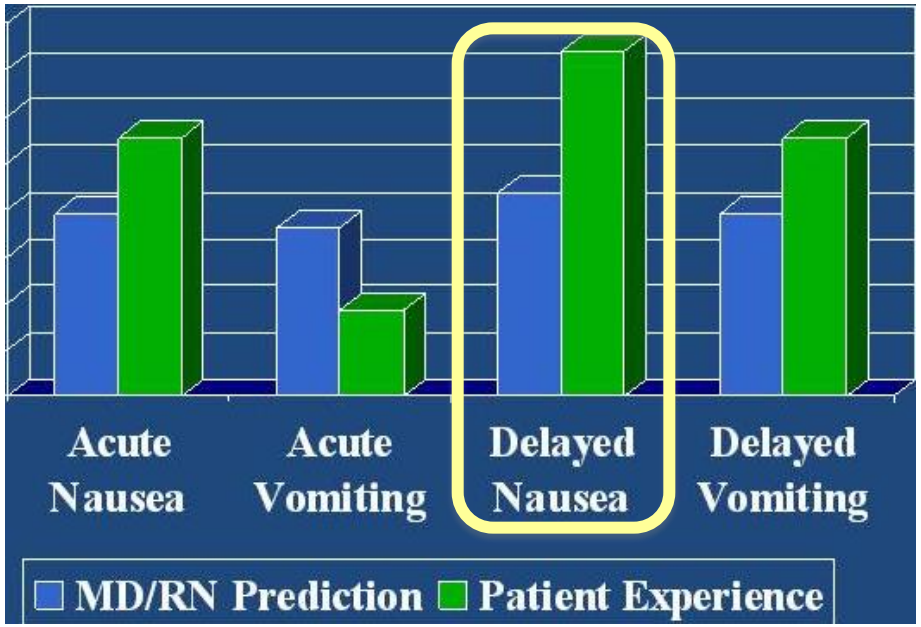
….Regardless of the ethnicity [MEC]

MEXICO



Valle, Curr Med Res Opin 22:2403, 2006

TAIWAN

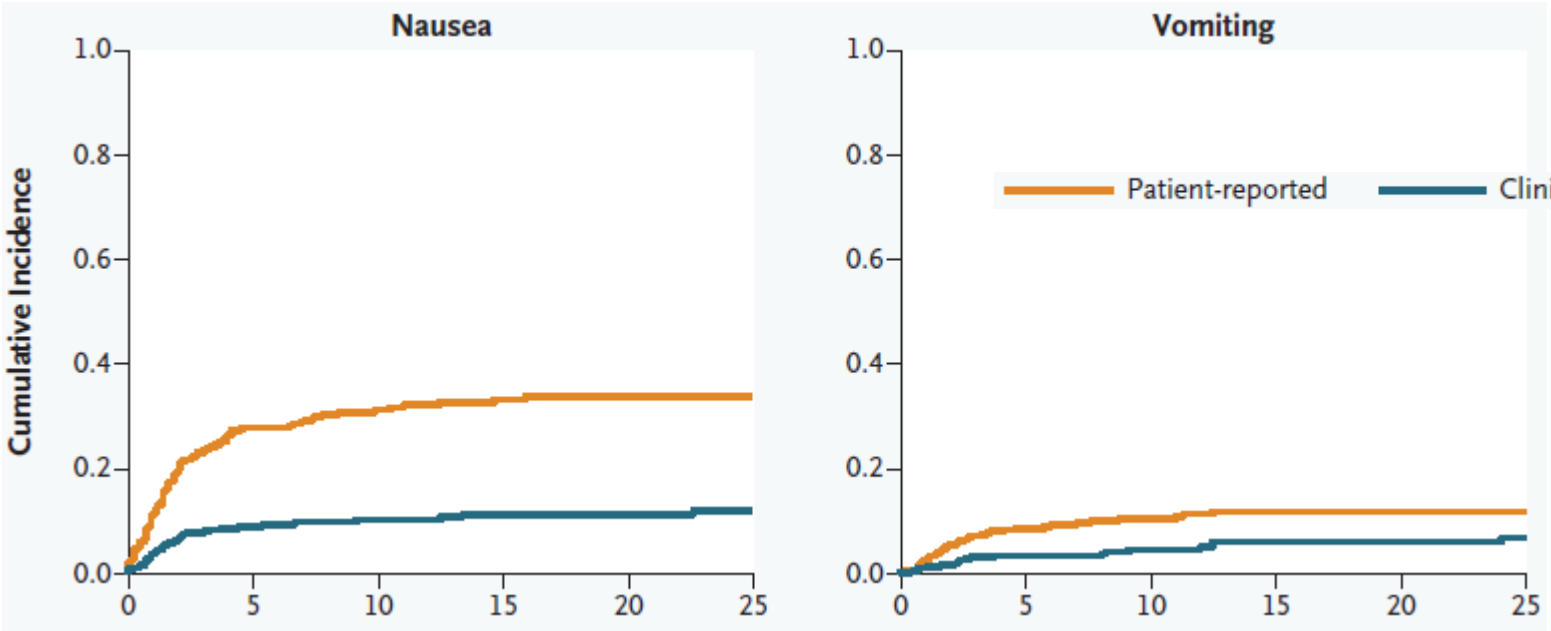


Liau, Support Care Cancer 13:277, 2005

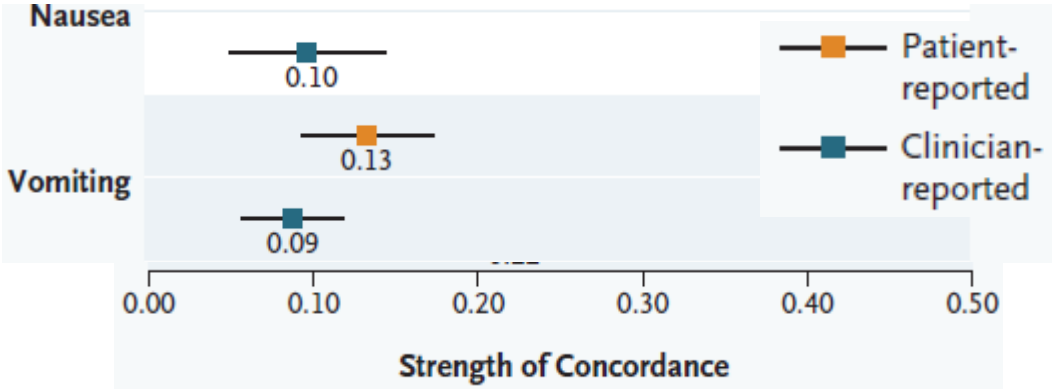
Modified by Grunberg S, ASCO 2012

The Missing Voice of Patients in Drug-Safety Reporting

Ethan Basch, M.D.



Cumulative Incidence of Adverse Symptom Events over Time as Reported by Patients versus Clinicians at Successive Office Visits



467 BC, LC, GU, GYN pts
4034 clinic visits at MSKCC

Symptomatic Toxicities Experienced During Anticancer Treatment: Agreement Between Patient and Physician Reporting in Three Randomized Trials

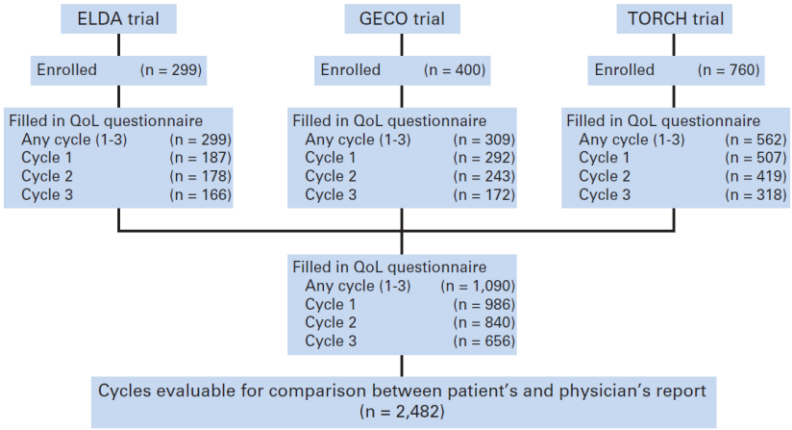


Table 2. Per-Patient Analysis of Association Between Patient (any severity) and Physician Reporting (any grade) of Toxicity

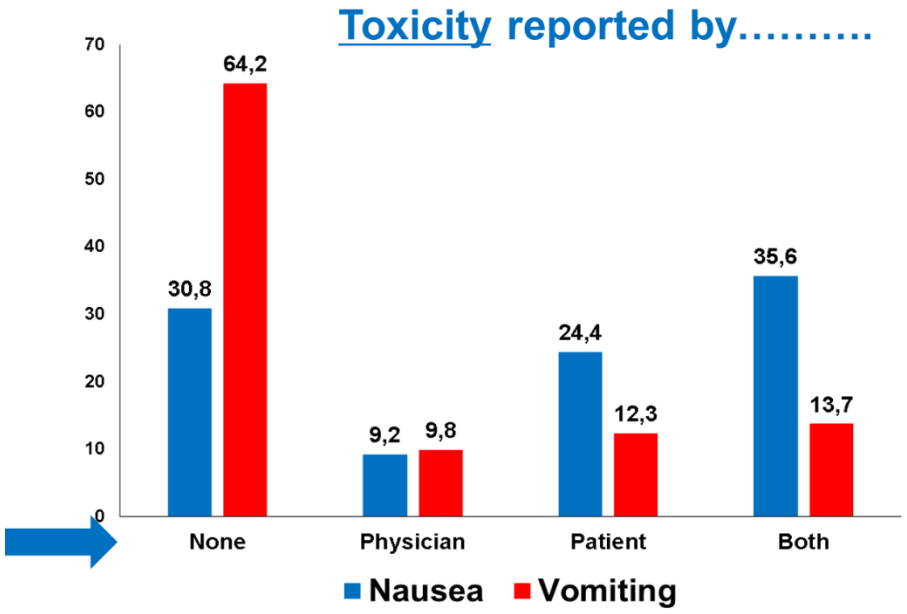
Toxicity	No. of Evaluable Patients*	Toxicity Reported by Neither Patient Nor Physician		Toxicity Reported by Physician but Not Patient		Toxicity Reported by Patient but Not Physician		Toxicity Reported by Both Patient and Physician		Cohen's κ	95% CI
		No.	%	No.	%	No.	%	No.	%		
Anorexia	1,090	383	35.1	28	2.6	505	46.3	174	16.0	0.15	0.12 to 0.19
Nausea	1,089	335	30.8	100	9.2	266	24.4	388	35.6	0.34	0.29 to 0.39
Vomiting	1,090	700	64.2	107	9.8	134	12.3	149	13.7	0.41	0.34 to 0.47
Constipation	1,087	501	46.1	32	2.9	384	35.3	170	15.6	0.24	0.20 to 0.29
Diarrhea	1,088	643	59.1	57	5.2	197	18.1	191	17.6	0.45	0.39 to 0.50
Hair loss	1,086	519	47.8	15	1.4	360	33.1	192	17.7	0.32	0.27 to 0.36

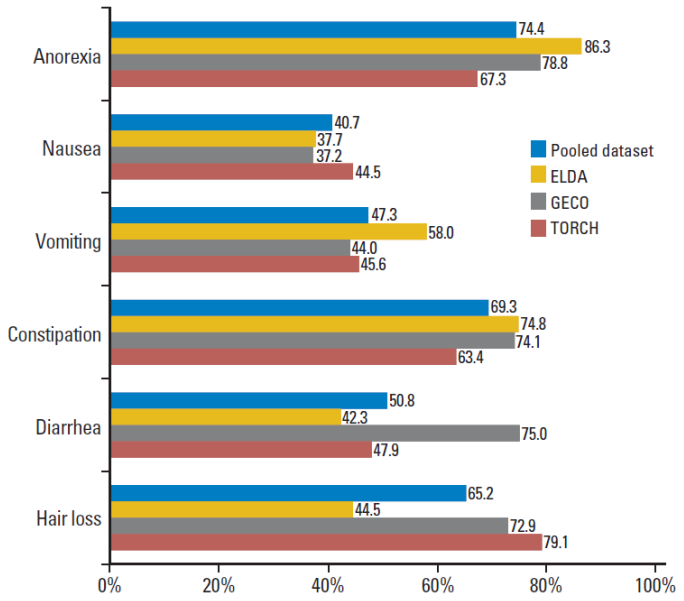
Conclusion

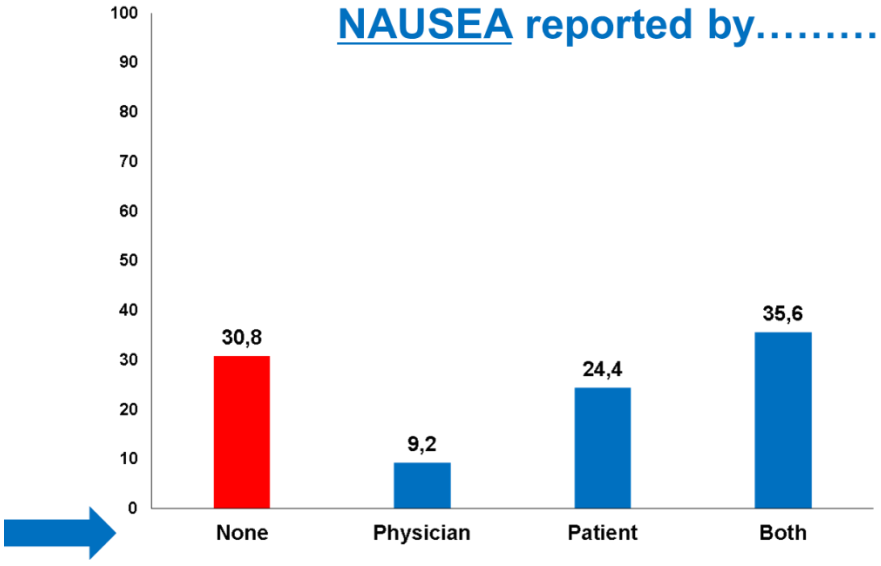
Subjective toxicities are at high risk of under-reporting by physicians, even when prospectively collected within randomized trials. This strongly supports the incorporation of patient-reported outcomes into toxicity reporting in clinical trials.

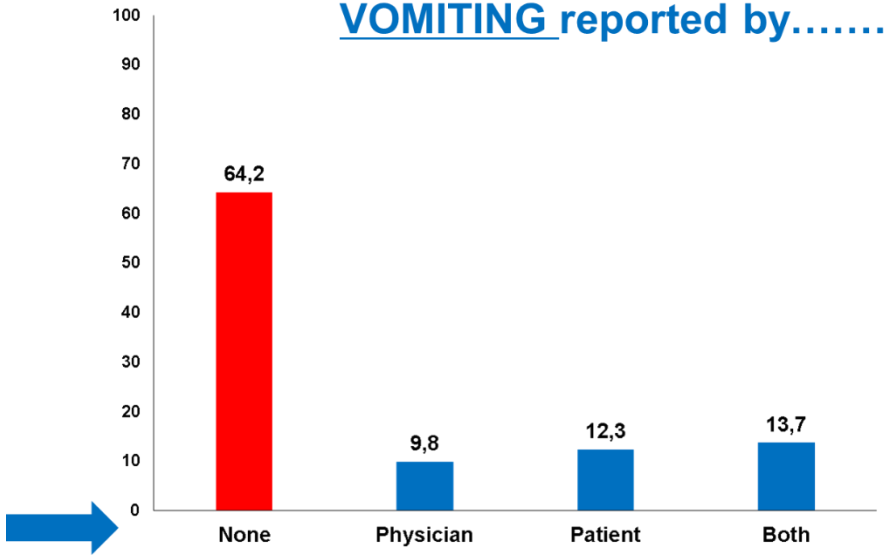
Di Maio M, JCO 2015

Symptomatic Toxicities Experienced During Anticancer Treatment: Agreement Between Patient and Physician Reporting in Three Randomized Trials





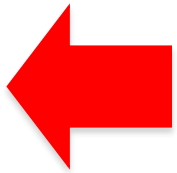




Di Maio M, JCO 2015

Reliability of adverse symptom [CTCAE] event reporting by clinicians

Symptom	ICC	95% CI
Constipation	0.48	0.36; 0.58
Diarrhea	0.58	0.49; 0.66
Dyspnea	0.69	0.62; 0.75
Fatigue	0.50	0.39; 0.59
Nausea	0.52	0.41; 0.60
Neuropathy	0.71	0.65; 0.76
Vomiting	0.46	0.34; 0.56



- *N=393*
- *Seen by 1st clinician in office, then 2nd clinician ~15 minutes later*

Two-point differences, ***which would likely affect treatment decisions,*** were most frequently seen among symptomatic patients for constipation (18%), ***vomiting (15%), and nausea (8%).***

Atkinson et al, Qual Life Res 2012

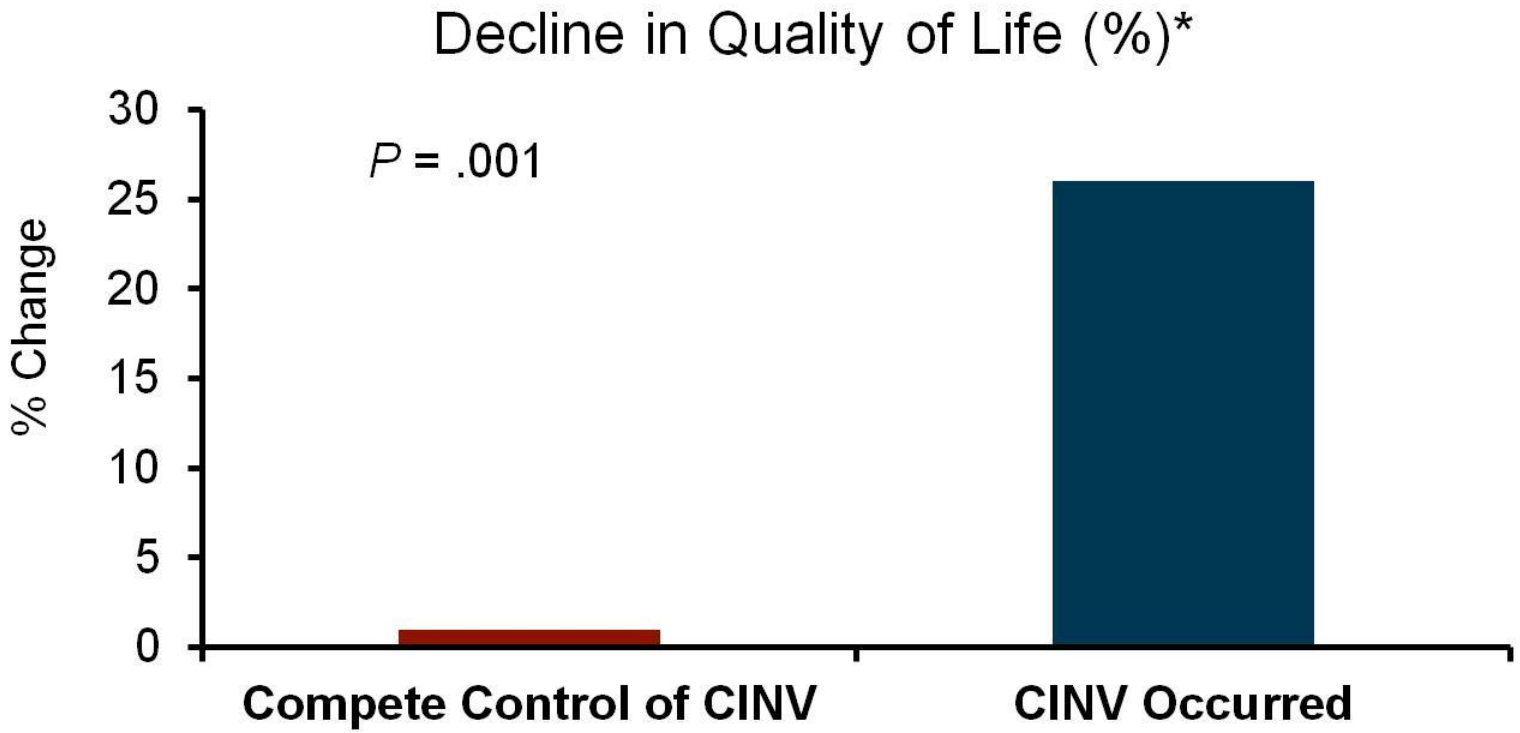
- CINV and QoL -

Why is that clinically relevant?

CINV may induce:

- Fluid and electrolyte balance
- Nutritional deficiencies
- Anorexia
- Pulmonary complications '*ab ingestis*', cough
- Reduction in the ability to perform daily activities
- Delays or interruptions of chemotherapy
- Poor compliance (relevant to oral therapies)
- Deterioration in the quality of life

Impact of CINV on Quality of Life: *Complete Control of CINV vs Failure to Control CINV*

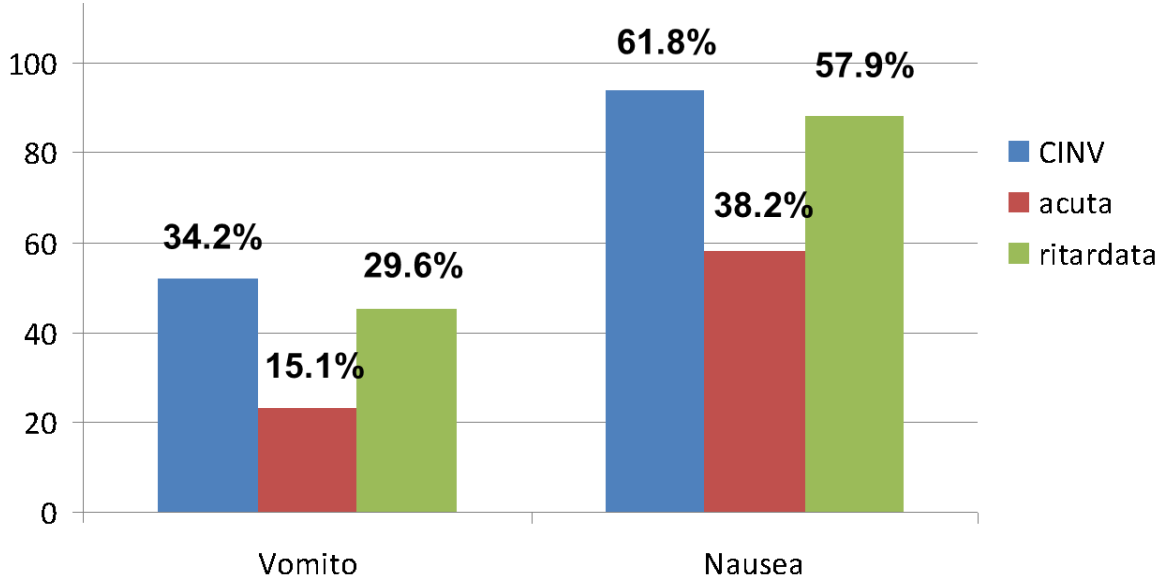


*Baseline QoL values determined immediately prior to chemotherapy, compared with 3 days after chemotherapy administration, using the patient-rated, validated QoL measure, the Functional Living Index – Emesis (FLIE).

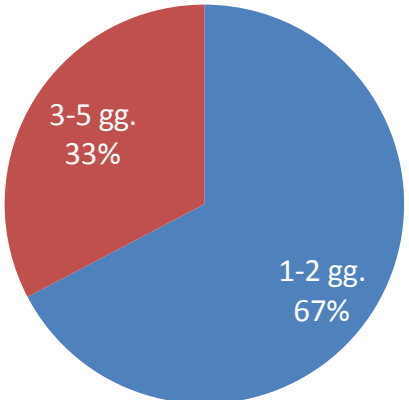
Lindley CM, et al. *Qual Life Res.* 1992;1:331-340.

Gralla RJ, Medscape 2013

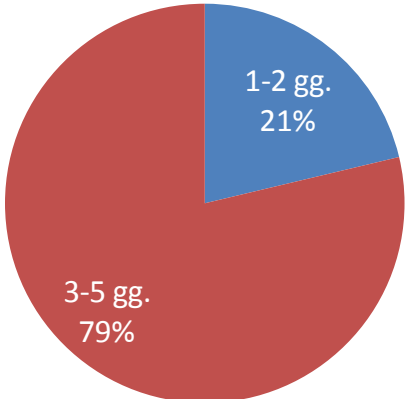
The impact of chemotherapy-induced nausea and vomiting on health-related quality of life



Durata del vomito (n=52)



Durata della nausea (n=94)



	Impatto sulla vita quotidiana	
	Vomito	Nausea
CINV (giorni 1-5)	**35/52 (67%)**	**72/94 (76%)**
acuta, non ritardata	4/7 (57%)	2/6 (33%)
ritardata, non acuta	16/29 (55%)	22/36 (61%)
sia acuta che ritardata	15/16 (94%)	48/52 (92%)

Ballatori E, SCC 2007

Issues for *CINV*

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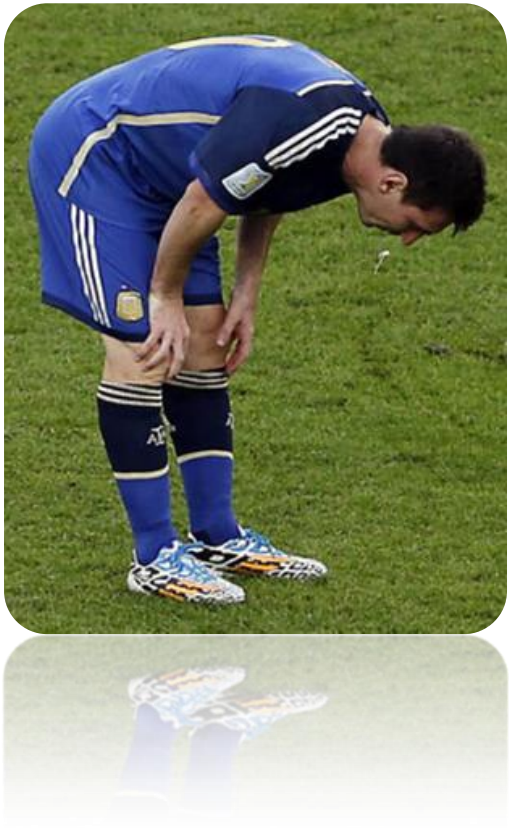


MAJOR ANTIEMETIC CLASSES

- Do we use Agents in these Classes Optimally? -

- **Corticosteroids**
  - Mechanism of action in CINV prevention is unknown
  - Side effects are limited by shortened course
  - Dexamethasone is typically used

- **Serotonin Antagonists**
  - Block binding of $5HT_3$ (serotonin) to the $5HT_3$ receptor
  - Includes:
    - First-generation $5HT_3$ receptor antagonists: dolasetron, granisetron, and ondansetron
    - Second-generation $5HT_3$ receptor antagonist: palonosetron

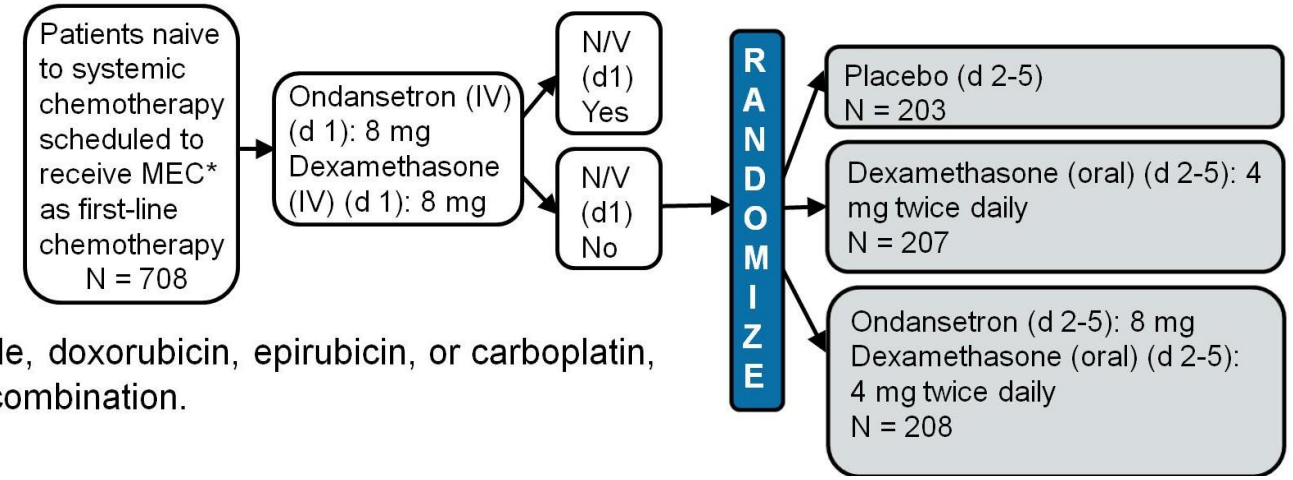
- **NK_1 Antagonists**
  - Blocks binding of substance P to the NK_1 receptor
  - Includes oral aprepitant and fosaprepitant (IV form of aprepitant)

MAJOR ANTIEMETIC CLASSES

- Do we use Agents in these Classes Optimally? -

- **Corticosteroids**
  - **Steroid Sparing**
- **Serotonin Antagonists**
- **NK_1 Antagonists**

The Italian Group for Antiemetic Research 2000



*Cyclophosphamide, doxorubicin, epirubicin, or carboplatin, either alone or in combination.

	Placebo	Dexamethsone (d 2-5)	Ondansetron + Dexamethasone (d 2-5)	*P* Value for Overall Comparison Between 3 Groups
No emesis (delayed period)	87.3%	92.3%	95.2%	.02
No moderate or severe nausea (delayed period)	81.8%	89.4%	93.3%	.002

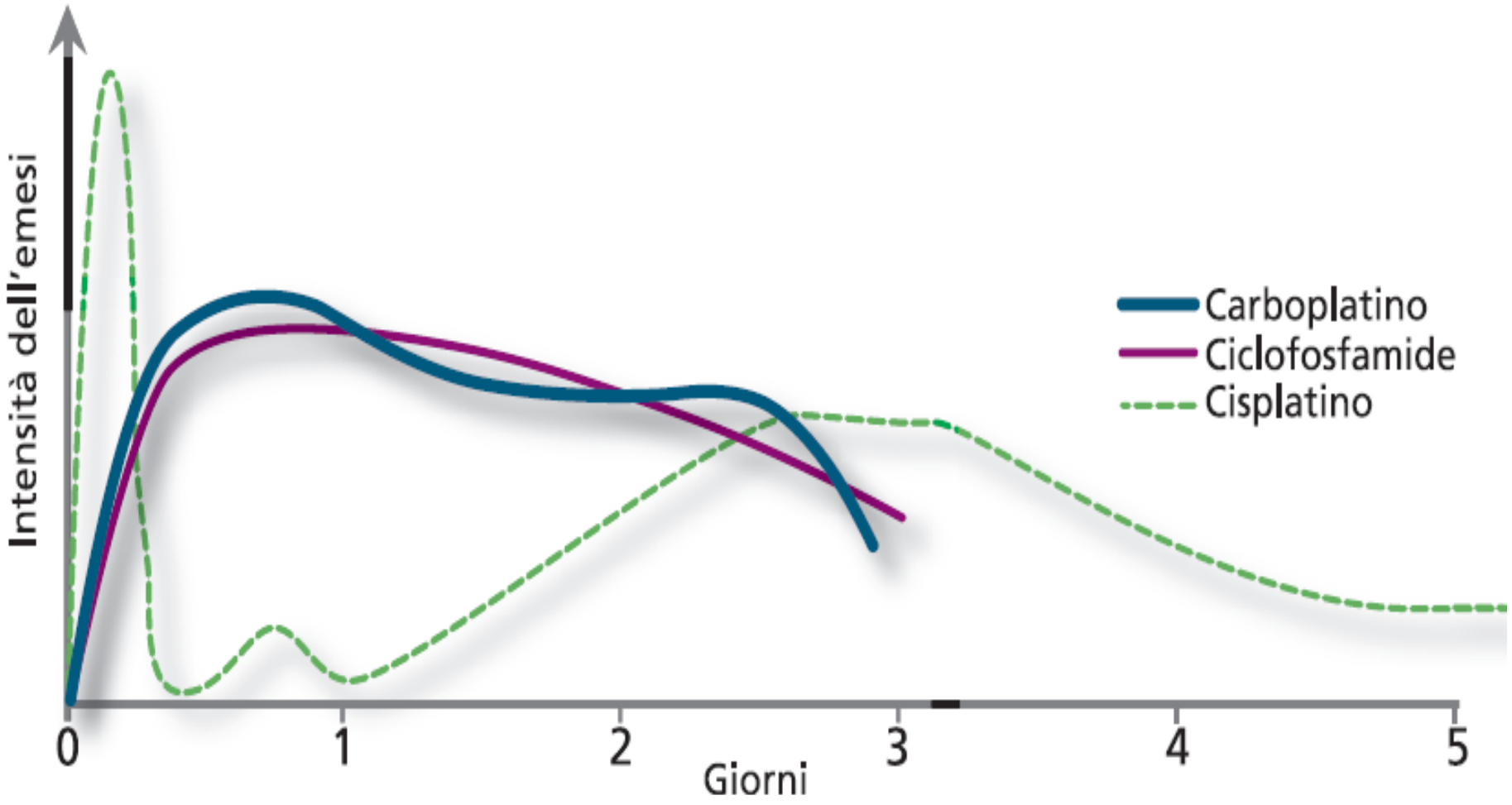
The Italian Group for Antiemetic Research. *N Engl J Med.* 2000;342:1554-1559.

- Conclusion: Dexamethasone alone is an optimal approach for the prevention of CINV during the delayed period in this patient population.

Raftopoulos H, Medscape 2013

DELAYED EMESIS

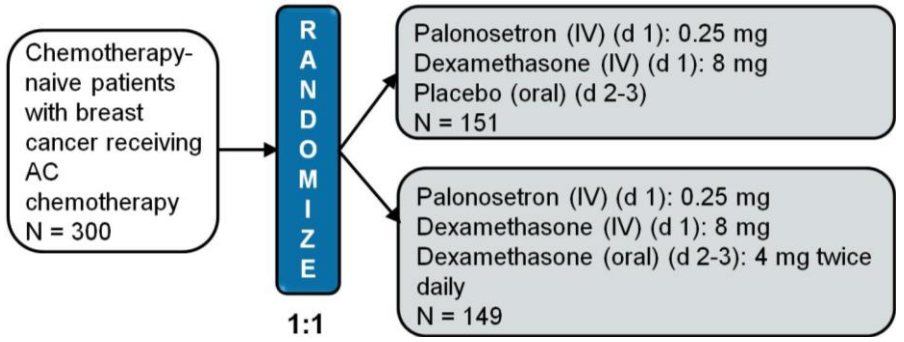
- Do we use Agents in these Classes Optimally? -



Aapro et al. Oncology 2005

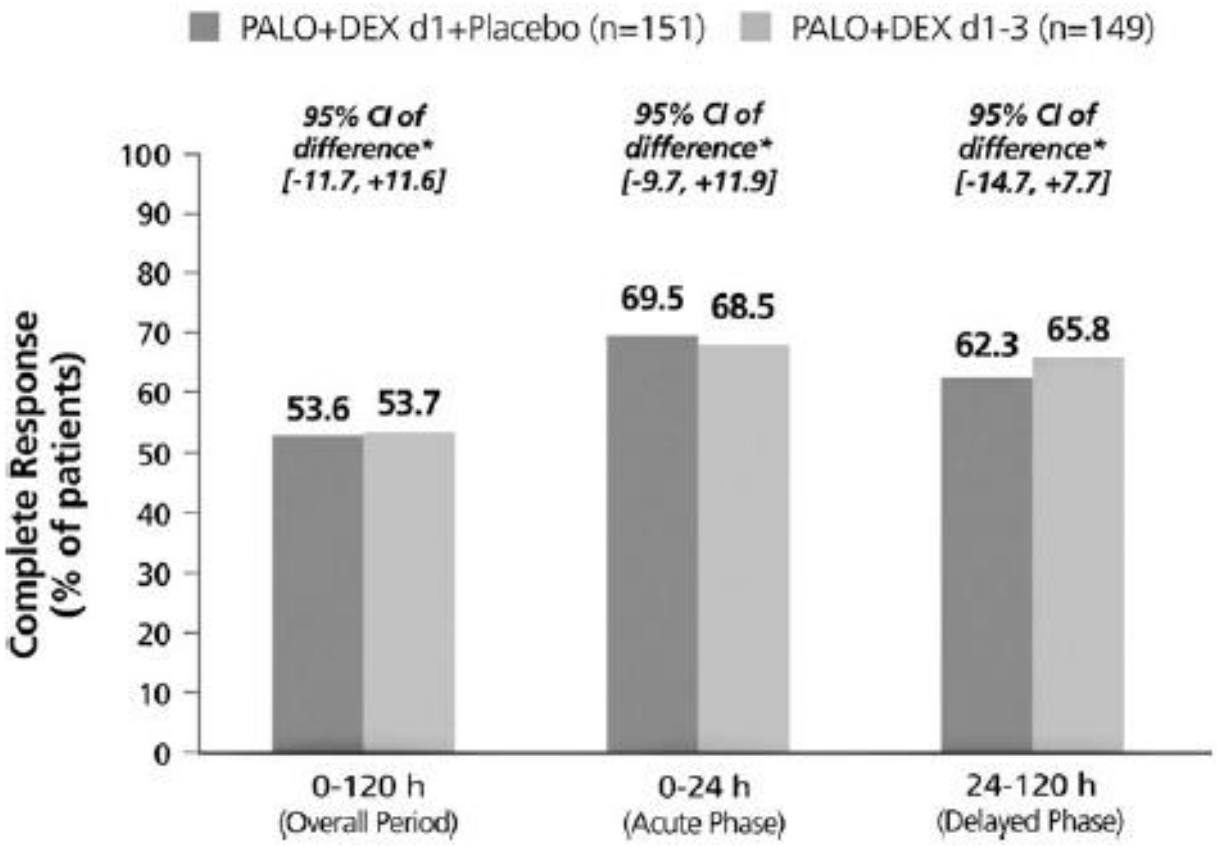
Double-blind, randomised, controlled study of the efficacy and tolerability of palonosetron plus dexamethasone for 1 day with or without dexamethasone on days 2 and 3 in the prevention of nausea and vomiting induced by moderately emetogenic chemotherapy

M. Aapro[1*], A. Fabi[2], F. Nolè[3], M. Medici[3], G. Steger[4], C. Bachmann[5], S. Roncoroni[6] & F. Roila[7]



DEX IN DELAYED EMESIS [AC]

- MBC.
- **ENDPOINT**: 5 DAY CR – Non-inferior ≤ 15%
- No nausea (delayed) favored DEX (62% vs 55%); no diff in FLIE (p=0.64) or side effects



Conclusion: In patients treated with a single injection of palonosetron on day 1, reducing dexamethasone is an option that is not associated with significant reduction in antiemetic control during the 5-day period or an impact on patient functioning.

Annals of Oncology 21: 1083–1088, 2010

Palonosetron in combination with 1-day versus 3-day dexamethasone for prevention of nausea and vomiting following moderately emetogenic chemotherapy: a randomized, multicenter, phase III trial

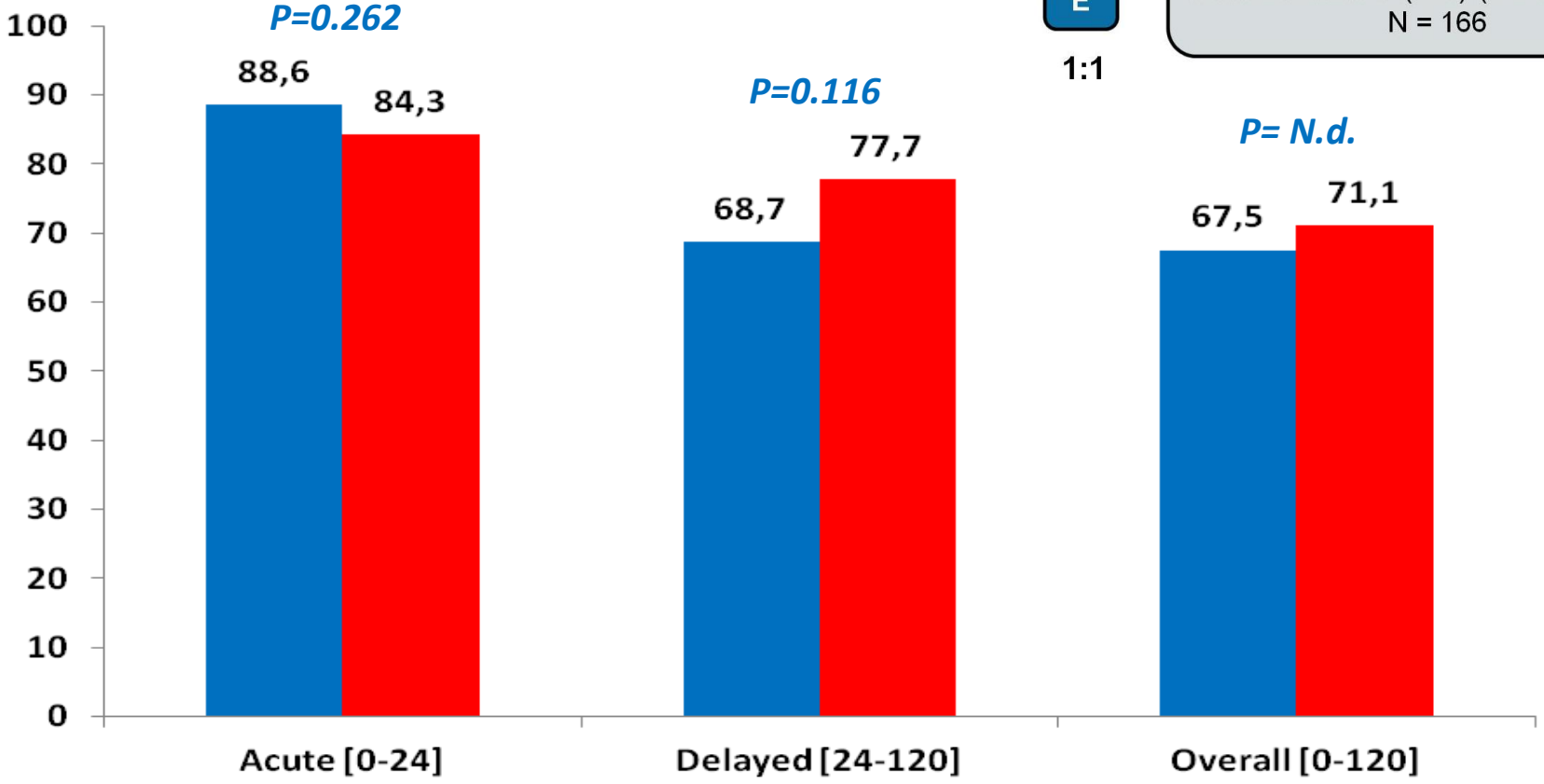
DEX IN DELAYED EMESIS [nonAC/AC]

Chemotherapy-naïve patients scheduled to receive AC- or non-AC-based MEC
N = 334

RANDOMIZE

1:1

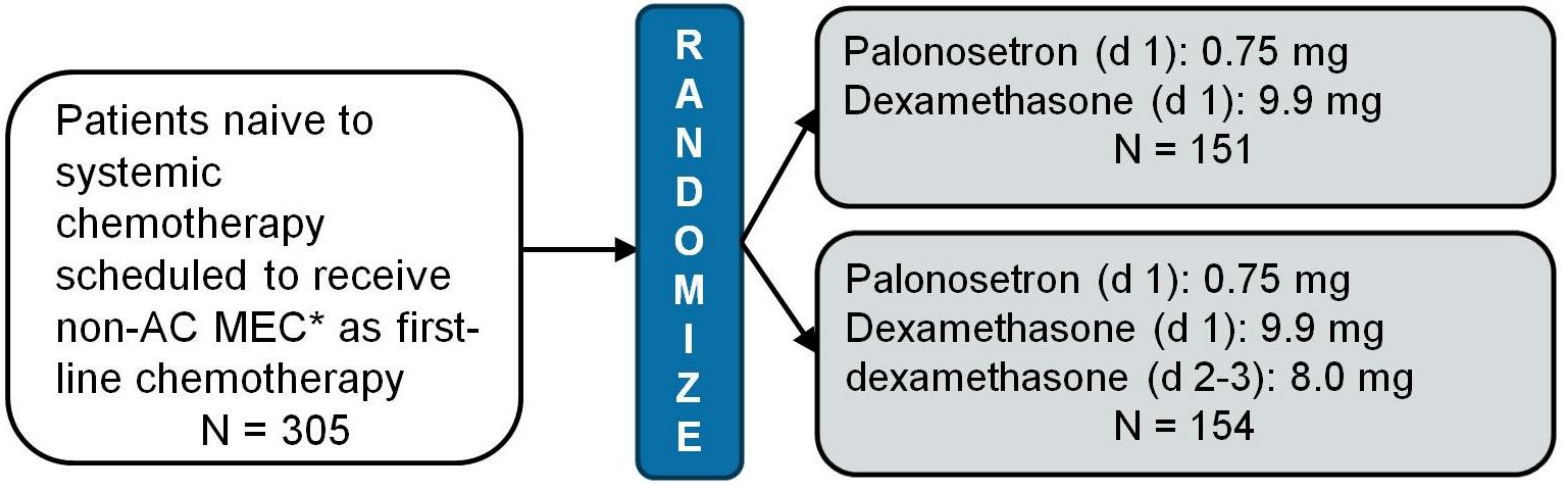
- Palonosetron (IV) (d 1): 0.25 mg
  Dexamethasone (IV) (d 1): 8 mg
  N = 166
- Palonosetron (IV) (d 1): 0.25 mg
  Dexamethasone (IV) (d 1): 8 mg
  Dexamethasone (oral) (d 2-3): 8 mg
  N = 166



Open-label, non inferiority trial (N=332)
Primary endpoint: Complete Response

Support Care Cancer (2011) 19:1217–1225

Steroid Sparing in Non-AC MEC



*72%-73% received oxaliplatin-based chemotherapy

Primary End Point:

- Overall CR† rate (0-120 h)

DEX IN DELAYED EMESIS [nonAC]

	Overall CR, %	Acute CR, %	Delayed CR, %
No DEX (d 2-3)	68.2	95.3	68.9
DEX (d 2-3)	64.7	94.7	66.0

	Overall Complete Control (CC), %	Acute CC, %	Delayed CC, %
No DEX (d 2-3)	66.2	95.3	66.9
DEX (d 2-3)	63.3	94.7	64.7

Sasaki K, et al. ECCO 2013. Abstract 1303

Raftopoulos H, Medscape 2013

Aprepitant Versus Dexamethasone for Preventing Chemotherapy-Induced Delayed Emesis in Patients With Breast Cancer: A Randomized Double-Blind Study

J Clin Oncol 31. © 2013

Fausto Roila, Benedetta Ruggeri, Enzo Ballatori, Albano Del Favero, and Maurizio Tonato

DEX IN DELAYED EMESIS [AC]

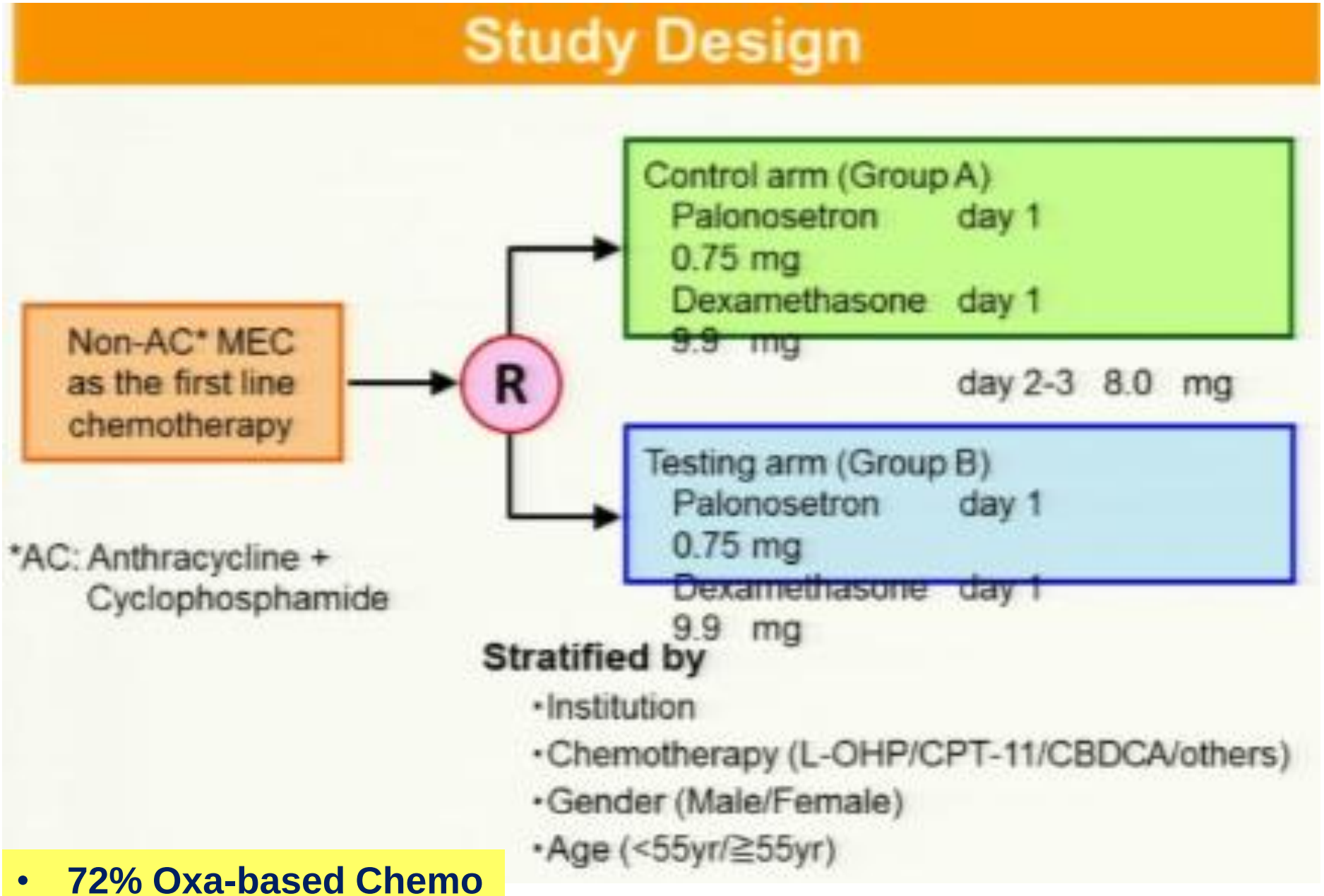
- 580 pts
- **All receiving PALO 0.25, DEX 8, APR day 1**
- **ENDPOINT**: Delayed Emesis, superiority fav. DEX (12%)
- No diff in FLIE (p=0.24); more imsonia/heartburn with DEX

Result	Dexamethasone Arm (n = 273) No.	%	Aprepitant Arm (n = 278) No.	%	*P*
Complete response	217	79.5	221	79.5	1.00
Complete protection	164	60.1	152	54.7	.23
Total control	131	48.0	120	43.2	.27
No vomiting	250	91.6	248	89.2	.39
No nausea	134	49.1	122	43.9	.24
No significant nausea	174	63.7	158	56.8	.10
No. of emetic episodes*					.07
Mean	5.7		9.2		
SD	6.5		9.4		
Maximum severity of nausea†					.26
Mean	42.8		45.5		
SD	25.9		24.1		
Duration of nausea, hours†					.13
Mean	14.1		16.6		
SD	18.4		21.4		

Conclusion

In patients with breast cancer treated with anthracycline plus cyclophosphamide chemotherapy and receiving the same antiemetic prophylaxis for acute emesis, dexamethasone was not superior to aprepitant but instead had similar efficacy and toxicity in preventing delayed emesis.

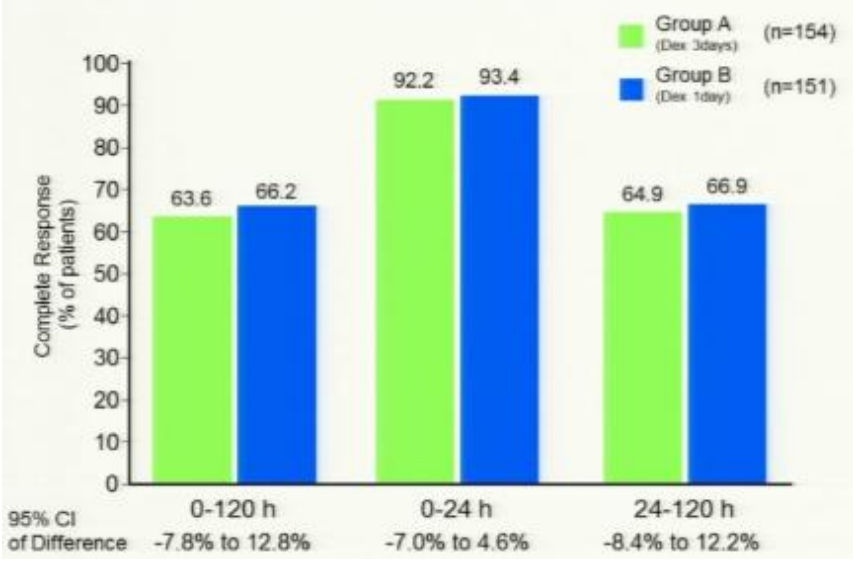
Study Design



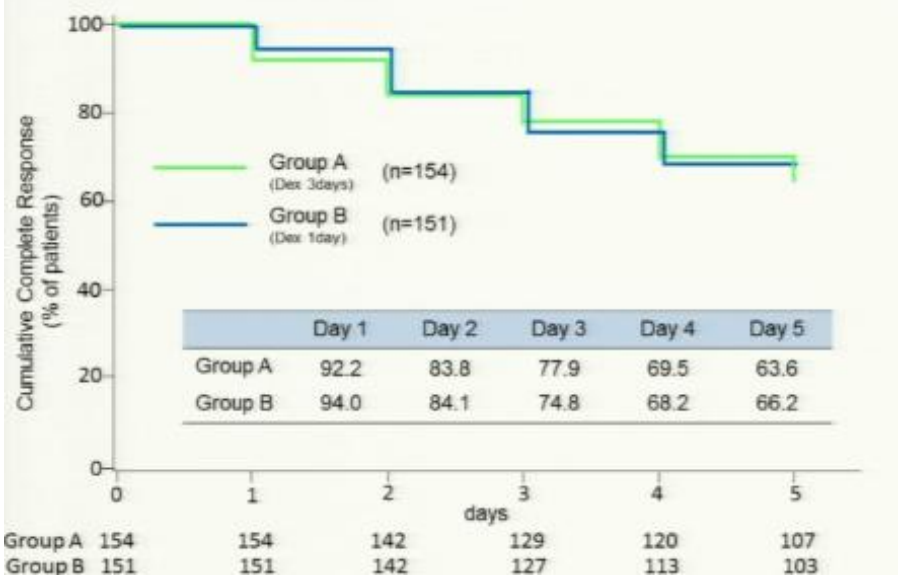
- **72% Oxa-based Chemo**
- **56% Males**

Isobe MASCC 2014

Complete Response Rate



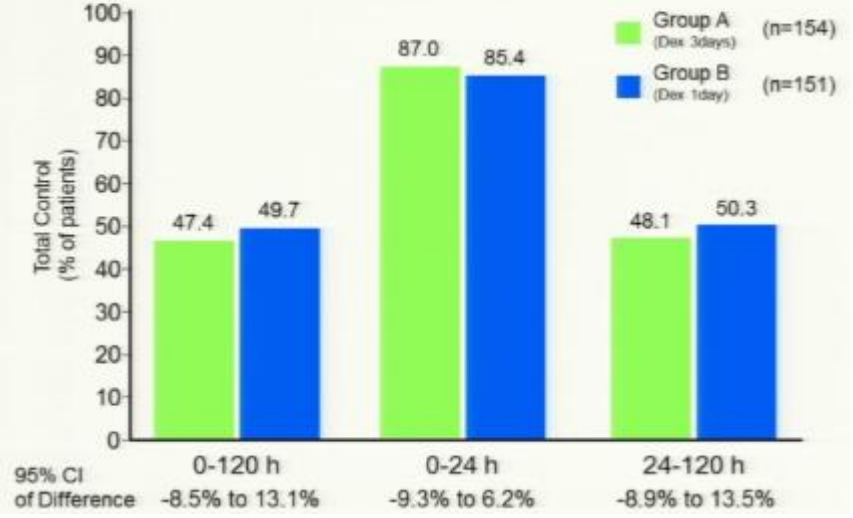
Cumulative Complete Response Rate



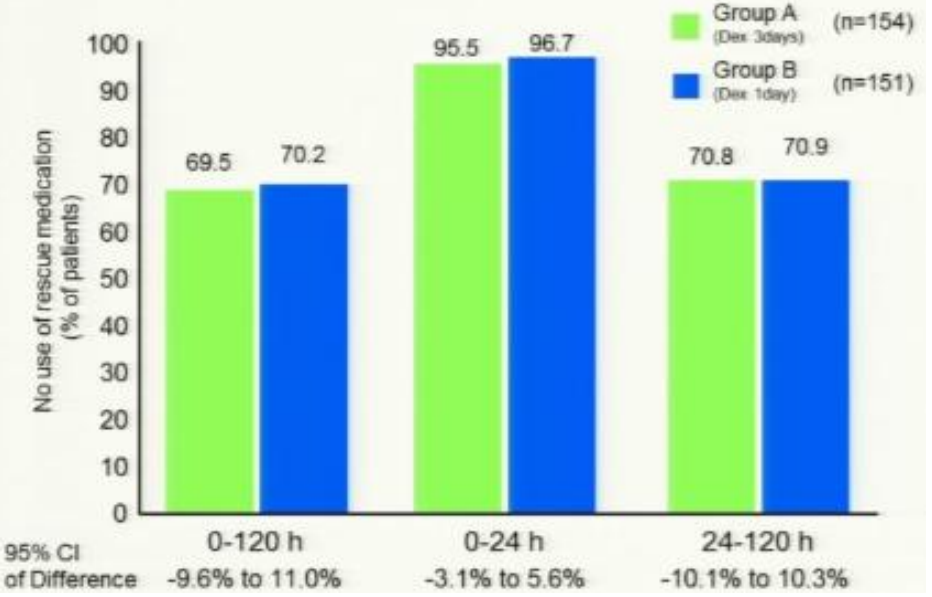
	Day 1	Day 2	Day 3	Day 4	Day 5
Group A	92.2	83.8	77.9	69.5	63.6
Group B	94.0	84.1	74.8	68.2	66.2

Group A	154	154	142	129	120	107
Group B	151	151	142	127	113	103

Total Control Rate



No use of rescue medication rate



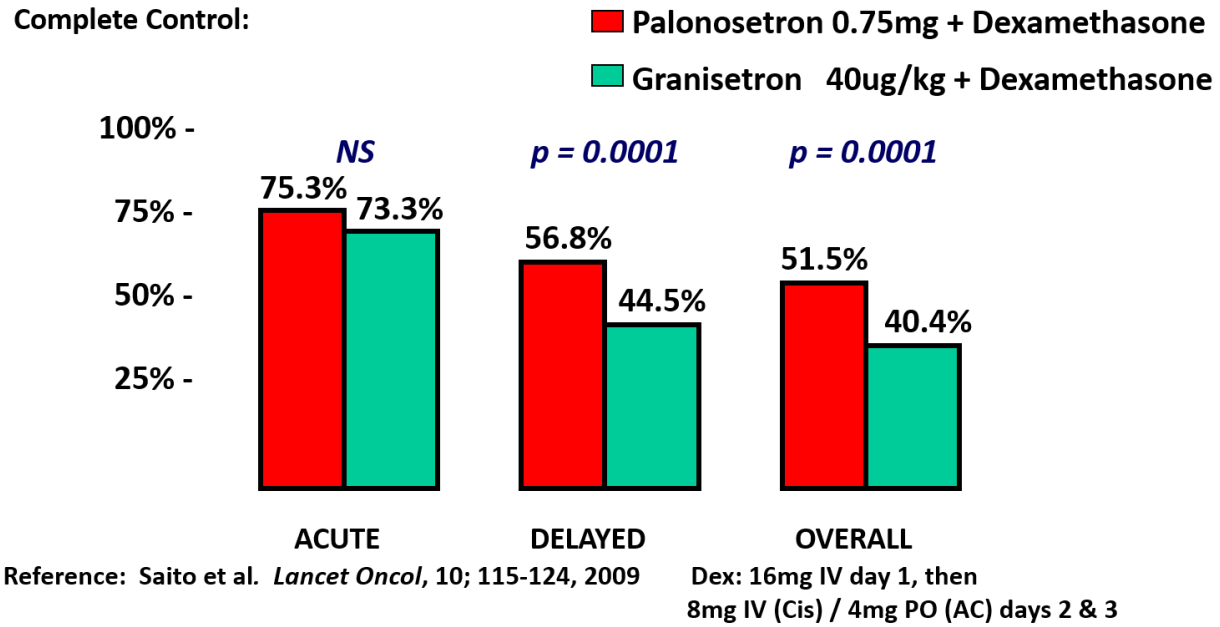
MAJOR ANTIEMETIC CLASSES

- Do we use Agents in these Classes Optimally? -

- Corticosteroids
- **Serotonin Antagonists**
  - Palonosetron
- **NK1 Antagonists**
  - Aprepitant
  - Fosaprepitant

‘New’ backbones from >2010

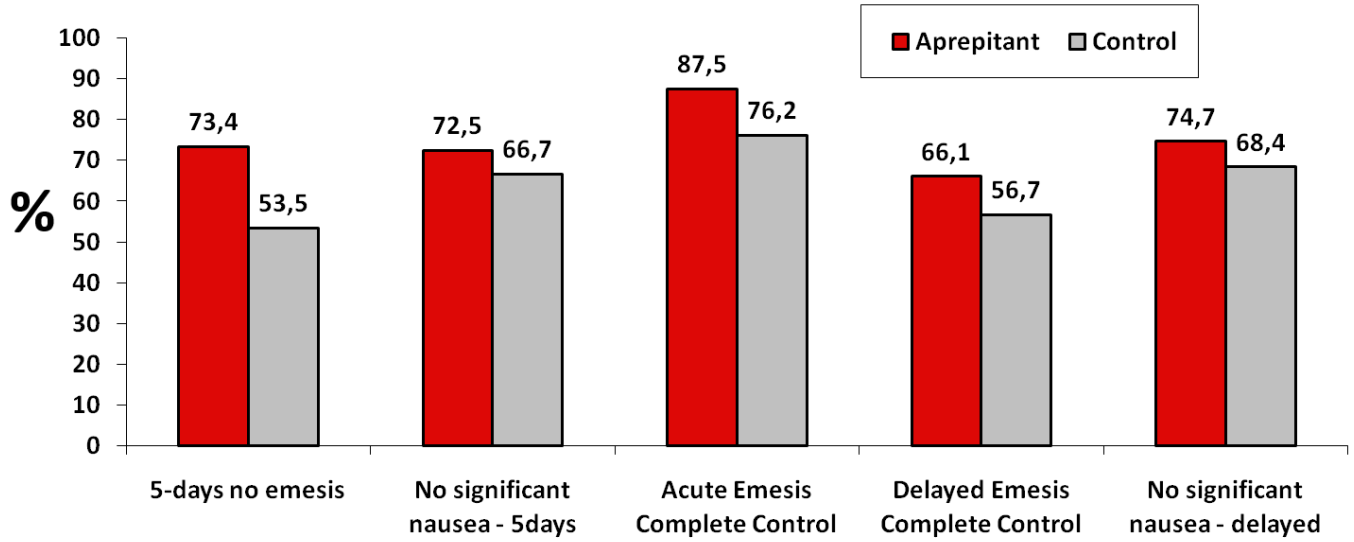
RANDOMIZED-DOUBLE BLIND TRIAL COMPARING:
PALO + DEX *versus* GRANI + DEX in EITHER CISPLATIN OR “AC / EC” (N = 1114)



Reference: Saito et al. *Lancet Oncol*, 10; 115-124, 2009

Dex: 16mg IV day 1, then 8mg IV (Cis) / 4mg PO (AC) days 2 & 3

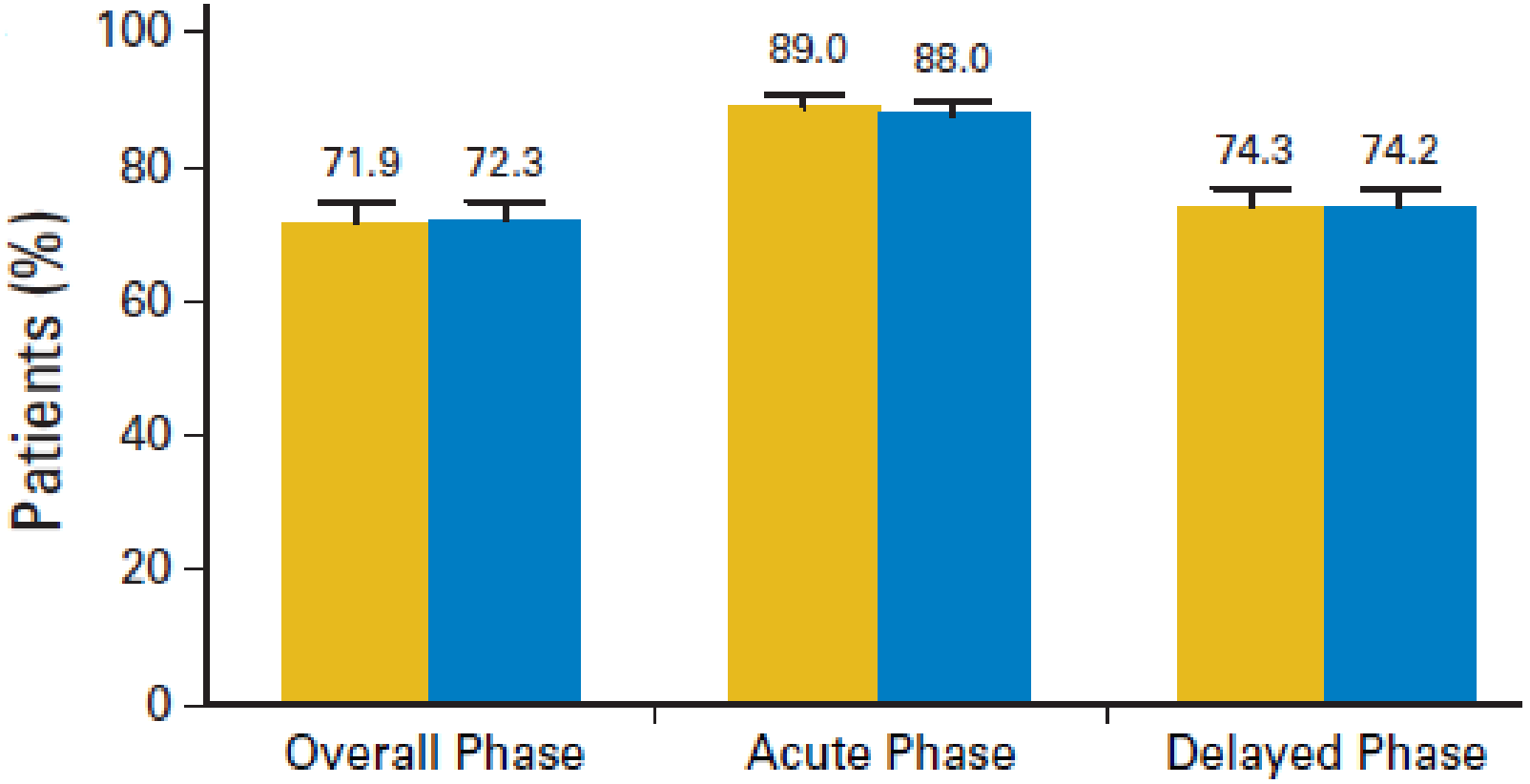
META-ANALYSIS IN 1527 PATIENTS:
The Magnitude of Benefit of adding Aprepitant



Gralla R, Raftopoulos H, Bria E, et al, ASCO 2008

Single-Dose Fosaprepitant for the Prevention of Chemotherapy-Induced Nausea and Vomiting Associated With Cisplatin Therapy: Randomized, Double-Blind Study Protocol—EASE

Steven Grunberg, Daniel Chua, Anish Maru, José Dinis, Suzanne DeVandry, Judith A. Boice, James S. Hardwick, Elizabeth Beckford, Arlene Taylor, Alexandra Carides, Fausto Roila, and Jørn Herrstedt



Randomly allocated
(n = 2,322)

VOLUME 29 · NUMBER 11 · APRIL 10 2011

JOURNAL OF CLINICAL ONCOLOGY

Background

- Moderate emetogenic chemotherapy:
  - Risk of emesis: 30-90%
  - Broad range of chemotherapeutic agents

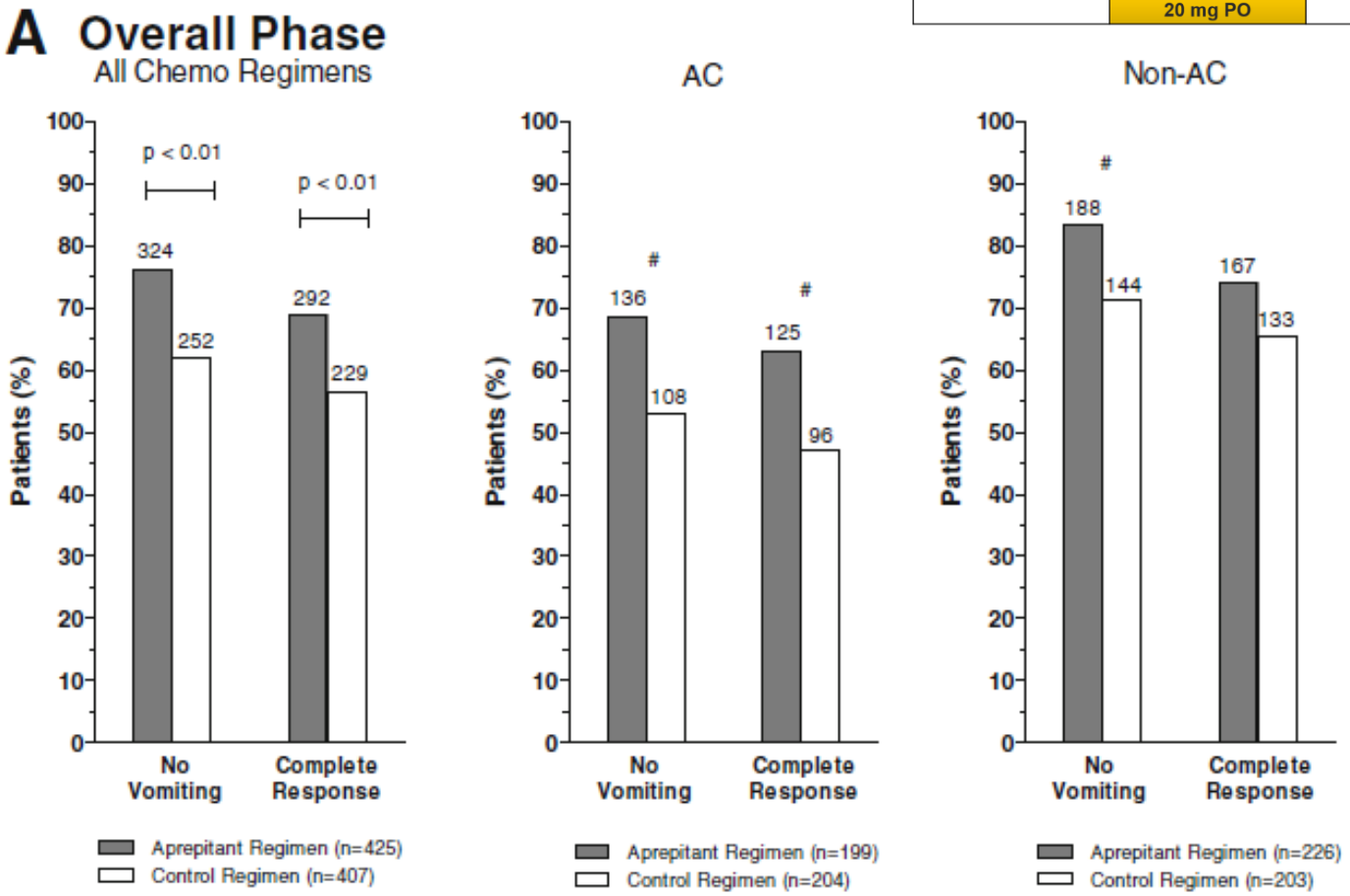
Present state:
To date, there are limited data supporting an NK_1 RA recommendation with other platinum agents such as carboplatin

Jordan MASCC 2014

Aprepitant for the prevention of chemotherapy-induced nausea and vomiting associated with a broad range of moderately emetogenic chemotherapies and tumor types: a randomized, double-blind study

Bernardo L. Rapoport · Karin Jordan · Judith A. Boice · Arlene Taylor · Carole Brown · James S. Hardwick · Alexandra Carides · Timothy Webb · Hans-Joachim Schmoll

	Day 1	Day 2	Day 3
Aprepitant regimen (n=430)	Aprepitant 125 mg PO	← Aprepitant 80 mg PO →	
	Ondansetron 8 mg PO bid		
	Dexamethasone 12 mg PO		
Control regimen (n=418)	Ondansetron 8 mg PO bid	Ondansetron 8 mg PO bid	Ondansetron 8 mg PO bid
	Dexamethasone 20 mg PO		



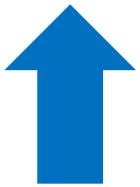
Support Care Cancer (2010) 18:423–431

Recent developments in the prevention of chemotherapy-induced nausea and vomiting (CINV): a comprehensive review

Benefit of 3-drug NK_1RA regimen over 2-drug $5\text{-}HT_3RA$ control in patients receiving Carboplatin

Overall (0–120 h)	APR + 5-HT_3RA + DEX	5-HT_3RA + DEX	Absolute difference
No emesis rate			
Gralla ($N = 192$)[a]	84%	70%	14%
Complete response			
Tanioka ($N = 91$)[b]	62%	52%	10%
Ito ($N = 134$)	80%	67%	14%
Yahata ($N = 324$)[c]	62%	47%	15%

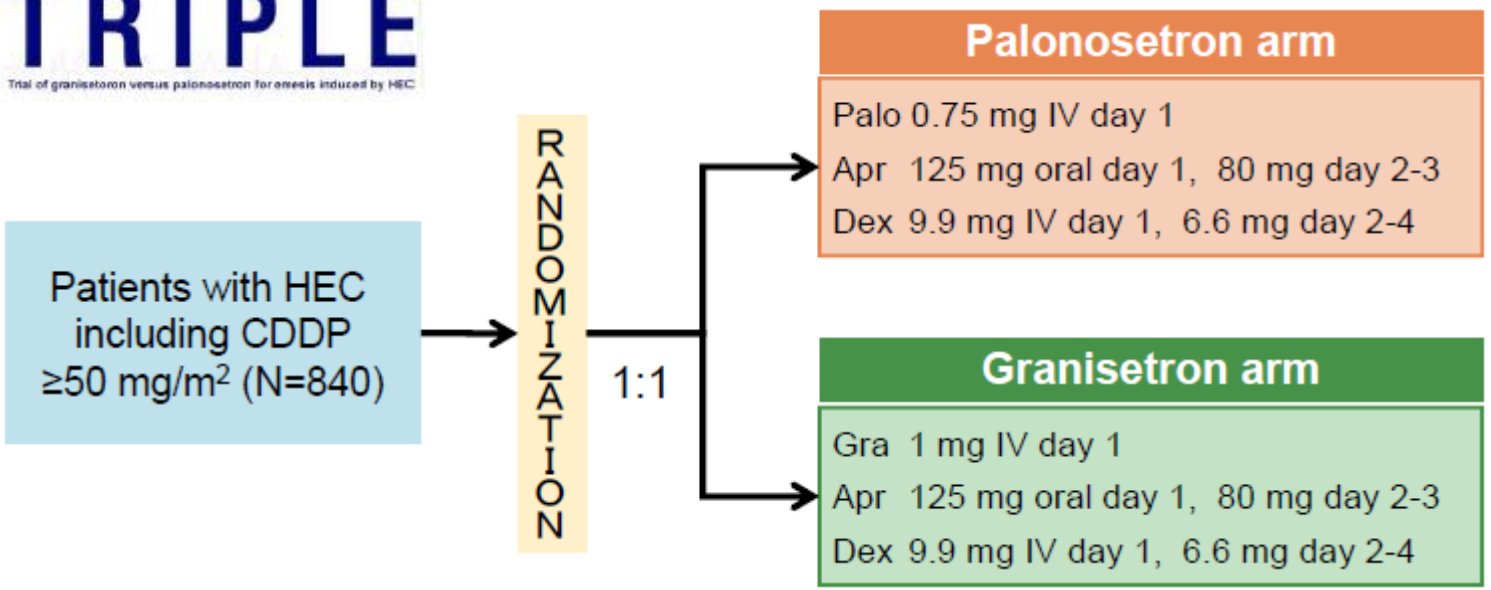
[a]*Post hoc* analysis of the Rapoport study in a subgroup of patients.
[b]Ninety-eight percent of patients received carboplatin-based chemotherapy.
[c]All patients received carboplatin and paclitaxel.
APR, aprepitant; DEX, dexamethasone.



Jordan K, Ann Oncol 2015

TRIPLE

Trial of granisetoron versus palonosetron for emesis induced by HEC



Primary endpoint:

- Complete response at overall (0-120 h) phase

Secondary endpoints:

- Complete response; acute (0-24 h), delayed (24-120 h)
- Complete control
- Total control
- Time to treatment failure
- Safety

Complete response: no emetic episodes and no rescue medication

Complete control: no emetic episodes, no rescue medication, and no nausea or low grade nausea

Total control: no emetic episodes, no rescue medication, and no nausea

Yamanaka et al, MASCC 2013

TRIPLE

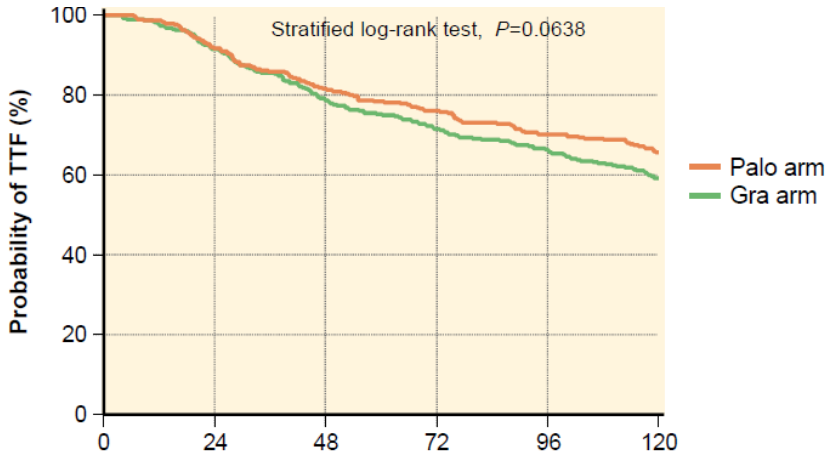
Trial of granisetoron versus palonosetron for emesis induced by HEC

Fuji Pharma Valley

Complete Response

	Palo arm (N=414)	Gra arm (N=413)	Odds ratio (95% CI)	*P*-value
Overall (0-120 h)	65.7%	59.1%	1.35 (0.99-1.82)	0.0539*
Acute (0-24 h)	91.8%	91.8%	1.00 (0.58-1.71)	1.0000
Delayed (24-120 h)	67.2%	59.1%	1.45 (1.07-1.96)	0.0142

* Asymptotic CMH test: *P*=0.0461



	Palo arm (N=415)			Gra arm (N=413)		
	Grade 1	Grade 2	Grade 3	Grade 1	Grade 2	Grade 3
Constipation	28.2%	22.4%	1.7%	30.0%	19.6%	1.5%
Hiccups	7.0%	6.0%	0.7%	5.6%	6.3%	0%
Hyperglycemia	2.9%	1.7%	0%	2.2%	0.7%	0.2%
Hyponatremia	2.2%	0%	0%	1.0%	0%	0.2%
Hypoalbuminemia	1.0%	0.5%	0%	2.2%	0.2%	0%
ALT increased	9.9%	0.5%	0%	9.9%	0.5%	0%
AST increased	2.9%	0%	0%	4.1%	0%	0%

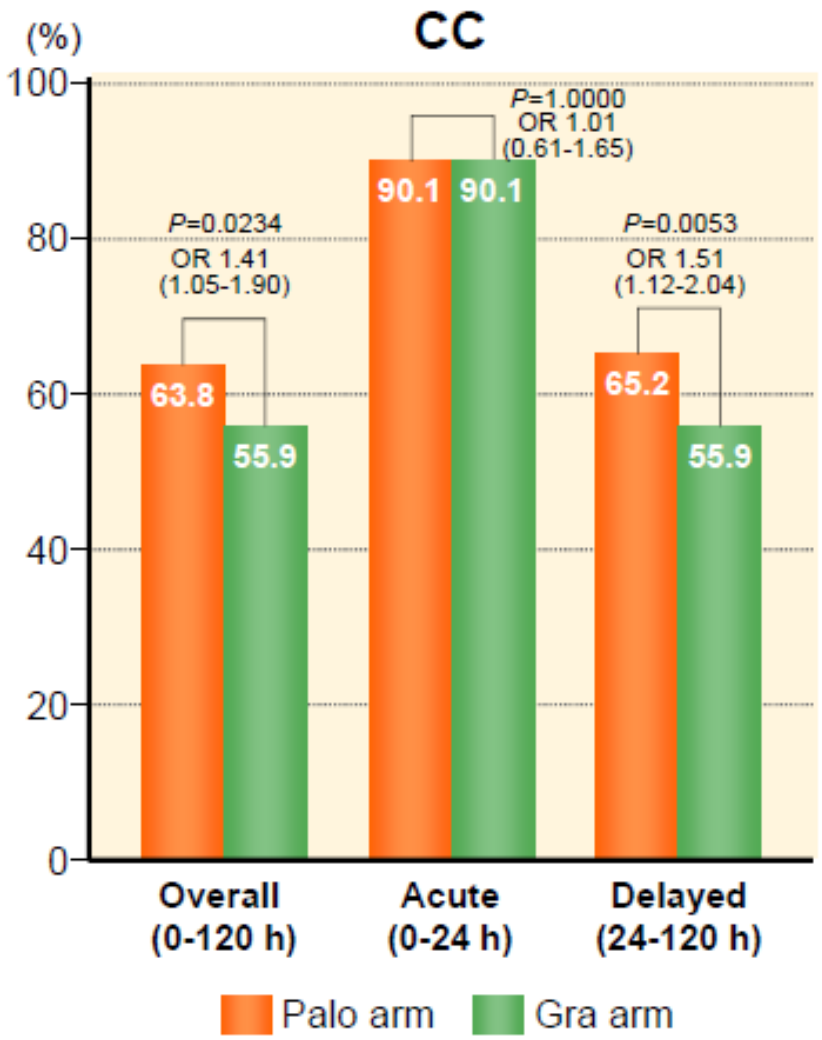
No grade 4 treatment-related adverse events were reported.

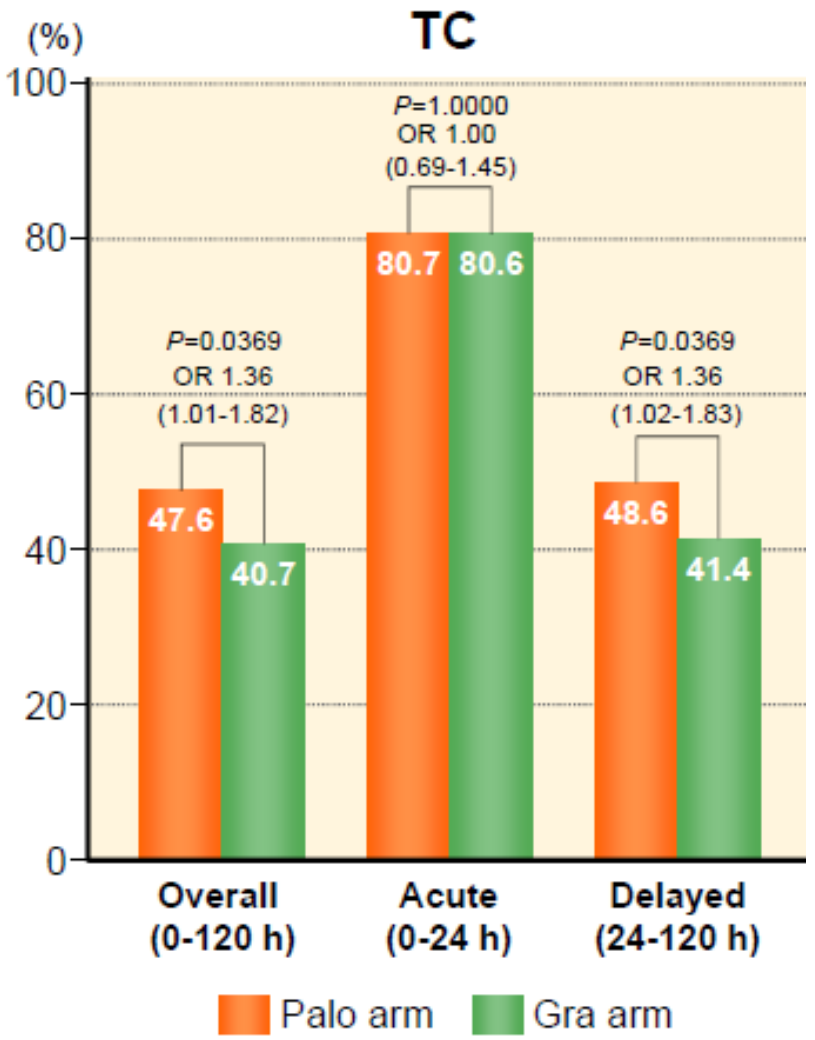
Yamanaka et al, MASCC 2013

TRIPLE

Trial of granisetoron versus palonosetron for emesis induced by HEC

Fuji Pharma Valley





Yamanaka et al, MASCC 2013

Aprepitant versus metoclopramide, both combined with dexamethasone, for the prevention of cisplatin-induced delayed emesis: a randomized, double-blind study

- **Day 2–4: APR 80 mg vs MTC 20 mg 4 times/day [All plus DEX 8 mg bid].**
- **Before Chemo, all patients received PALO i.v. 0.25 + DEX 12 mg + APR 125 mg**

ACUTE

Results	MTC + DEX arm (n = 137)		APR + DEX arm (n = 147)		P
	N	%	N	%	
Complete response[a]	130	94.9	139	94.6	1.00
Complete protection[b]	122	89.1	127	86.4	0.59
Total control[c]	119	86.9	117	79.6	0.12
No vomiting	132	96.4	141	95.9	1.00
No nausea	119	86.9	118	80.3	0.16
No significant nausea	123	89.8	129	87.8	0.71
No. of emetic episodes[d]					
Mean	4.4		2.8		0.14
SD	3.2		2.6		
Maximum severity of nausea[e]					
Mean	43.7		34.0		0.14
SD	21.6		21.7		
Duration of nausea, hours[e]					
Mean	4.2		2.7		0.22
SD	5.3		3.2		

DELAYED

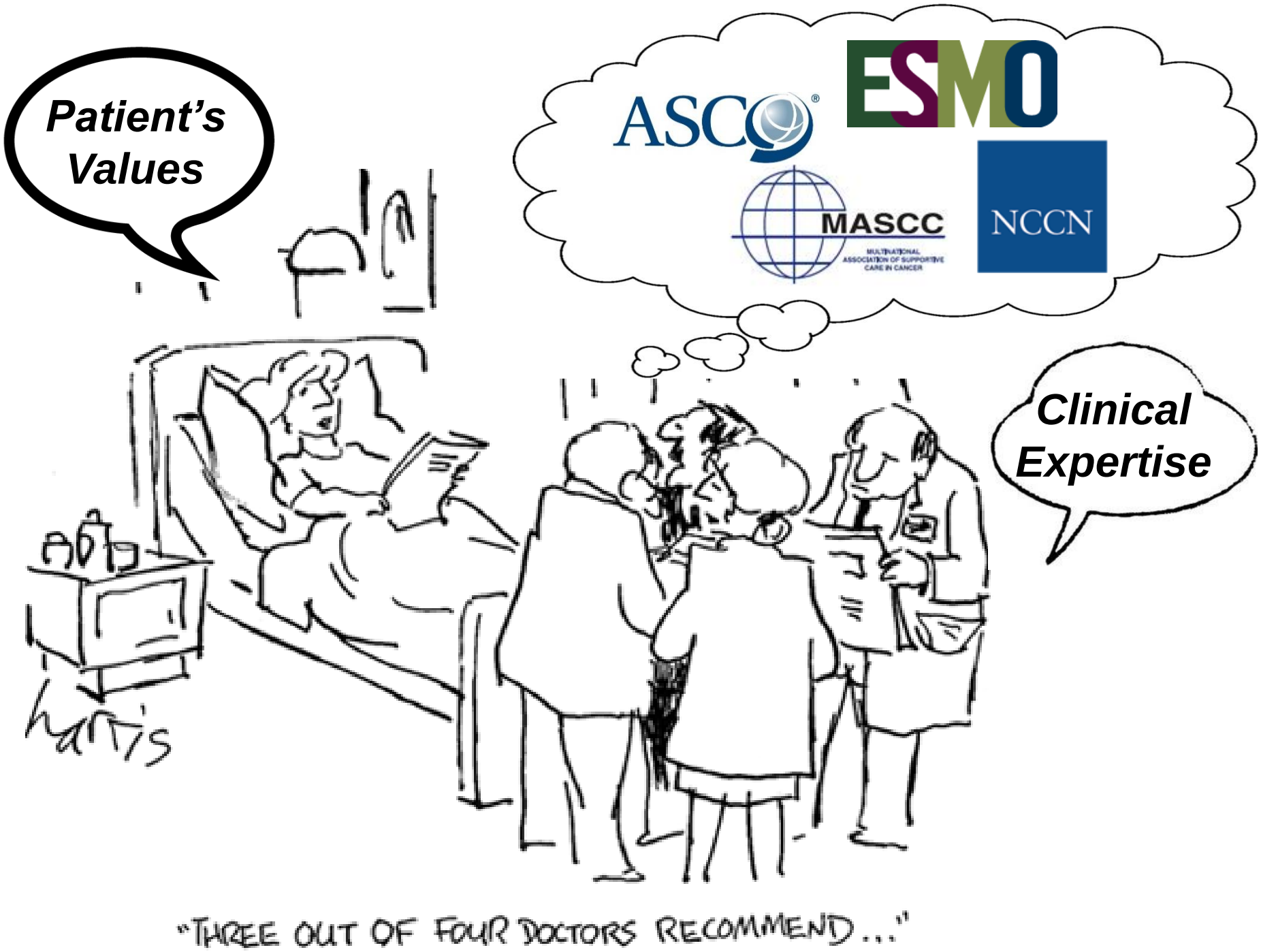
Results	MTC + DEX arm (n = 137)		APR + DEX arm (n = 147)		P
	N	%	N	%	
Complete response[a]	113	82.5	118	80.3	0.38
Complete protection[b]	102	74.5	108	73.5	0.90
Total control[c]	97	70.8	102	69.4	0.90
No vomiting	120	87.6	129	87.8	1.00
No nausea	100	73.0	105	71.4	0.80
No significant nausea	111	81.0	114	77.6	0.56
No. of emetic episodes[d]					
Mean	7.9		8.4		0.67
SD	7.4		11.8		
Maximum severity of nausea[e]					
Mean	44.8		44.9		0.68
SD	25.5		26.2		
Duration of nausea, hours[e]					
Mean	13.5		15.4		0.71
SD	16.5		19.0		

Conclusions: In cancer patients submitted to cisplatin-based chemotherapy, receiving the same antiemetic prophylaxis for acute emesis, A + D is not superior to M + D in preventing delayed emesis, and both treatments present similar toxicity.

Roila F, Ann Oncol 2015

Issues for *CINV*

- Do we reliably measure that?
- Do we use agents optimally?
- Are **guidelines useful** for clinical practice?
- What is new for CINV in 2015?
- Are we missing something?


Patient's Values
ASCO
ESMO
MASCC
MULTINATIONAL ASSOCIATION OF SUPPORTIVE CARE IN CANCER
NCCN
Clinical Expertise
"THREE OUT OF FOUR DOCTORS RECOMMEND..."

Antiemetic Guidelines Groups

	MASCC/ESMO	ASCO	NCCN
Who judges the evidence?	**25 International AE experts - multidisciplinary**	**c. 20 ASCO member AE experts + HSR individuals**	**Small NCCN group**
Who does the major update?	**25 International AE experts – multidisciplinary**	**Subgroup**	**Small NCCN group**
Highly evidence based?	**Yes**	**Yes**	**More Opinion than the others**
Frequently updated?	**Yes**	**No**	**Yes**
Main distribution:	**Print: *Supp Care Cancer* + Other Jnl** **Web: MASCC.org**	**Print: *JCO***	**Print: Pamphlets** **Web: NCCN.org**

Gralla RJ, Medscape 2013

ANTIEMETIC GUIDELINE PROCESS

Matti Aapro, MD
Enzo Ballatori, PhD
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Lawrence Einhorn, MD
Birgitte Espersen, RN
Petra Feyer, MD
Richard Gralla, MD
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Karin Jordan, MD
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Ernesto Maranzano, MD
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Gary Morrow, PhD
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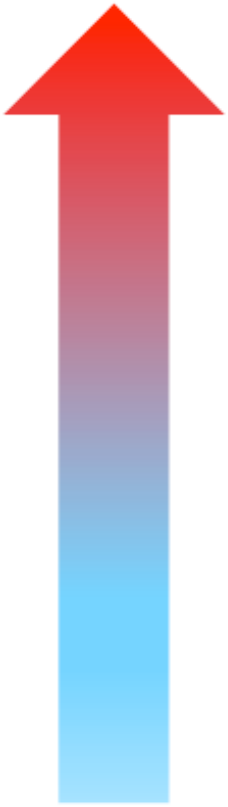
Bernardo Rapoport, MD
Cynthia Rittenberg, RN, MN, AOCN
Fausto Roila, MD
Mitsue Saito, MD
Maurizio Tonato, MD
David Warr, MD

Annals of Oncology 21 (Supplement 5): v232–v243, 2010

Guideline update for MASCC and ESMO in the prevention of chemotherapy- and radiotherapy-induced nausea and vomiting: results of the Perugia consensus conference

EMETOGENIC POTENTIAL of I.V. Agents

- Based on MASCC / ASCO / ESMO Guidelines -



Chemotherapy	Risk	Examples
High	> 90%	Cisplatin, streptozocin, carmustine, dacarbazine
Moderate	30–90%	Carboplatin, cyclophosphamide, doxorubicin, ifosfamide, oxaliplatin, irinotecan, alemtuzumab, azacitidine, bendamustine
Low	10–30%	Etoposide, gemcitabine, 5-FU, docetaxel, paclitaxel, cetuximab, catumaxomab, panitumumab
Minimal	< 10%	Vinca alkaloids, bleomycin, bevacizumab

Basch E et al. J Clin Oncol. 2911; 29:4198-4198 (ASCO Guideline).
Roila, F. et al Ann Oncol. 2010;21:v232–v243.

Courtesy of Jordan J, 2014

- The Process -

What are the criteria for consensus?

- **Degree of consensus required**:
  - 67% or greater agreement among the panelists was required to change a guideline.
- **Basis of evidence to change an existing guideline**:
  - Compelling evidence was required based on well-conducted trials, generally with a comparator felt to be:
    - ***Consistent with guidelines***
    - ***Representing best practice.***
- **Generally at least a 10% difference was considered to be the minimum degree of benefit sufficient for change.**

2013 MASCC/ESMO Antiemetic Guideline Recommendations: Acute Setting

Emetic Risk Group	Antiemetics
High (HEC)	5HT3 + DEX + APR or FOS
Anthracycline + Cyclophosphamide (AC)	5HT3* + DEX + APR or FOS
Moderate (other than AC) (MEC)	PALO + DEX
Low	DEX OR 5HT3 OR DRA
Minimal	No routine prophylaxis

5HT3 = serotonin receptor antagonist

DEX = DEXAMETHASONE

APR = APREPITANT; FOS= FOSAPREPITANT

PALO = PALONOSETRON

DRA = dopamine receptor antagonist

* NOTE: If the NK1 receptor antagonist is not available for AC chemotherapy palonosetron is the preferred 5-HT3 receptor antagonist.

MASCC/ESMO. www.mascc.org.

Gralla RJ, Medscape 2013

2013 MASCC/ESMO Antiemetic Guideline Recommendations: Delayed Setting

Emetic Risk Group	Antiemetics
High (HEC)	DEX* + APR*
Anthracycline + Cyclophosphamide (AC)	APR or none†
Moderate (other than AC) (MEC)	DEX
Low	No routine prophylaxis
Minimal	No routine prophylaxis

DEX = DEXAMETHASONE | APR= APREPITANT

* DEX only if FOSAPREPITANT used on Day 1
† If FOSAPREPITANT used on Day 1

MASCC/ESMO. www.mascc.org.

Gralla RJ, Medscape 2013

2013 MASCC/ESMO Antiemetic Guideline Recommendations:

HEC

a. Hesketh PJ, et al. *J Clin Oncol.* 2003;21:4112-4119; b. Poli-Bigeli S, et al *Cancer.* 2003;97:3090-3098.

AC

Warr DG, et al. *J Clin Oncol.* 2005; 23:2822-2830.

Non-AC MEC

a. Schwartzberg L, et al. *Support Care Cancer.* 2013 Oct 19. [Epub ahead of print]; b. Gralla R, et al. *Ann Oncol.* 2003;14:1570-1577; c. Eisenberg P, et al. *Cancer.* 2003;98:2473-2482; d. Aapro MS, et al. *Ann Oncol.* 2006;17:1441-1449; e. Saito M, et al. *Lancet Oncol.* 2009;10:115-124.

Gralla RJ, Medscape 2013

High Level of Agreement Across 3 Major Antiemesis Guidelines: Similarities and Differences

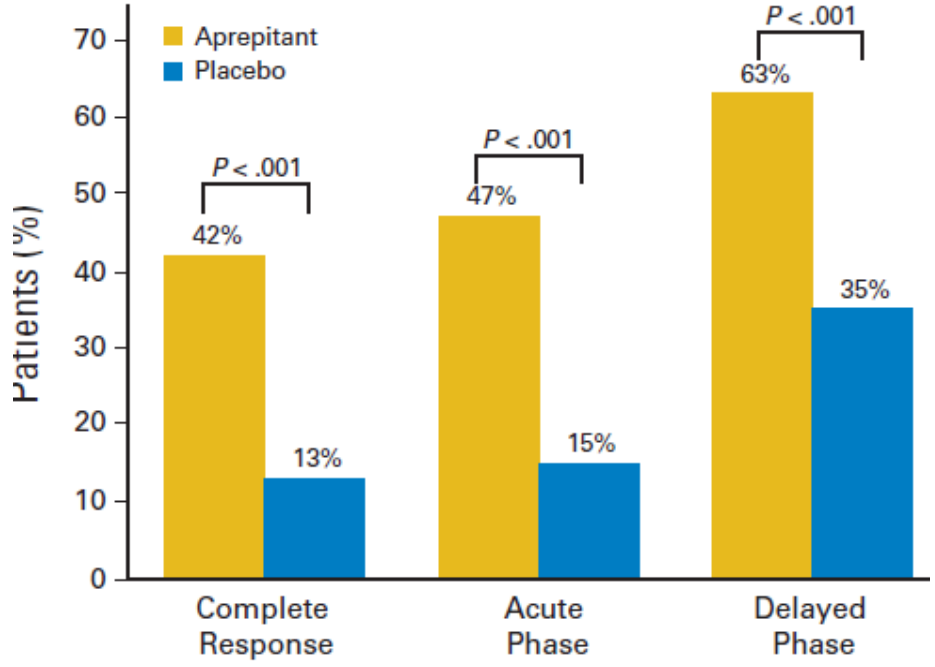
MASCC/ESMO[a], ASCO[b], NCCN[c]	• Triple therapy ($5HT_3$ RA + APR + DEX) are recommended for patients receiving HEC or AC • Oral aprepitant and IV fosaprepitant are considered to be clinically equivalent • PALO is the preferred $5HT_3$ RA in patients receiving MEC
ASCO[b], NCCN[c]	• Classify AC as HEC
NCCN[c,d]	• PALO is the preferred $5HT_3$ RA for patients receiving MEC and HEC

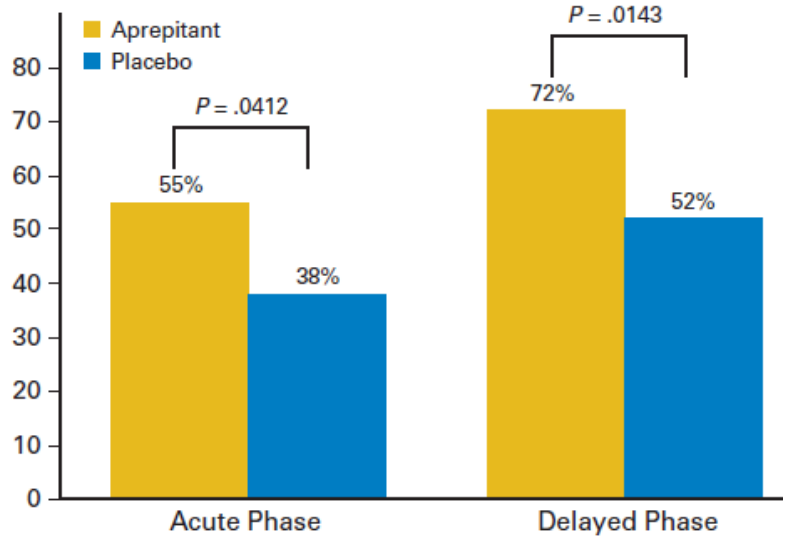
a. MASCC/ESMO. www.mascc.org; b. Basch E, et al. *J Clin Oncol.* 2011;29:4189-4198; c. NCCN. www.nccn.org. d. Saito M, et al. *Lancet Oncol.* 2009;10:115-124.

Gralla RJ, Medscape 2013

Randomized, Double-Blind, Placebo-Controlled, Phase III Cross-Over Study Evaluating the Oral Neurokinin-1 Antagonist Aprepitant in Combination With a 5HT3 Receptor Antagonist and Dexamethasone in Patients With Germ Cell Tumors Receiving 5-Day Cisplatin Combination Chemotherapy Regimens: A Hoosier Oncology Group Study

Days 1-2	Day 3	Days 4-5	Days 6-7	Day 8
Dexamethasone 20 mg + 5HT3-RA	Aprepitant 125 mg + 5HT3-RA	Aprepitant 80 mg + 5HT3-RA	Aprepitant 80 mg + dexamethasone 4 mg twice per day	Dexamethasone 4 mg twice per day
Dexamethasone 20 mg + 5HT3-RA	Placebo + 5HT3-RA	Placebo + 5HT3-RA	Placebo + dexamethasone 8 mg twice per day	Dexamethasone 4 mg twice per day





Albany C et al, JCO 2012

MAJOR ANTIEMETIC CLASSES AND GUIDELINES

- Based on MASCC / ASCO / NCCN / ESMO Guidelines -

CLASS OF AGENT:	CHANGES LIKELY:
Corticosteroids	- Highly Emetic - Moderately Emetic *'Wiser' Use*
Serotonin Antagonists	- Highly Emetic - Moderately Emetic *Increased Palo suggested*
NK_1 Antagonists	- Highly Emetic - Moderately Emetic *'Smarter' NK_1 (APR/Fosa) use*

Modified by Gralla R, ECCO-ESMO 2009

Recent developments in the prevention of chemotherapy-induced nausea and vomiting (CINV): a comprehensive review

Emetic risk category and guideline recommendations for the acute phase

Emetic risk category	Emetic risk	Chemotherapy examples	Recommended antiemetics	MASCC/ESMO	ASCO	NCCN
High	>90%	Cisplatin	NK_1RA	√	√	√
		Carmustine	5-HT_3RA[a]	√	√	√
		Dacarbazine	DEX	√	√	√
AC[b]	85%	Cyclophosphamide	NK_1RA	√	√	√
		Doxorubicin	5-HT_3RA[a]	√	√	√
		Epirbubicin	DEX	√	√	√
Moderate	30%–90%	Carboplatin	NK_1RA	–	[c]	[d]
		Ifosfamide	Palonosetron	√	√	√
		Oxaliplatin	DEX	√	√	√
		Irinotecan				

[c]May consider.

[d]'In select patients where appropriate' (e.g. carboplatin, doxorubicin, epirubicin, ifosfamide, irinotecan, methotrexate).

Jordan K, Ann Oncol 2015

Recent developments in the prevention of chemotherapy-induced nausea and vomiting (CINV): a comprehensive review

Recently approved antitumor agents with:

- **No emetogenicity classification**

No classification by any guideline		Classified only by NCCN	
Afatinib	Obinutuzumab	Ado-trastuzumab emtansine	Pertuzumab
Belinostat	Pembrolizumab	Crizotinib[a]	Pomalidomide
Ceritinib	Ramucirumab	Dabrafenib	Ponatinib
Ibrutinib	Siltuximab	Ofatumumab	Sorafenib
Idelalisib		Paclitaxel albumin	Trametinib

Jordan K, Ann Oncol 2015

Do Guidelines Improve Emetic Control?
- Adherence to Guidelines -

- **Adherence to (MASCC) guidelines significantly improves CINV control**
- **Utilization effects of adopting MASCC guidelines:**
  - Marked ***decrease of 5-HT3*** in the delayed emesis period
  - ***Increased*** use of ***corticosteroids***
  - ***Increased*** use of ***aprepitant***
  - *Estimated* ***equal*** or ***decreased total costs***

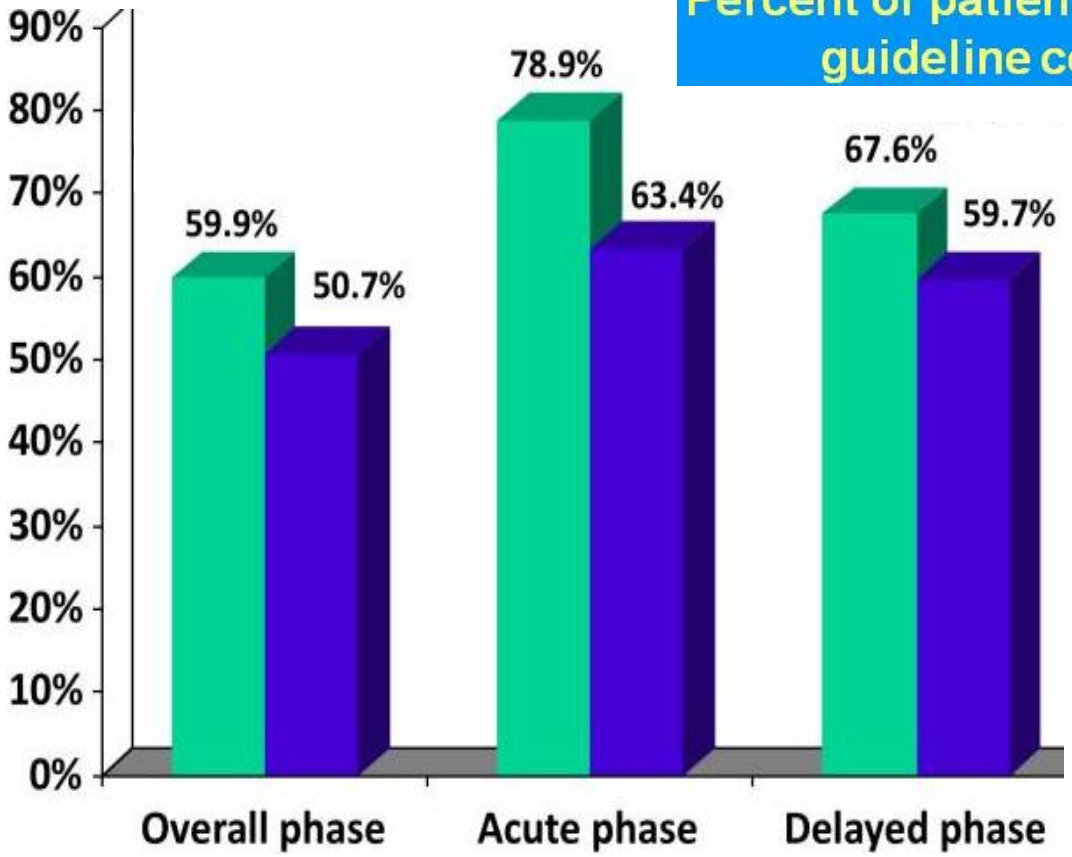
PEER Investigators, Ann Oncol 2012
INSPIRE Investigators, J Oncol Practice 2013
Molassotis et al, JPSM 2013
O'Kane et al. Proc. MASCC 2009
De Moor et al. Proc. ASCO 2013

The effect of guideline-consistent antiemetic therapy on chemotherapy-induced nausea and vomiting (CINV): the Pan European Emesis Registry (PEER)

M. Aapro[1*], A. Molassiotis[2], M. Dicato[3], I. Peláez[4], Á. Rodríguez-Lescure[5], D. Pastorelli[6], L. Ma[7], T. Burke[7], A. Gu[7], P. Gascon[8] & F. Roila[9]; on behalf of the PEER investigators

Chemotherapy	Acute phase (day 1) GCCP	Delayed phase (days 2–4) GCCP
HEC	Corticosteroid + NK1-RA + 5HT3-RA[a]	Corticosteroid days 2–4 + NK1-RA days 2–3
Female AC	Corticosteroid + NK1-RA + 5HT3-RA[a]	Corticosteroid +/or NK1-RA days 2–3[c]
MEC	Corticosteroid + 5HT3-RA[a,b]	Corticosteroid +/or 5HT3-RA days 2–3[c]

Percent of patients with Complete Response among guideline consistency groups, by phase

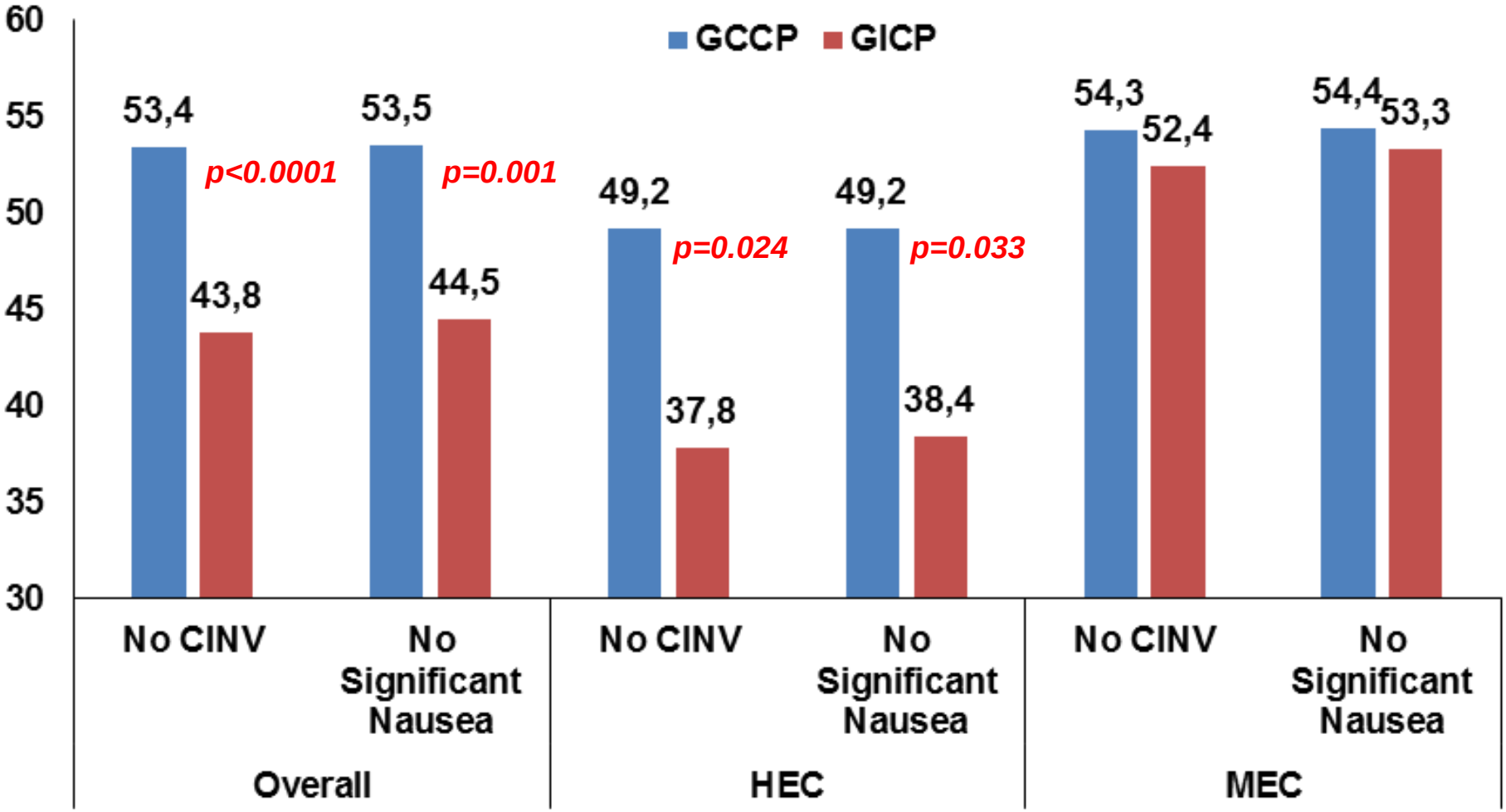


Annals of Oncology
doi:10.1093/annonc/mds021

Antiemetic Guideline Consistency and Incidence of Chemotherapy-Induced Nausea and Vomiting in US Community Oncology Practice: INSPIRE Study

By James W. Gilmore, PharmD, Nancy W. Peacock, MD, Anna Gu, MD, PhD, Stephen Szabo, MD, Melissa Rammage, PharmD, MS, Joyce Sharpe, RN, OCN, Sally T. Haislip, RPh, Toni Perry, RN, Tim L. Boozan, RN, Katherine Meador, RN, Xiting Cao, PhD, and Thomas A. Burke, PharmD, PhD

N (pts) = 1,295



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Evaluation of Risk Factors Predicting Chemotherapy-Related Nausea and Vomiting: Results From a European Prospective Observational Study

Alexander Molassiotis, RN, PhD, Matti Aapro, MD, Mario Dicato, MD, FRCP, Pere Gascon, MD, PhD, Sylvia A. Novoa, MD, Nicolas Isambert, MD, Thomas A. Burke, PhD, Anna Gu, MD, PhD, and Fausto Roila, MD

N (pts) = 991

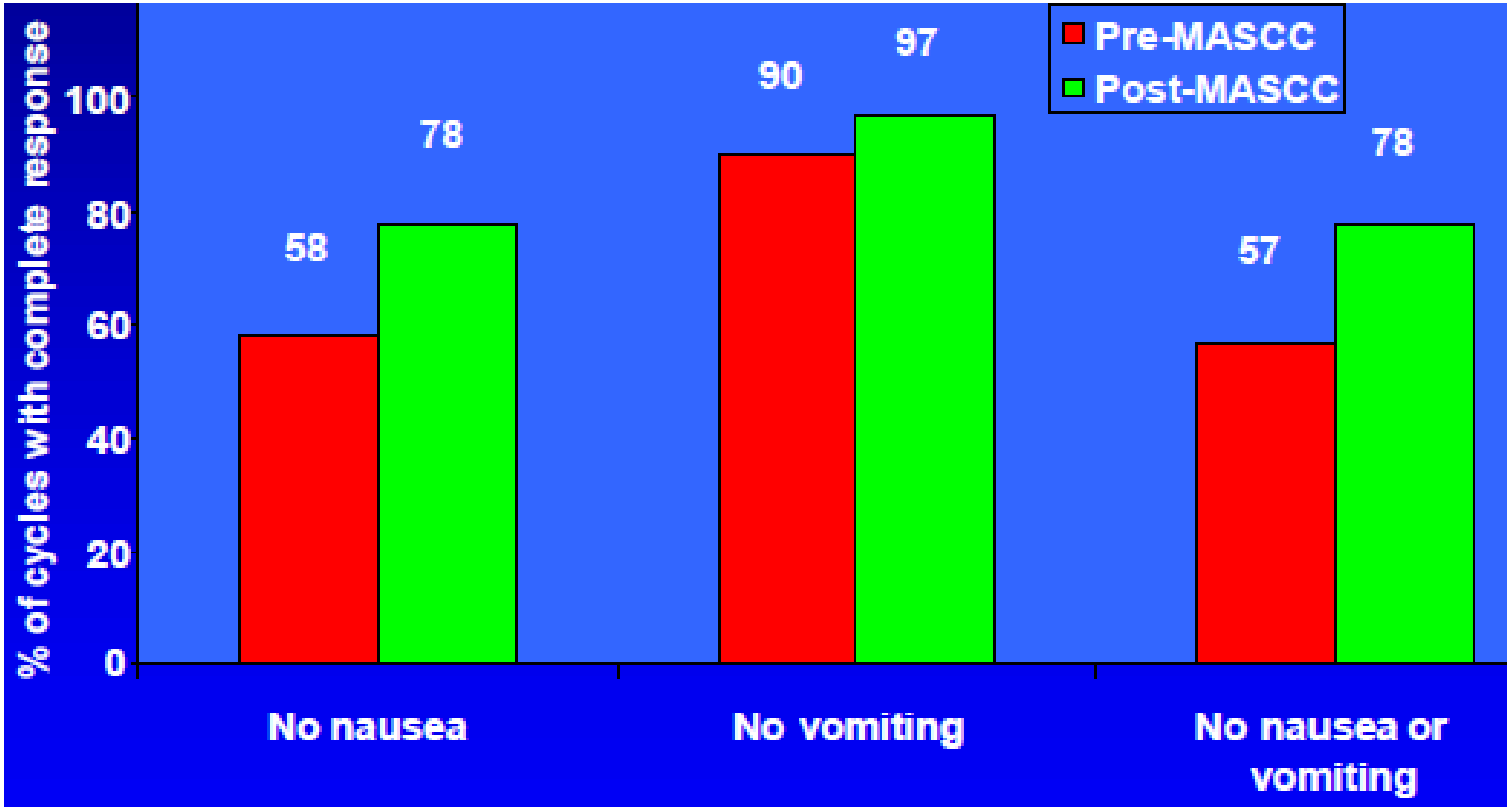
	OR (95% CI)	*P-value*
Guidelines Consistency	**1.56 (1.09-2.24)**	***<0.0001***
Age		
<50	0.40 (0.25-0.64)	*<0.0001*
50-64	0.54 (0.36-0.81)	*0.0029*
Sex	0.65 (0.42-0.98)	*0.0409*
Previous N/V	0.51 (0.34-0.76)	*0.0164*
Pre-chemo anxiety (>50)	0.37 (0.20-0.68)	*0.0015*
CR 1° course	6.63 (4.80-9.17)	*<0.0001*

Overall Phase, N (pts) = 517

Do Guidelines Improve Emetic Control?

COMPLETE CONTROL OF NAUSEA AND VOMITING

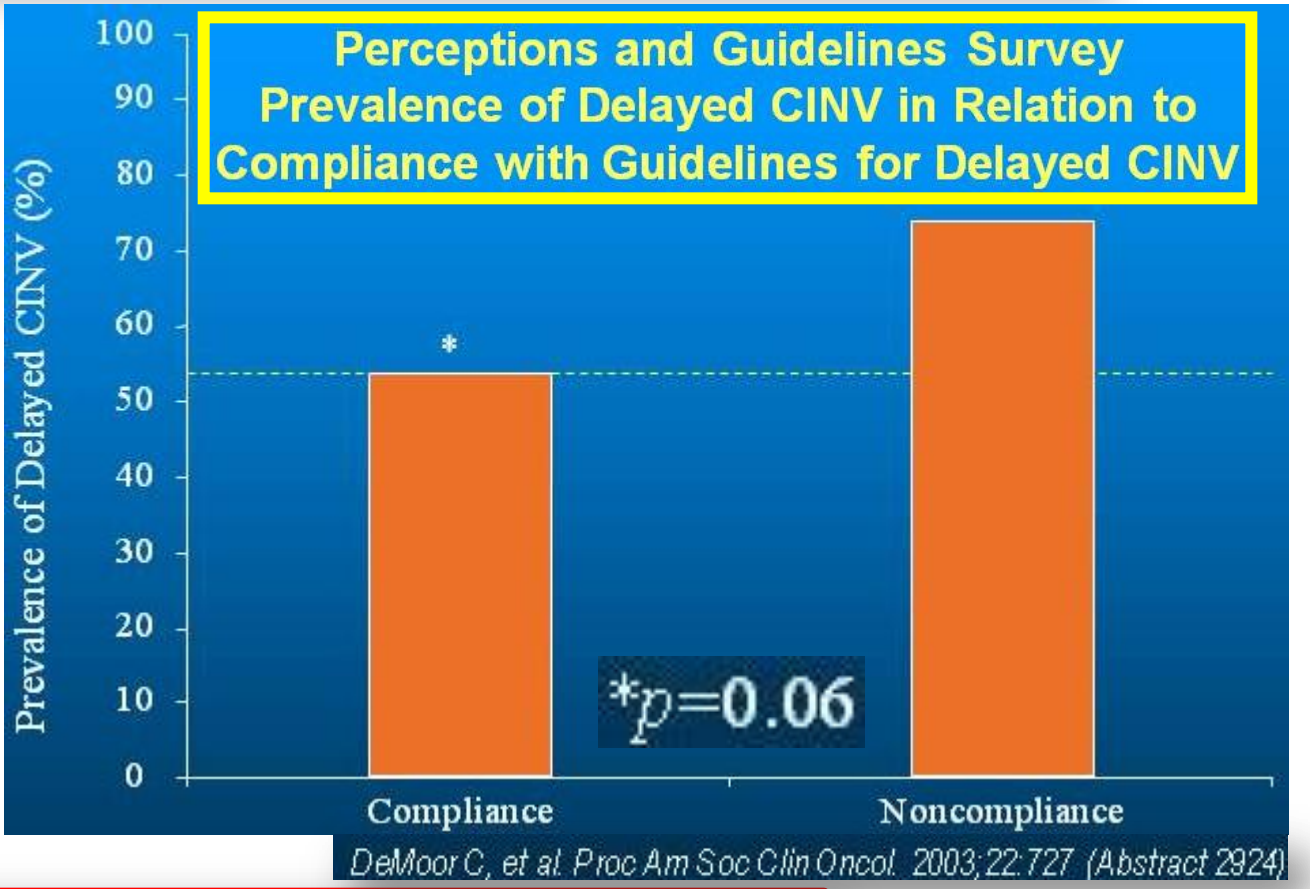
	BEFORE MASCC GUIDELINES (n = 100)	*AFTER* MASCC GUIDELINES (n = 100)
DDP	**54%** (95% CI 44-63)	**81%** (95% CI 73-88)
L-OHP	**53%** (95% CI 43-62)	**83%** (95% CI 75-90)



Modified - O'Kane et al. Proc MASCC 2009

WHAT SHOULD BE THE IMPACT OF GUIDELINES?

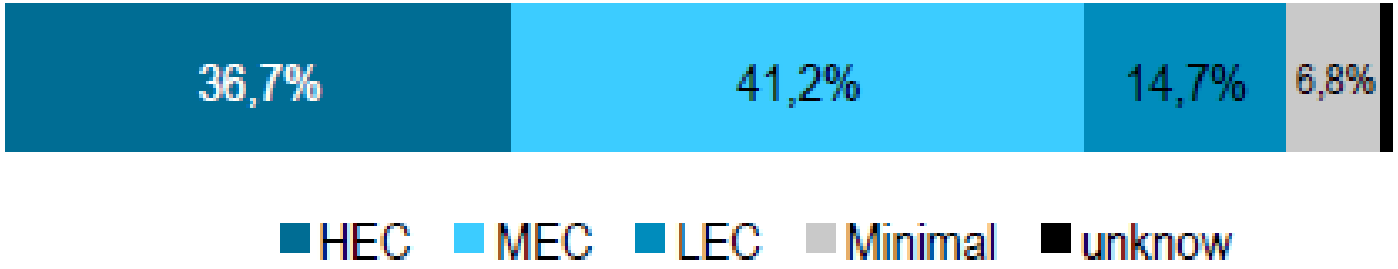
ASCO Annual '12 Meeting



Treatment per MASCC guideline increases control of N/V compared to control regimens used in studies by about 10%

Aapro M, Educational ASCO 2012

Adherence to Guidelines remains Suboptimal



Main charateristics of patients treated with chemotherapies and receiving antiemetics

	HEC Pts.
NSCLC	1,795 (22.1%)
Breast	1402 (17.3%)
SCLC	722 (8.9%)
Total	8116 (100%)
Pt-based	5,731 (70.6%)
NK-1 use	2035 (25.1%)

	MEC Pts.
CRC	2,732 (30.0%)
NHL	2,179 (23.9%)
Breast	548 (6.0%)
Total	9,115 (100%)
AC-based	1,749 (19.2%)
NK-1 use	491 (5.4%)

	LEC Pts.
MM	987 (20.8%)
Pancreas	834 (17.5%)
Breast	602 (12.7%)
Total	4,756 (100%)
Tx-based	945 (19.9%)
NK-1 use	63 (1.3%)

Ref.: Adapted from Ricarte C, Anger C – 38th ECC 2013; P099

Avoidable Hospitalisations

A retrospective study of 154 patients with GI malignancies

Table 2. Reasons for Hospital Admissions

Reason	Hospitalizations							
	All		Potentially Avoidable					
			Yes		No			
	No.	%	No.	%	No.	%	OR*	95% CI
No. of hospitalizations	201	100	39	19	162	81		
Categorical reason for hospitalization								
Treatment complication/adverse effect	57	28	9	23	48	30	Reference	
Cancer symptom	107	53	25	64	82	51	1.8	0.7 to 4.9
Noncancer medical condition	19	9	3	8	16	10	1.1	0.2 to 5.8
Planned hospitalization	18	9	2	5	16	10	0.4	0.0 to 3.8
Symptomatic reason for hospitalization†								
Fever/infection	54	27	12	31	42	26	1.1	0.3 to 3.2
Abdominal pain, undifferentiated	25	12	2	5	23	14	0.3	0.1 to 1.4
GI tract obstruction	19	9	3	8	16	10	0.5	0.0 to 5.1
Asthenia/dehydration	17	8	5	13	12	7	2.0	0.6 to 7.0
Ablation procedure	15	7	2	5	13	8	0.4	0.1 to 3.0
Nausea/vomiting	15	7	3	8	12	7	1.0	0.2 to 6.0
Other‡	56	28	12	31	44	27	1.9	0.8 to 4.8

Abbreviation: OR, odds ratio.
*ORs adjusted for clustering by patient (154 unique patients).
†For each row under the subheading, the reference level is patients without the listed characteristic.
‡Other symptomatic reasons for hospitalization representing less than 5% of admissions included biliary obstruction (eight hospitalizations), neurologic complaints (seven), thrombosis (seven), diarrhea (six), dyspnea (six), cardiovascular complaints (five), bleeding (four), renal failure (three), and miscellaneous complaints (10).

Nausea and vomiting acounted for 7% of the hospitalisations

Brooks GA, et al. J Clin Oncol. 2014;32(6):496-503.

Courtesy of Jordan J, 2014

Barriers to Physician Adherence

1. **Knowledge**
   - Lack of awareness of, and familiarity with, the guideline
2. **Attitudes**
   - Disagreement with evidence-based medicine and specific guidelines
   - Lack of belief in guideline efficiency and ability to comply with guideline recommendations
3. **Behaviour**
   - Patient preferences
     - Patients try to limit their number of medications

Cabana M, et al. JAMA. 1999;282:1458-1465.

Courtesy of Jordan J, 2014

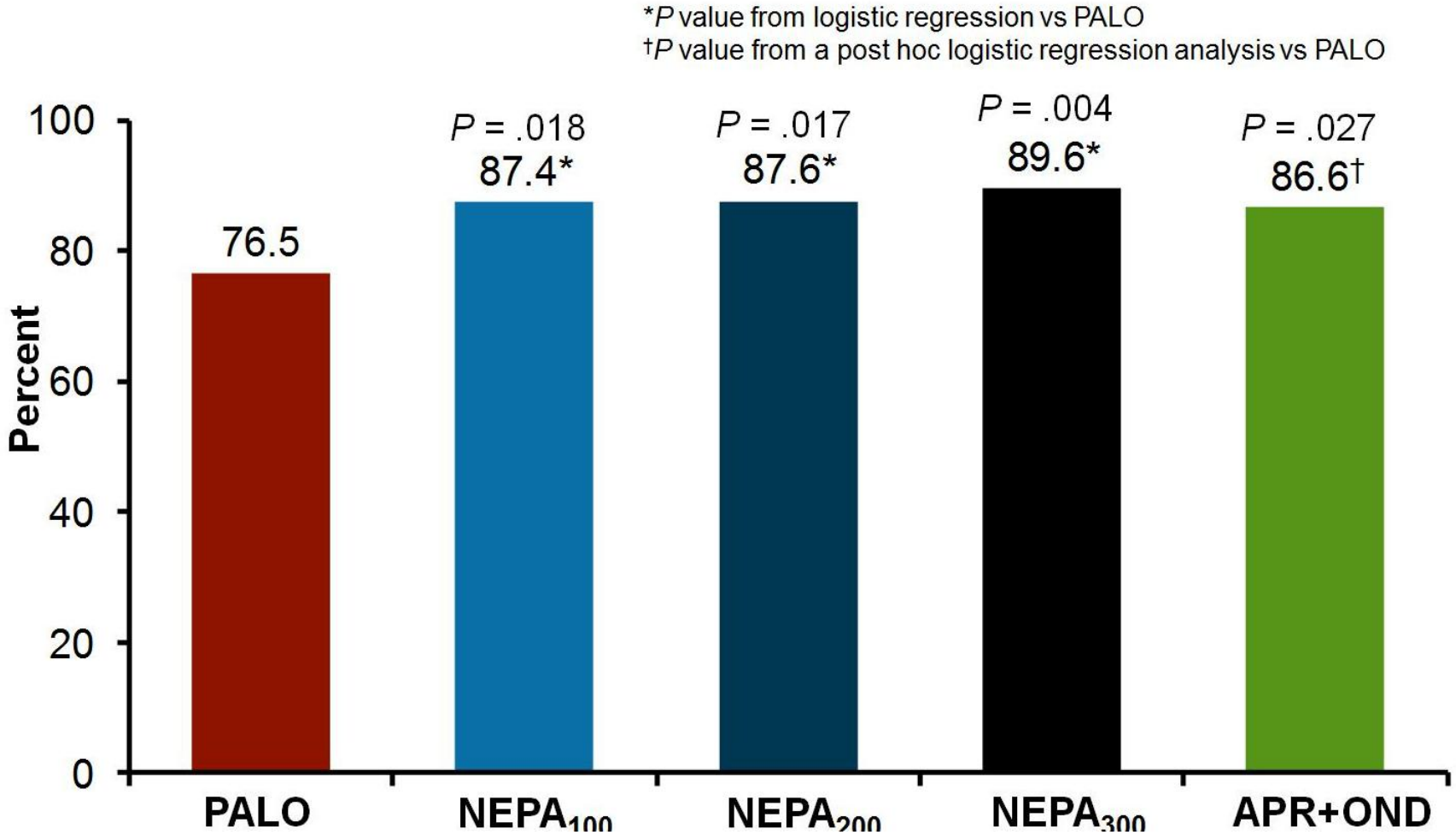
Issues for *CINV*

- Do we reliably measure that?
- Do we use agents optimally?
- Are guidelines useful for clinical practice?
- What is **new** for CINV in 2015?
- Are we missing something?

NEPA: Phase 2 Netupitant Dose-finding Study

Overall CR Rates

HEC



Hesketh P, Annals of Oncology 2014

Oral NEPA + Oral DEX vs Oral Palonosetron + Oral DEX in AC-based MEC

Multinational, Randomized, Double-blind Phase 3 Study

AC

Chemotherapy-naive patients scheduled to receive AC-based MEC
N = 1455

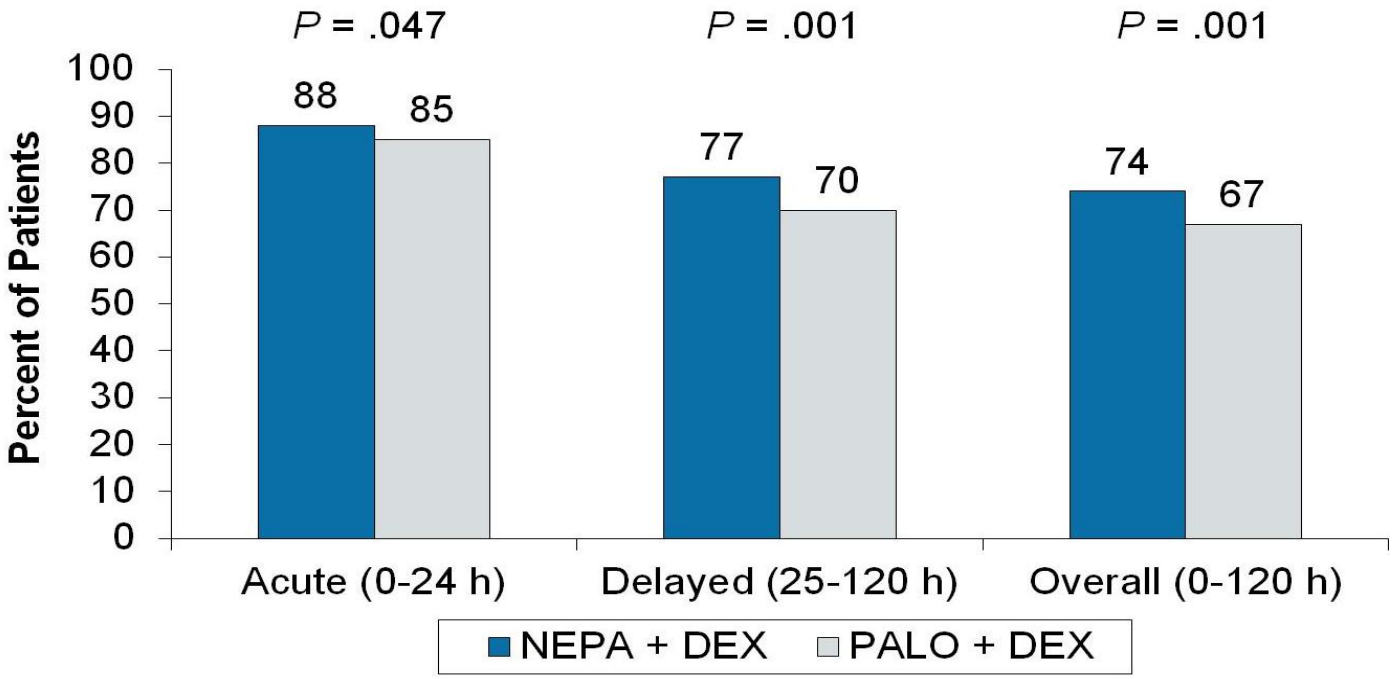
RANDOMIZE

1:1

- Oral NEPA (netupitant 300 mg + oral palonosetron 0.50 mg) + oral dexamethasone 12 mg -- d 1 only
  N = 724
- Oral palonosetron 0.50 mg + oral dexamethasone 20 mg -- d 1 only
  N = 725

Primary End Point:

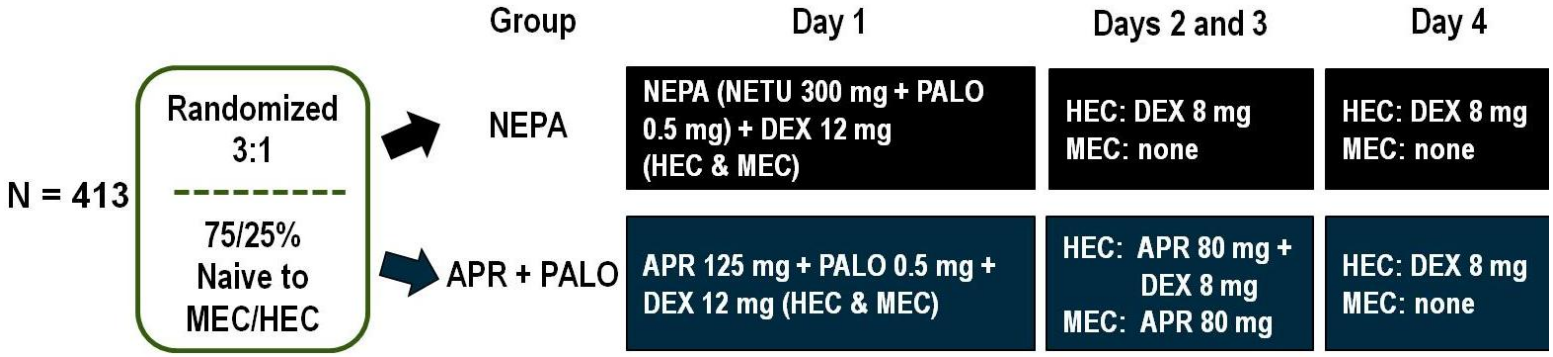
- CR rate (delayed period; 25-120 h)

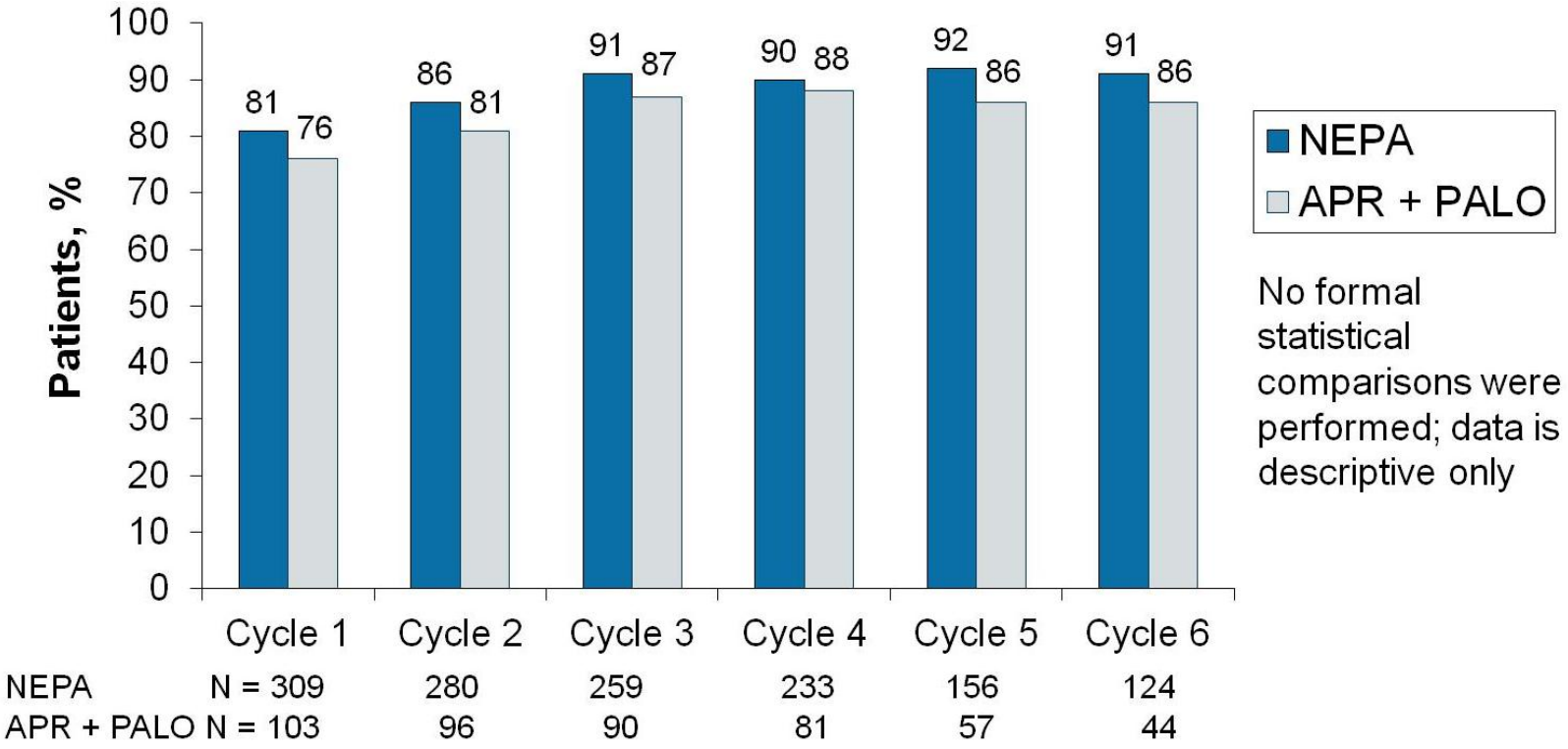


Aapro M, Annals of Oncology 2014

NEPA for CINV Following MEC/HEC

Phase 3 Trial Overall CR Rates/6 Cycles





Gralla RJ, Annals of Oncology 2014

Recent developments in the prevention of chemotherapy-induced nausea and vomiting (CINV): a comprehensive review

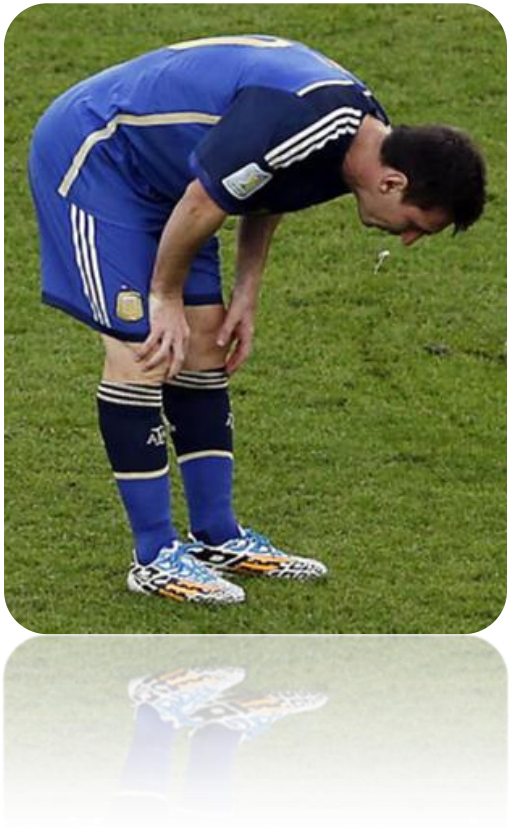
Overview of cycle 1 efficacy for Rolapitant

Patients (%)	Study 1 (AC/non-AC MEC)			Study 2 (HEC)			Study 3 (HEC)		
	Rolapitant + GRAN + DEX (N = 666)	GRAN + DEX (N = 666)	P value	Rolapitant + GRAN + DEX (N = 264)	GRAN + DEX (N = 262)	P value	Rolapitant + GRAN + DEX (N = 271)	GRAN + DEX (N = 273)	P value
Complete response									
Acute	83.5	80.3	0.143	83.7	73.7	0.005	83.4	79.5	0.233
Delayed	71.3	61.6	<0.001	72.7	58.4	<0.001	70.1	61.9	0.043
Overall	68.6	57.8	<0.001	70.1	56.5	0.001	67.5	60.4	0.084
No significant nausea									
Acute	82.1	84.7	0.193	86.4	79.4	0.035	90.0	85.7	0.119
Delayed	72.7	69.4	0.194	73.5	64.9	0.034	74.5	68.9	0.137
Overall	70.6	66.5	0.118	71.6	63.0	0.037	72.7	67.8	0.203

Jordan K, Ann Oncol 2015

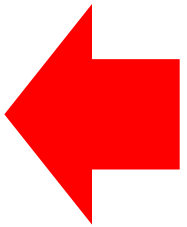
Issues for *CINV*

- Do we reliably measure that?
- Do we use agents optimally?
- Are guidelines useful for clinical practice?
- What is new for CINV in 2015?
- Are we **missing something**?



ANTIEMETIC RESEARCH
-Emerging Area of Focus: Controlling Nausea

- **Methodology Issues: Nausea**
  - Should nausea be a primary endpoint in many clinical trials?
  - We need characterization of the nausea
    - onset, duration, intensity….
  - Consistency in reporting nausea among papers: mean/median; and < 5 mm, and < 25 mm
  - Affect of functional impact



- **A MASCC Work shop on nausea is necessary**

Modified from Gralla R, 2009

BUT WHAT IS NAUSEA?

ASCO Annual '12 Meeting

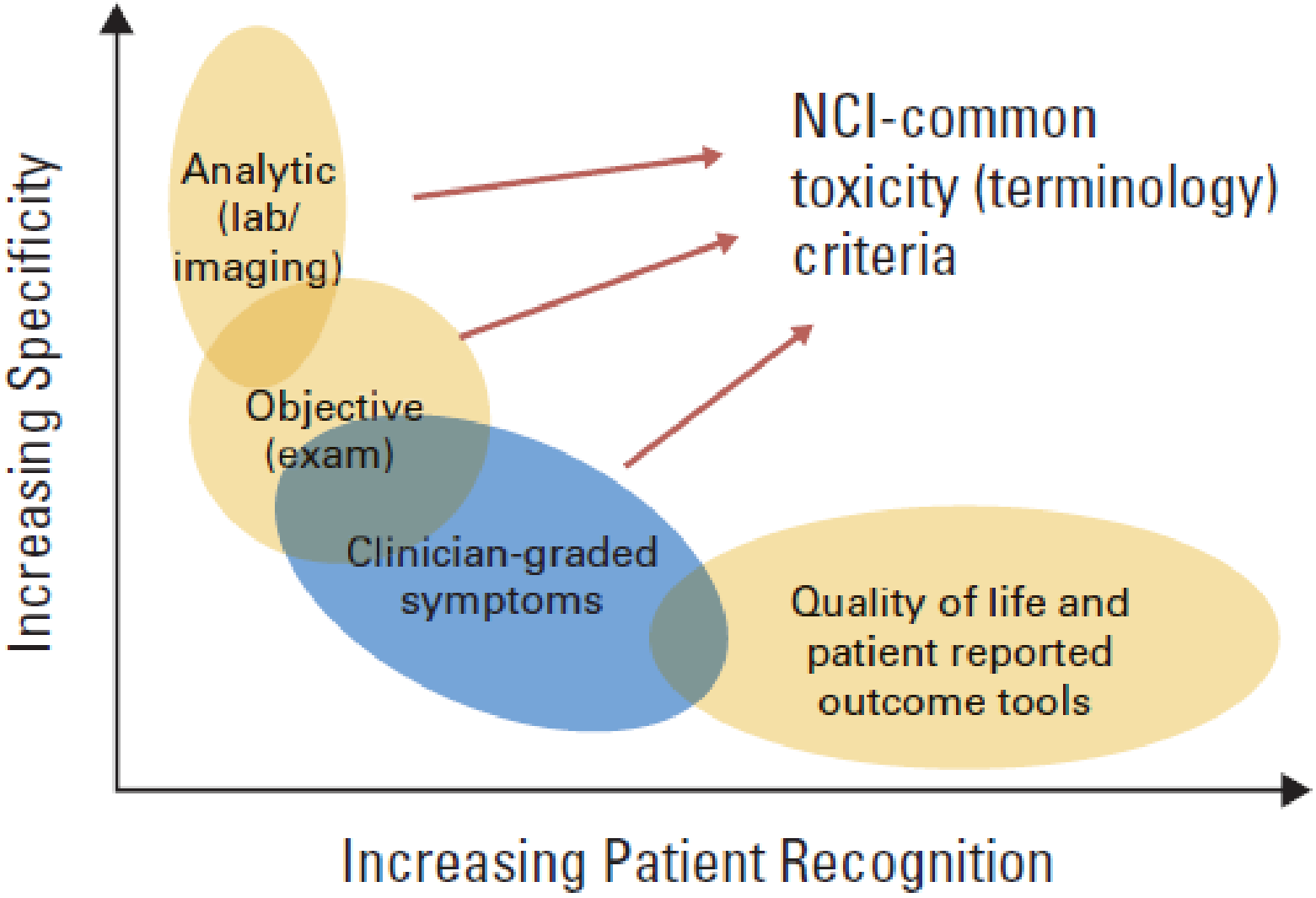
- Nausea is subjective; Vomiting is objective. Therefore the accurate measurement of Nausea is more of an obstacle
- It is more difficult to interpret an animal model of Nausea than an animal model of Vomiting

For PATIENTS nausea (if they understand the word at all) often means « feeling bad »

Aapro M & Grunberg S, Educational ASCO 2012

Patient-Reported Outcomes and the Evolution of Adverse Event Reporting in Oncology

Andy Trotti, A. Dimitrios Colevas, Ann Setser, and Ethan Basch



VOLUME 25 · NUMBER 32 · NOVEMBER 10 2007

JOURNAL OF CLINICAL ONCOLOGY

Patient-Reported Outcomes and the Evolution of Adverse Event Reporting in Oncology

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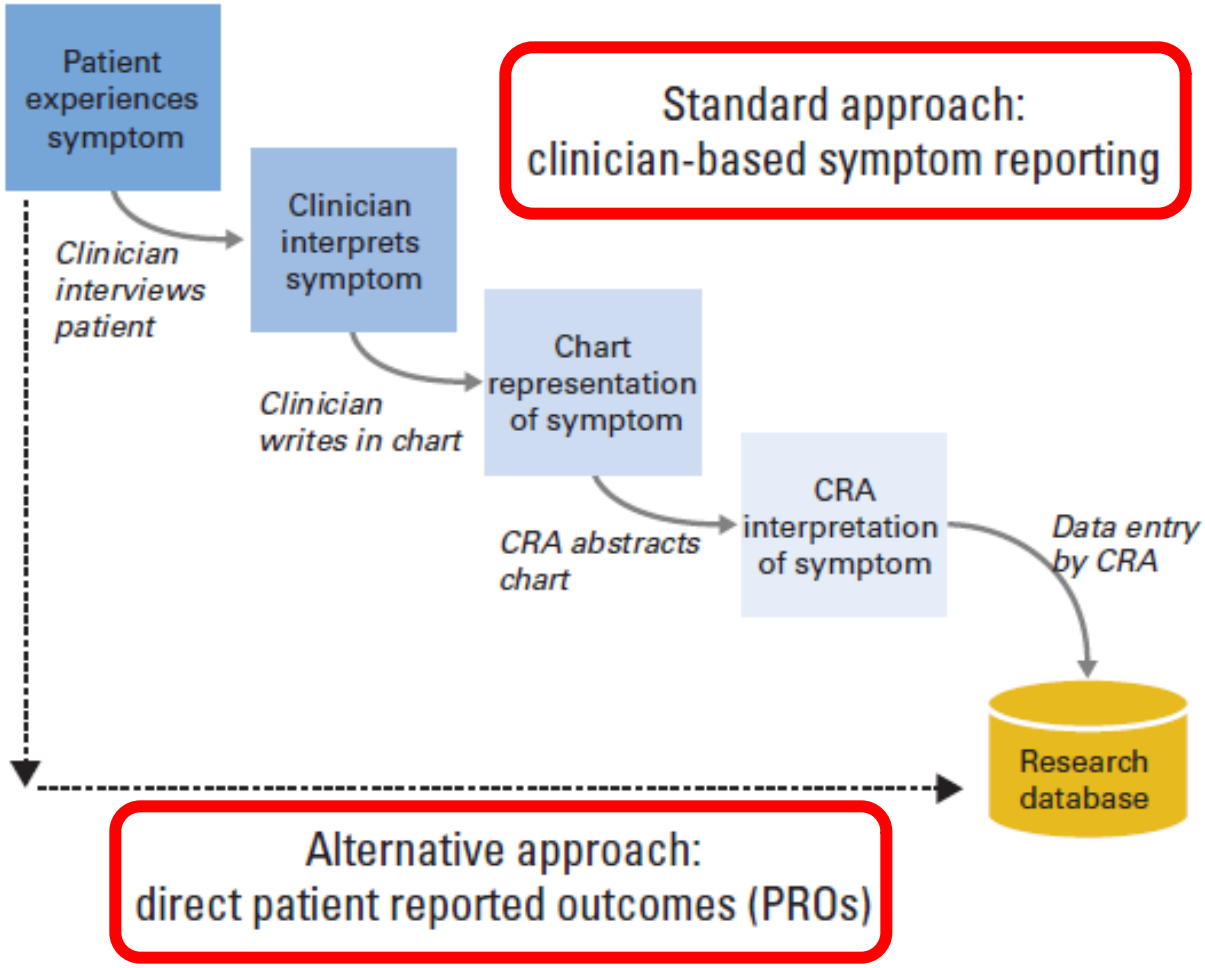


"How do '*subjective*' measures (such as nausea) compare with *'objective*' measures?"

VOLUME 25 · NUMBER 32 · NOVEMBER 10 2007

JOURNAL OF CLINICAL ONCOLOGY

How Do We Measure Patient Comfort During Treatment?

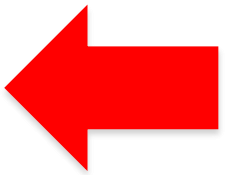
Assessment and documentation of symptoms, particularly those that are clearly subjective (PROs), is essential to provide effective treatment *(*S. Börjeson, *Cancer Nursing*, 1997)

Patient Monitoring

- In clinic
- Telephone follow- up

Tools

- Patient diary
- **Visual analog scale (VAS)**
- **Verbal category scale (VCS)**



Courtesy of Gralla, 2013

ANTIEMETIC TREATMENT
- Assessing Effectiveness [NAUSEA]-

NAUSEA

- Intensity (Patient-generated “VAS”)
- Time of onset and duration
- Presence or absence: *Complete Control*

Question: How much nausea do you have?

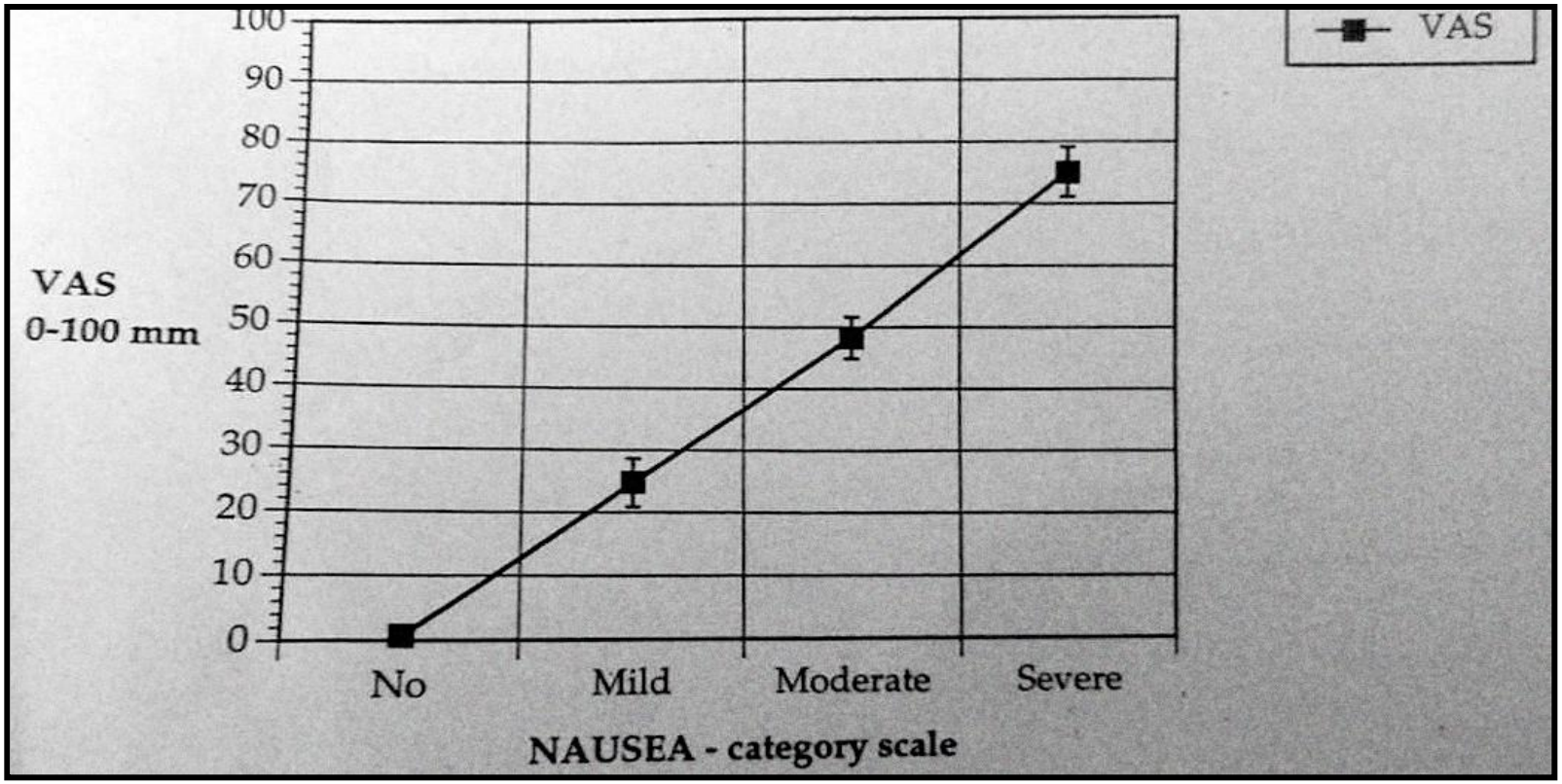
VAS:

None **As much as it could be**

Modified - Courtesy of Gralla, 2013

Relating *VAS Scores* to *Verbal Categorical Scale Scores*

Based on 348 Simultaneous Ratings



Mean visual analog scale ratings (with 95% confidence intervals) corresponding to each category on the verbal categorical scale

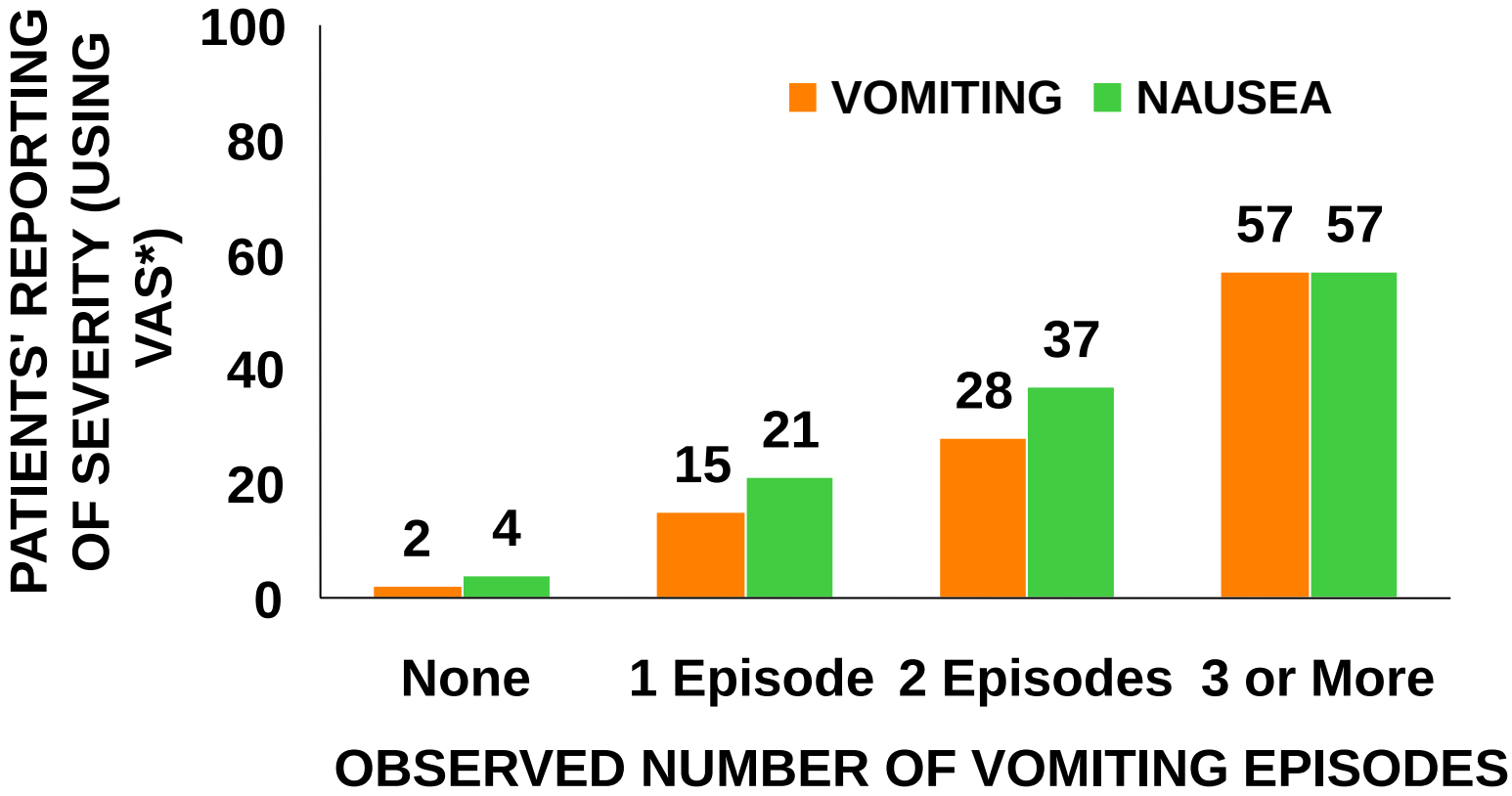
S. Börjeson et al, *Cancer Nursing* 1997

Courtesy of Gralla, 2013

ANTIEMETIC CONTROL

- Correlation of Nausea with Vomiting (119 Patients) -

(Correlation of ***Observed*** and ***Reported*** Effects)



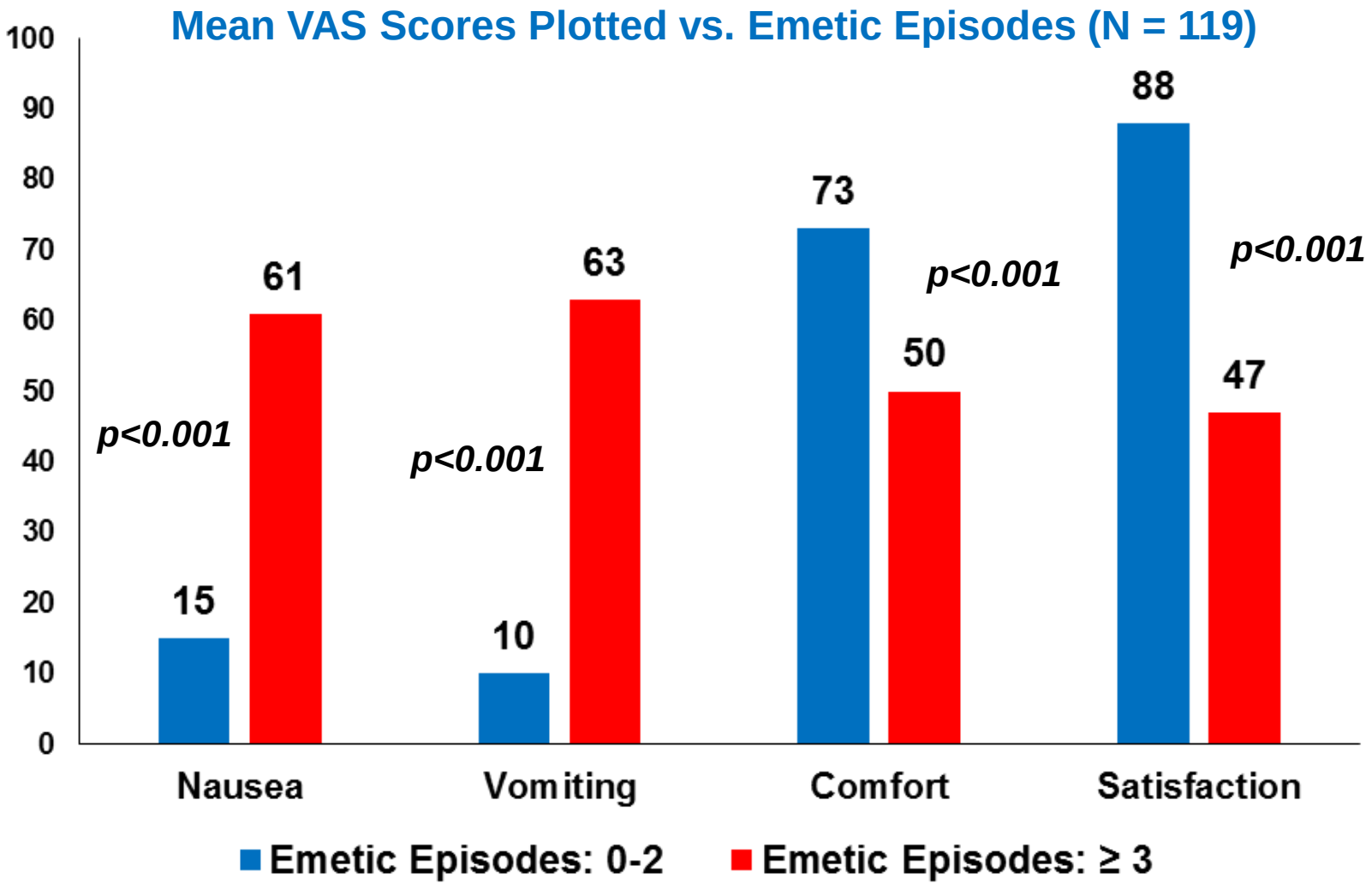
0 = The Least, 100 = The Most

Reference: Clark et al, ONS, 1985.

Modified - Courtesy of Gralla, 2013

OBSERVED EMETIC CONTROL AND PROs:

Focus on Nausea Control



Courtesy of Gralla, 2013

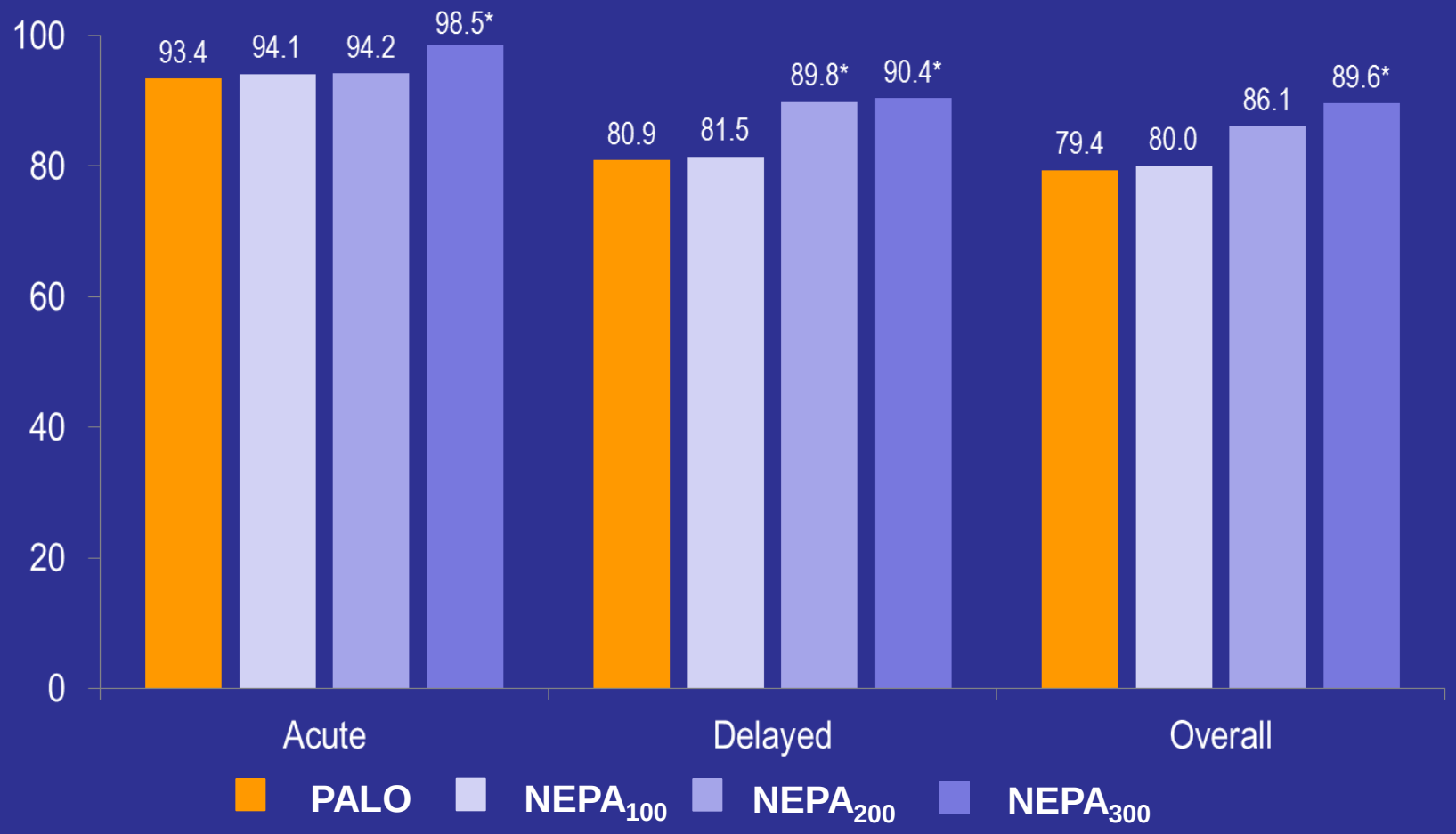
Measuring Nausea:
Key-Points

- VAS provide ***reproducible*** and ***accurate*** measures of the PROs [Nausea]
  - The VAS score itself should be reported
- The concordance was:
  - ***Excellent:*** between VAS scores and the observed number of vomiting episodes
  - ***Well***: between VAS Scores and Categorical Scales of Nausea
- The numerical scale for Nausea, based on the VAS, has been shown to have good psychometric properties
- It may be that both VAS scores and verbal categorical scores give complementary information.

Courtesy of Gralla, 2013

Efficacy of NEPA (Netupitant + PALO) for prevention of CINV following HEC

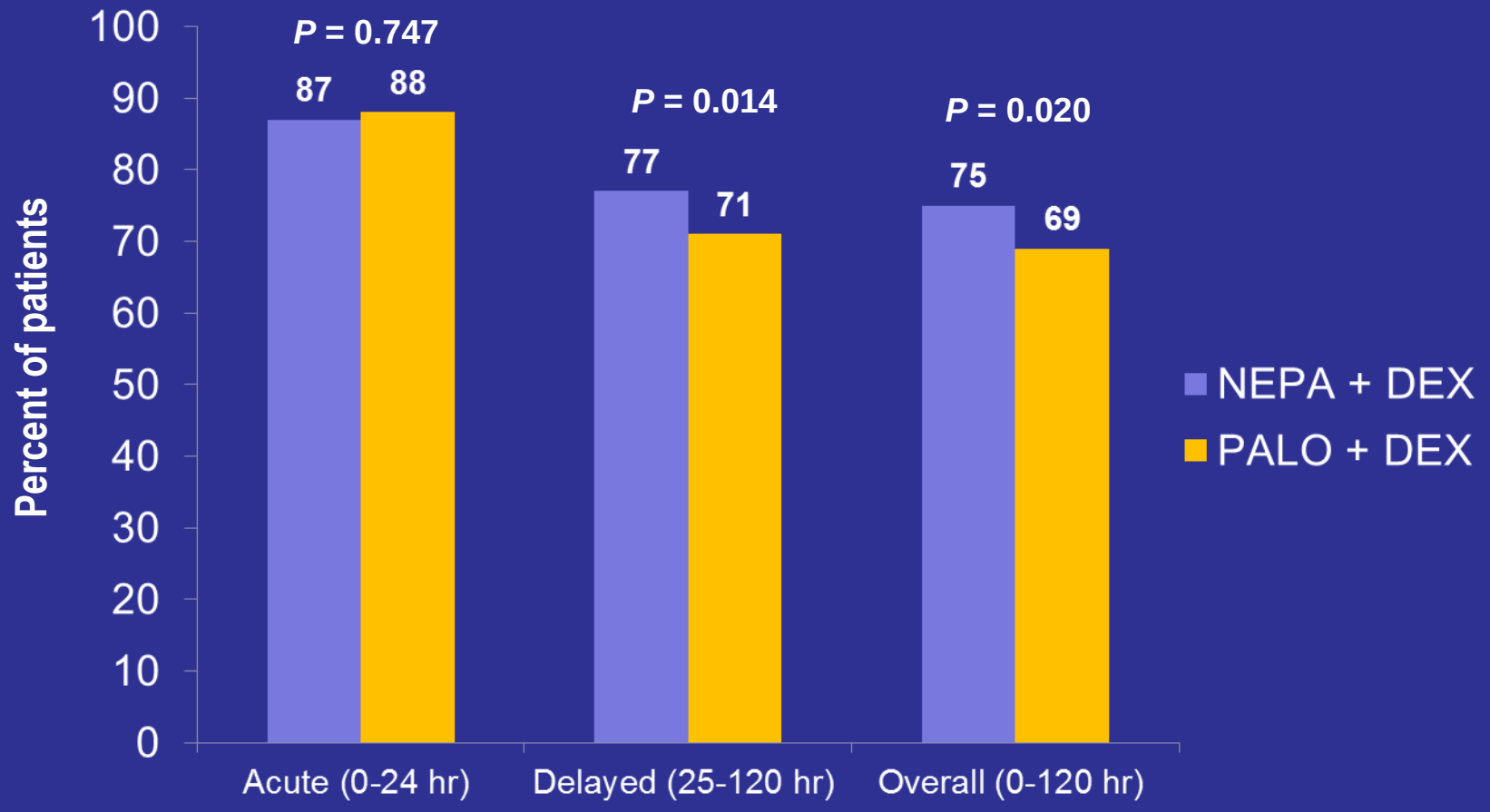
No Significant Nausea (Maximum VAS < 25 mm)



* P ≤ 0.05 compared with PALO; not adjusted for multiple comparisons

Phase 3 study of [NEPA + PALO] versus [PALO] for prevention of CINV following MEC

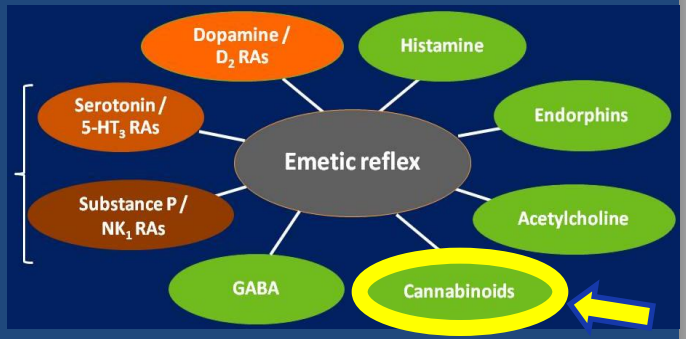
No Significant Nausea Rates (Maximum VAS Score <25 mm)



Nausea and Appetite

ASCO Annual '12 Meeting

- Several agents that have appetite stimulating properties also have anti-nausea properties
  - Corticosteroid
  - Megestrol
  - Olanzapine
  - Dronabinol

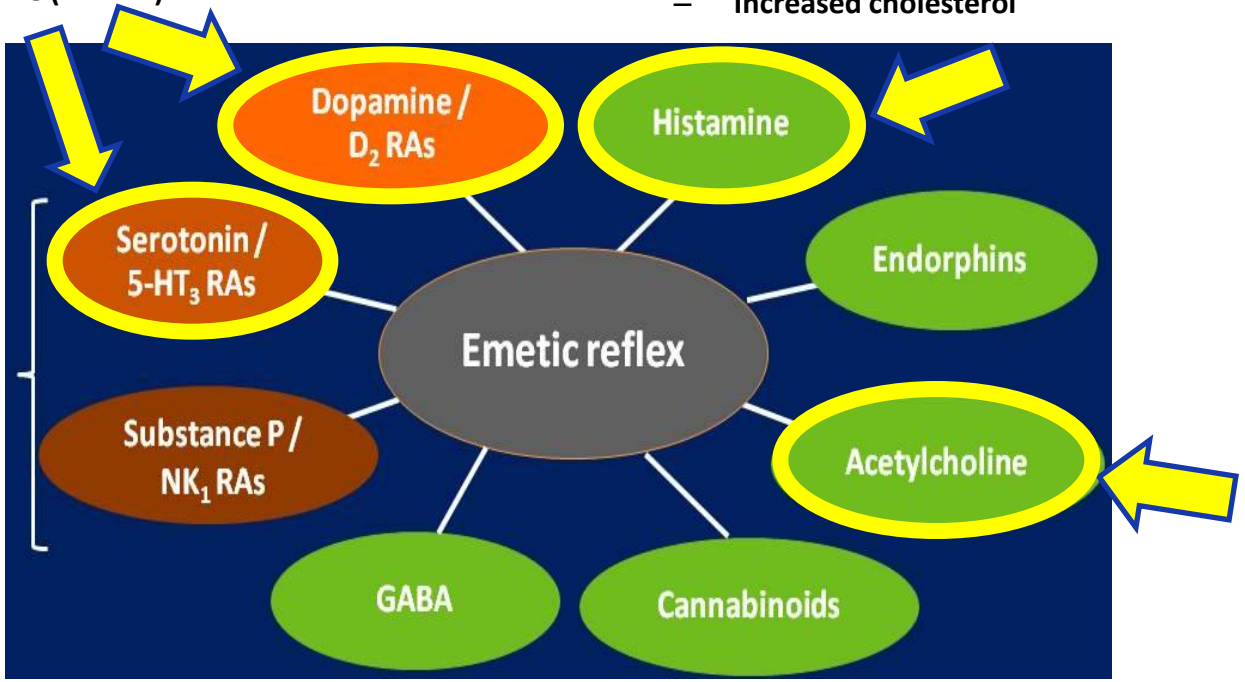


- Nausea/anorexia may be a more valid construct than nausea/vomiting
- A low-dose anti-nausea agent might complement anti-vomiting agents

Modified by Grunberg S & Clark-Snow, Educational ASCO 2012

‘New’ Options: OLANZAPINE

- **Athypical antipsychotic**
- **Broad spectrum of activity against:**
  - Dopamine (D1, D2, D3 and D4)
  - Serotonin (5HT2A. 5HT2C, 56HT3, 5HT6)
  - Catecholamines (alfa-1 adrenergic)
  - Histamine (H1)
  - Acetylcolhine (m1-m4)
- **Side effetcs:**
  - Sedation
  - Dizziness
  - Weight gain
  - Extrapyramidal symptoms
  - Metabolic syndrome
  - Onset of diabetes mellitus
  - Increased cholesterol

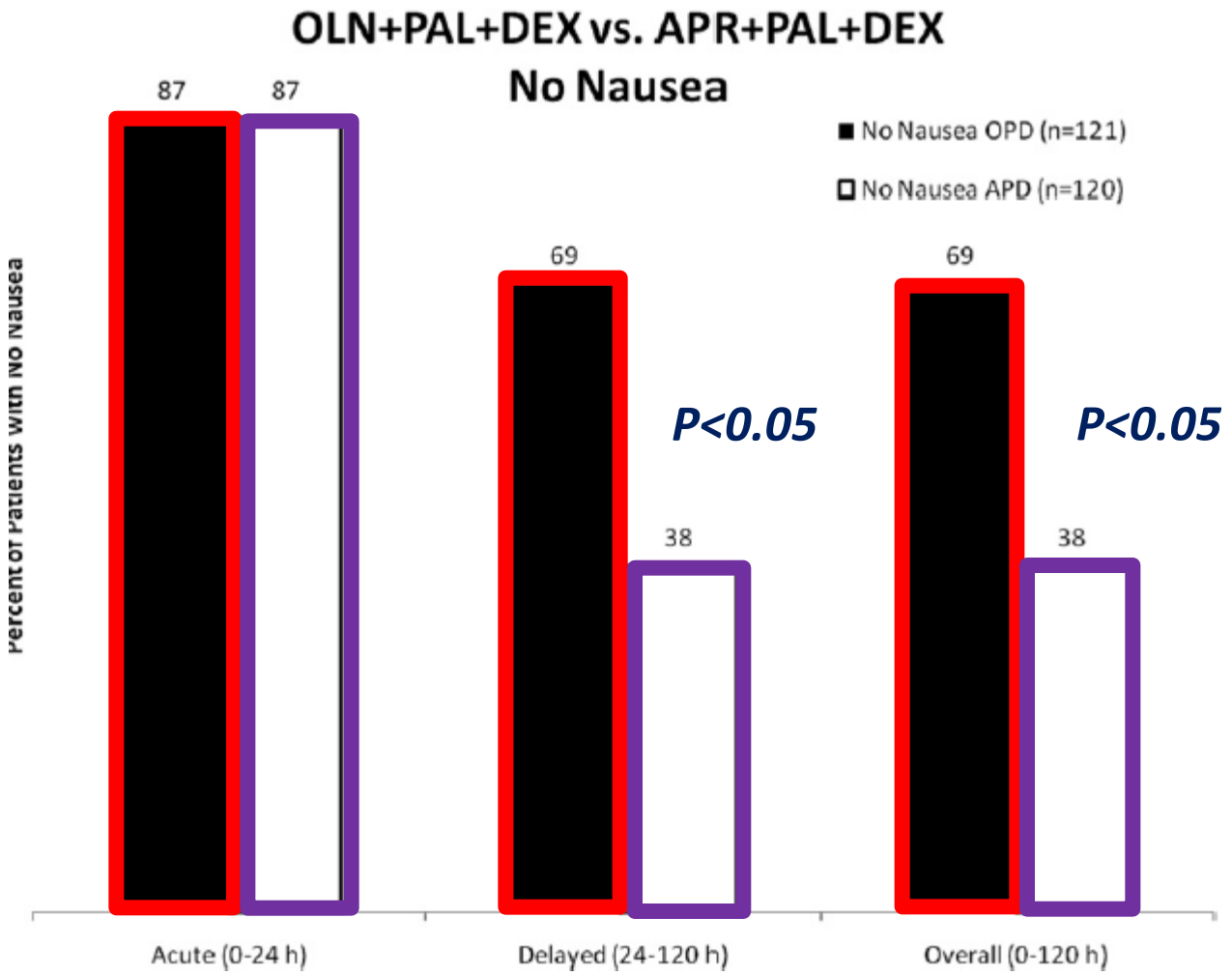


Modifed – Gunberg S, ASCO 2012; Bosnjiak MASCC 2014

Olanzapine Versus Aprepitant for the Prevention of Chemotherapy-Induced Nausea and Vomiting: A Randomized Phase III Trial

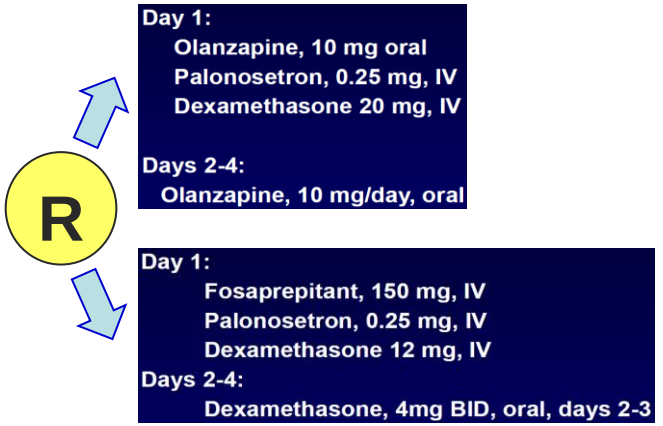
Rudolph M. Navari, MD, PhD, Sarah E. Gray, BS, and Andrew C. Kerr, BS

Nausea (Scale of 0–10, MDASI)

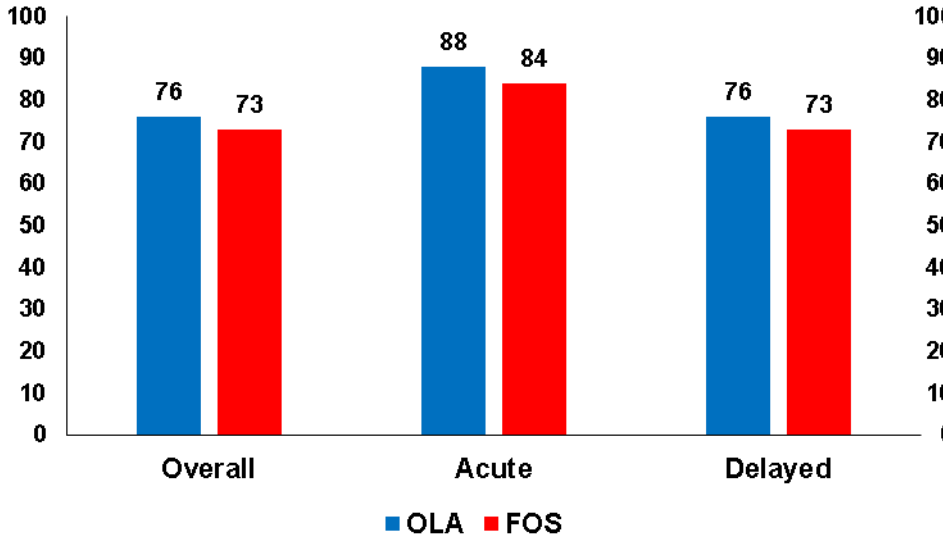


Olanzapine (OLN) Versus Fosaprepitant (FOS) for the Prevention of Chemotherapy-Induced Nausea and Vomiting (CINV) in Patients Receiving Concurrent Chemo-Radiation Treatment: A Randomized, Double-Blind, Phase III Trial.

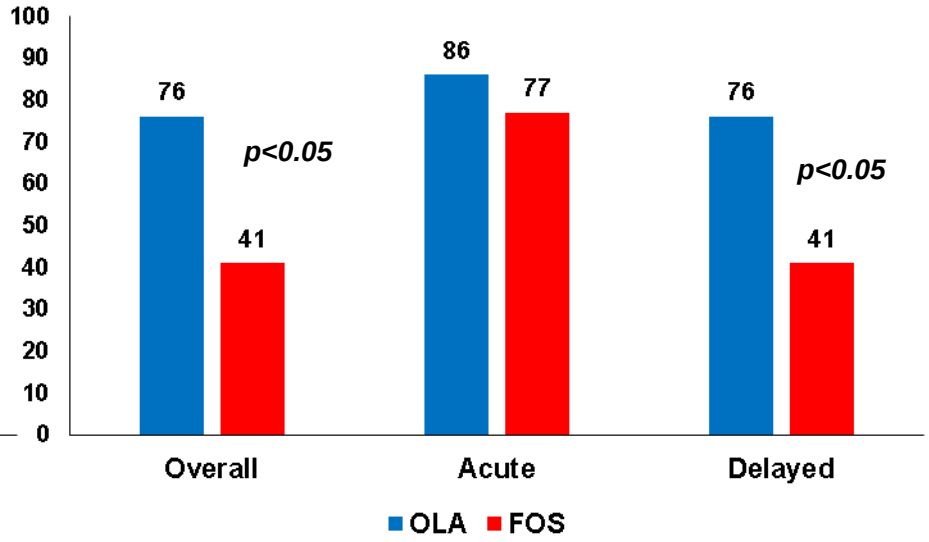
- Patients unrgoing concurrent 60-70 Gy RT (Random after 2 wks of RT) prior to DDP (≥70 mg/mq) + 5FU (HEC)
- Advanced Esophageal and HNC
- End-point:
  - Complete response (No emesis, no rescue 24 hours, days 2-5, and 120 hours CT)
  - Control of nausea (No nausea, 0 on scale of 0-10 24 hours, days 2-5, and 120 hours CT)



Complete Control



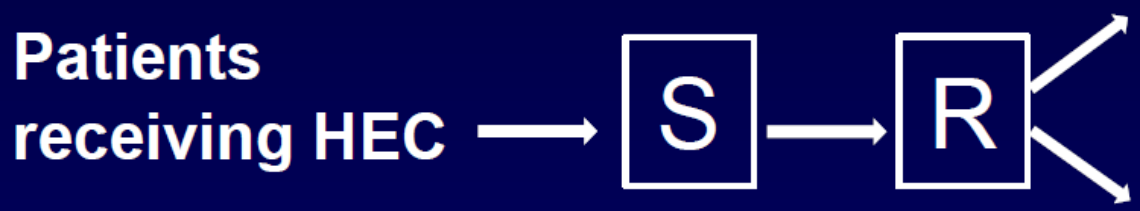
No Nausea



Navari R, ASCO 2015

Olanzapine for Preventing CINV Alliance A221301

Results consistent with current NCCN guidelines recommending olanzapine regimen as an option for CINV prophylaxis for patients receiving HEC



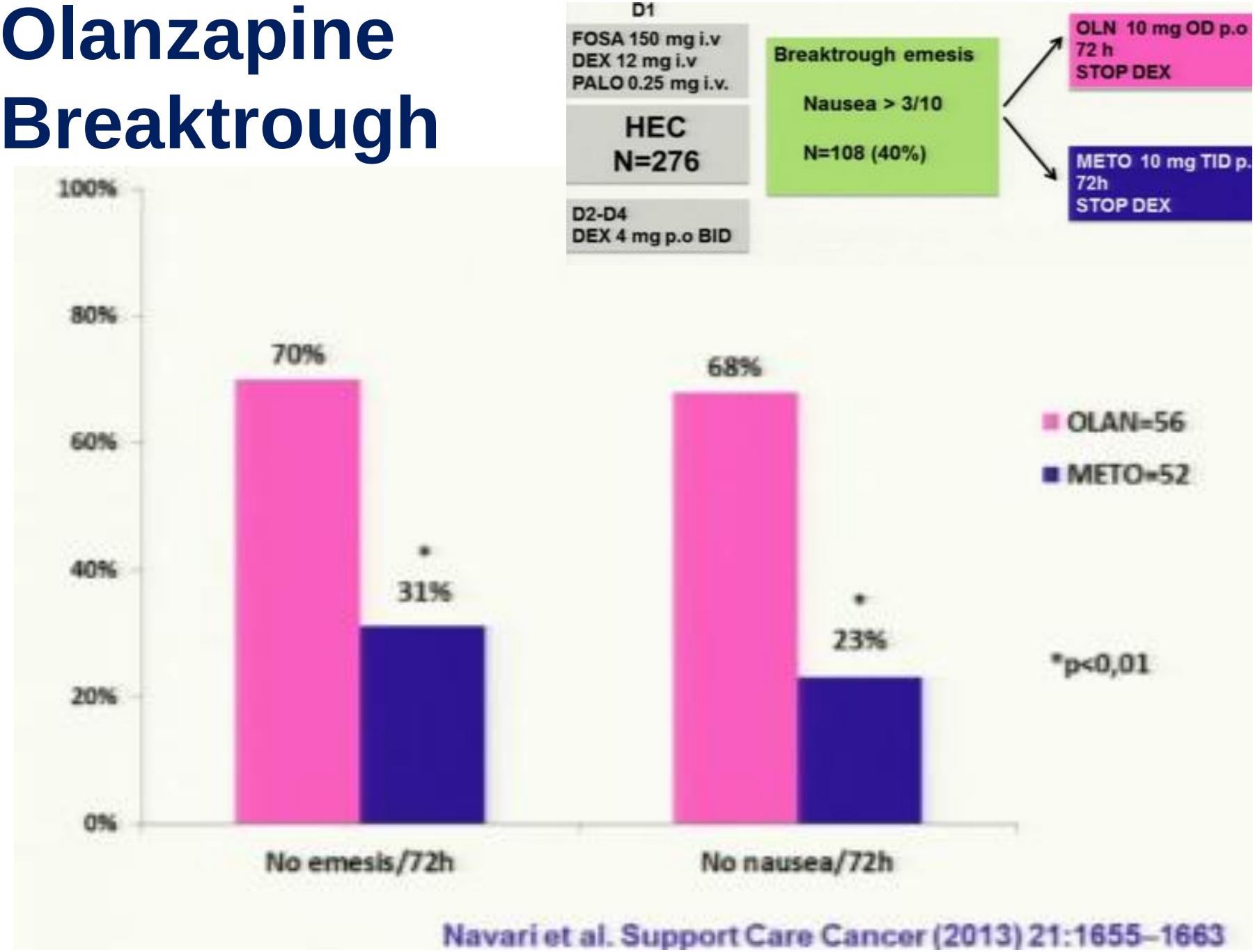
Endpoints

Primary: No nausea

Secondary: Compete response (no emesis, no rescue)

Navari R, ASCO 2015

Olanzapine Breaktrough



Navari et al. Support Care Cancer (2013) 21:1655–1663

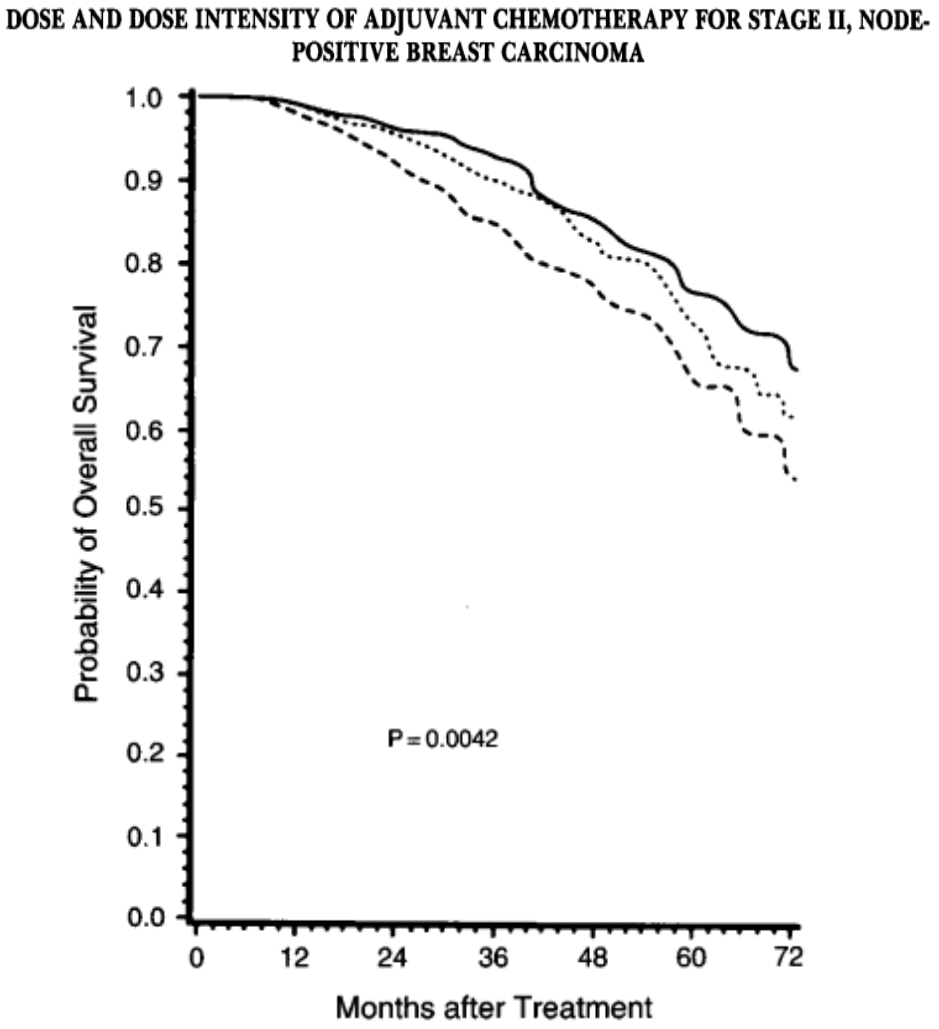
THE MULTIPLE ROLES FOR 'SUPPORTIVE CARE' IN CANCER

- Reduce or eliminate associated symptoms and side-effects
- Preserve or improve quality of life
- Permit safe out-patient treatment
- **Enhance the use of the most effective anti-neoplastic agents**

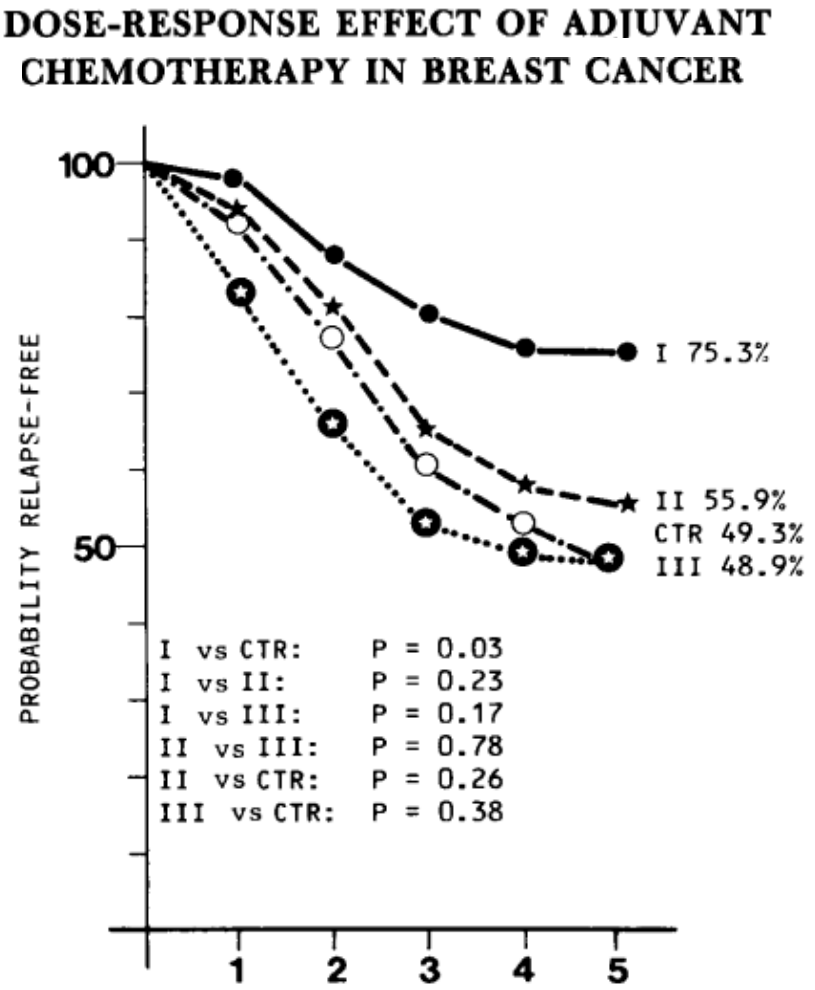
MASCC
MULTINATIONAL ASSOCIATION OF SUPPORTIVE CARE IN CANCER

Modified - Courtesy of Gralla R, 2009

Breast Cancer: RDI and outcome



Wood WC, NEJM 1994



Bonadonna G, NEJM 1994

Decreasing CINV may improve RDI and outcome?

Propensity score matching

Jan. 2008～Dec. 2012, 504 pts treated with A

AP group : 205 pts, nAP group 299 pts

↓

propensity score (PS)*

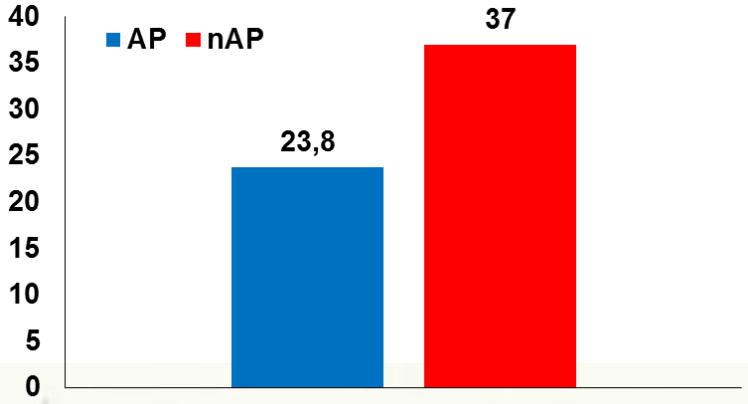
↓

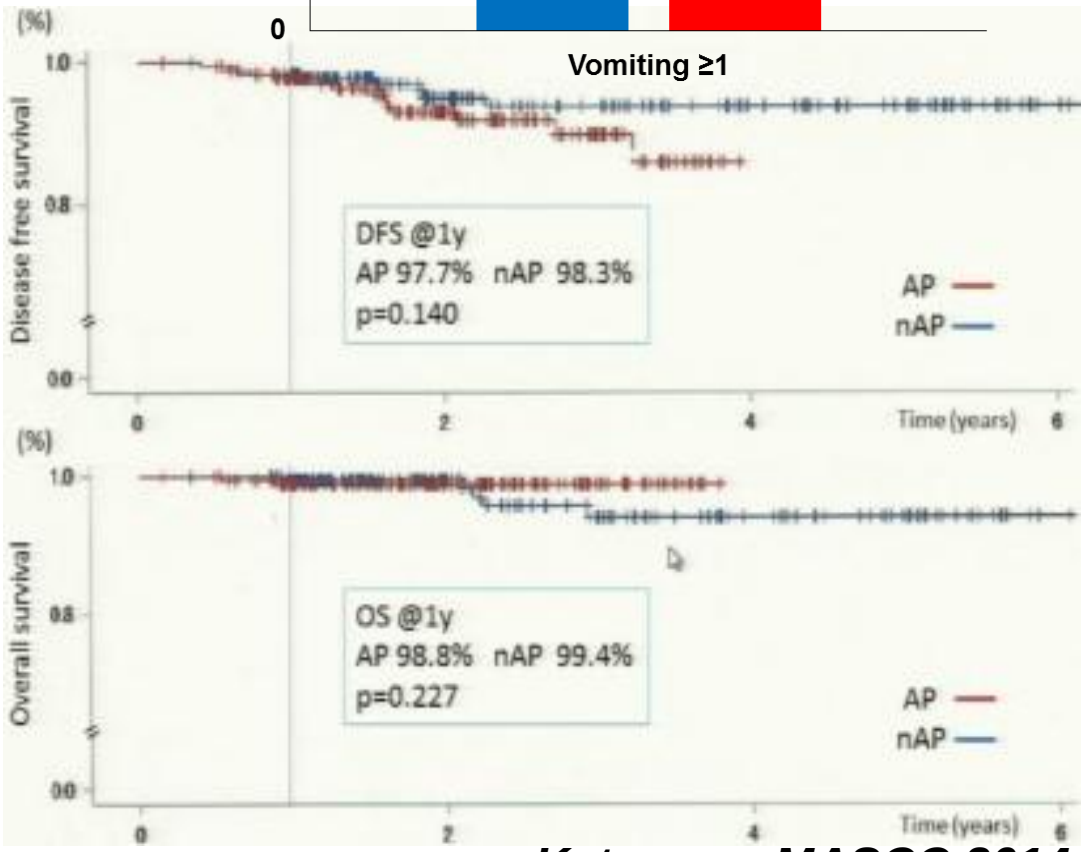
AP group : 181 pts, nAP group 181 pts

adjustment variables (age, BMI, use of taxanes, dose of corticosteroids and institute)

- **nAP group**
  - – Corticosteroid* on day 1 (iv) and day 2-4 or 5 (oral)
  - – 5HT3 receptor antagonist** on day 1 (iv)
- **AP group**
  - – oral aprepitant 125 mg on day 1, then 80 mg on days 2 and 3
  - – corticosteroid on day 1 (iv) and day 2-4 or 5 (oral)
  - – 5HT3 receptor antagonist on day 1 (iv)

* : dexamethasone, betamethasone ** : granisetron, palonosetron, ramosetron





Katayama MASCC 2014

Conclusions

- Findings from CINV clearly indicate that this is a ***Patient-Centered Care***
- Evidence that ***clinicians underestimate*** incidence and severity of vomiting and (particularly) nausea
- Use ***guidelines*** to improve control!
  - Triple-drug approach is THE standard in the majority of settings
  - CINV control has significant implications for QoL and outcome
- New options to meet patient compliance are under investigation
- Pivotal data indicate that PROs can be adopted:
  - High degree of patient engagement and compliance
  - Validations are needed to assess how much may reliably complement clinician-reported data.
- Staff education is essential!
  - Monitor symptoms throughout treatment
  - Collection of PROs via checklist reviewed by staff