complete response (no vomiting and no rescue antiemetic use 0-120 hours after chemotherapy).

If we are to optimize the care of our patients, we need to standardize CINV study end points. We would also request that all of the currently published studies allow open access to their full data so that this process can begin.[5] This would allow clinicians and patients to compare different regimens on a more level playing field. Standardization of data collection and reporting would also allow objective cross-trial comparisons and meta-analyses to better inform treatment guidelines and health policy. Finally, if we as oncologists are unable to decide which end points to report, then surely it is time to ask our patients what they believe to be the most important clinical parameters that should be measured and reported in the real-world setting?

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Aprepitant Versus Dexamethasone for Delayed Emesis: What Is the Role of the 5-Hydroxytryptamine Type 3 Receptor Antagonist Palonosetron?

To the Editor: We would like to comment on the recently published study by Roila et al[1] and to respond to the authors' discussion of our own work. The hypothesis underlying the study was that in the pivotal trial by Warr et al,[2] aprepitant had proved superior to ondansetron against delayed emesis as the result of a carryover effect on the protection against acute emesis caused by an anthracycline plus cyclophosphamide (AC). The current superiority trial,[1] which was prematurely closed because of accrual difficulties, suggests that either aprepitant or dexamethasone can be recommended, but because of the lower cost of corticosteroids, dexamethasone should be chosen as prophylaxis for delayed emesis caused by AC.

The authors highlight that only an appropriate methodology allows us to identify the role of an agent in the delayed phase. In view of this, we do not understand the decision of the investigators to use palonosetron; we also fail to understand why there is no comment about it in the article.[1] The choice of palonosetron as the 5-hydroxytriptamine type 3 receptor antagonist can represent a methodologic pitfall for a trial that is designed to target delayed emesis. A large superiority trial comparing palonosetron with granisetron, both combined with dexamethasone given once per day for 3 days, demonstrated that the complete response (CR) was similar in the acute phase but significantly superior with palonosetron in the delayed phase (57% *v* 44.5%; $P < .001$) in the setting of cisplatin and AC chemotherapy.[3] In a noninferiority trial comparing palonosetron plus either dexamethasone given once or once per day for 3 days, the dexamethasone-sparing regimen achieved delayed protection similar to that found with multiday dexamethasone dosing[4] (Table 1). The 1-day regimen that included low-dose dexamethasone provided protection against acute emesis similar to that observed in the control arm (ondansetron plus high-dose dexamethasone) of the trial by Warr et al,[2] but a higher proportion of women receiving the dexamethasone-sparing regimen experienced delayed CR compared with those receiving ondansetron also on days 2 and 3 (Table 1). And last but not least, the recent results of a large phase III trial by Aapro et al[5] indicate that palonosetron plus a single, day-1-only, 20-mg dose of dexamethasone provided acute protection similar to that of the three-drug regimen used in the trial by Roila et al[1] and also achieved delayed CR in the vast majority of patients (Table 1). These results are particularly relevant to clinical practice if clinicians choose not to use a neurokinin-1 receptor antagonist (NK-1RA). Acute and delayed findings from this trial[5] also compare well with those observed in the pivotal trial by Warr et al[2] (Table 1). Likewise, the delayed CR rate that was observed in the second Aapro trial[5] confirms and reinforces previous results showing that not all women undergoing AC need additional dexamethasone doses when a combination of palonosetron plus dexamethasone is administered on day 1.[4,6]

We regret that despite this evidence, the article by Roila et al[1] is remarkable for the absence of any attempt to place the findings in the context of other existing and relevant knowledge. The authors should also have a more conservative approach when they speculate on the meaning of their findings. In daily clinical practice, an Italian patient would need to take a large number of dexamethasone tablets (available only at a dose of either 0.5 or 0.75 mg) to comply with the recommended daily dose of 8 mg for delayed prophylaxis. Therefore, the choice between the two drugs should be made after considering not only the differences in terms of efficacy, safety, and cost, but also feasibility and convenience. Our opinion is not that dexamethasone would be ineffective against delayed emesis, as erroneously stated by the authors. However, we can customize the prophylaxis to avoid giving unnecessary

Table 1. Phase III Trials With Different Antiemetic Regimens in Patients With Breast Cancer Undergoing AC Treatment

Author and Year	Antiemetic Treatment	No. of Patients	Study Period	CR (%)		*P*
				Exp	Control	
Warr et al, 2005[2]	Exp: Day 1: APR + ONDA + DEX (12 mg) Days 2 and 3: APR	433	Day 1	76	69	.03
	Control: Day 1: ONDA + DEX (20 mg) Days 2 and 3: ONDA	424	Days 2-5	55	49	.06
Aapro et al, 2010[4]	Exp: Day 1: PALO (0.25 mg) + DEX (8 mg) Days 2 and 3: placebo	151	Day 1	69.5	68.5	.57
	Control: Day 1: PALO (0.25 mg) + DEX (8 mg) Days 2 and 3: DEX (8 mg)	149	Days 2-5	62	66	.25
Roila et al, 2014[1]	Exp: Day 1: APR + PALO (0.25 mg) + DEX (8 mg) Days 2 and 3: DEX (8 mg)	273	Day 1	88	85	.39
	Control: Day 1: APR + PALO (0.25 mg) + DEX (8 mg) Days 2 and 3: APR	278	Days 2-5	79.5	79.5	1.00
Aapro et al, 2013[2]	Exp: Day 1: NEPA + DEX (12 mg)	724	Day 1	88	85	.04
	Control: Day 1: PALO (0.50 mg) + DEX (20 mg)	725	Days 2-5	77	69.5	.001

Abbreviations: AC, anthracycline plus cyclophosphamide; APR, standard-dose aprepitant; CR, complete response (no vomiting and no rescue antiemetics); DEX, dexamethasone; Exp, experimental; NEPA, combination of netupitant and palonosetron; ONDA, ondansetron (8 mg twice per day orally); PALO, palonosetron (0.25 mg intravenously or 0.50 mg orally).

additional doses (and adverse effects such as insomnia and heartburn) of dexamethasone to women undergoing AC. It would seem important to note that recent results of treatment with a fixed-dose combination of the NK-1RA netupitant and palonosetron plus 1-day dexamethasone further demonstrate the value of a simplified, single-day prophylaxis[5] (Table 1).

The use of palonosetron does not allow us to be confident that the same CR results in the delayed phase would be obtained if an older antagonist was administered on day 1. It seems unreasonable to use only one of the three capsules available in the aprepitant package. In daily clinical practice, real options for antiemetic prophylaxis in patients undergoing AC still remain: either the 3-day standard aprepitant regimen (fosaprepitant is not available in Italy) or palonosetron plus dexamethasone, as recommended by guidelines, when an NK-1RA is not available.[7,8]

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