Efficacy of olanzapine for the prophylaxis and rescue of chemotherapy-induced nausea and vomiting (CINV): a systematic review and meta-analysis

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Objective

Investigate the efficacy of olanzapine in relation to other antiemetics in the prophylaxis and rescue of CINV, as reported by randomized controlled trials (RCT)

- A literature search was conducted in Ovid MEDLINE from 1946 to June Week 1 2015, EMBASE and EMBASE Classic from 1947 to 2015 Week 24, and the Cochrane Central Register of Controlled Trials up until 2015
- RCTs were included if they compared olanzapine to other antiemetics in either a prophylaxis or breakthrough setting, with at least one of the endpoints – no emesis, or no nausea
- The primary endpoints were the percentage of patients achieving no emesis or no nausea in the acute, delayed and overall phases

Results

• 13 eligible RCTs were identified – 10 in the preventative setting and 3 in the breakthrough setting

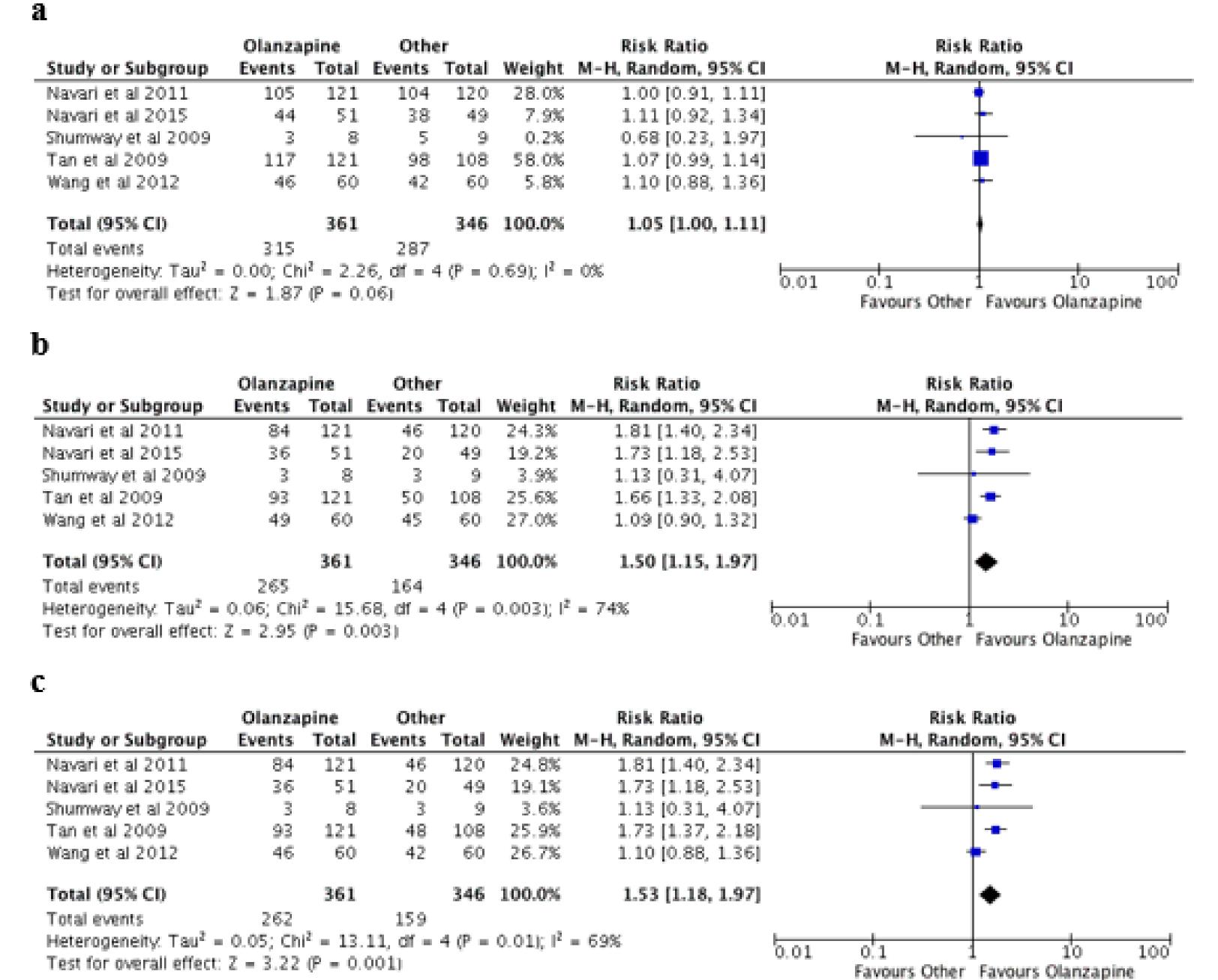
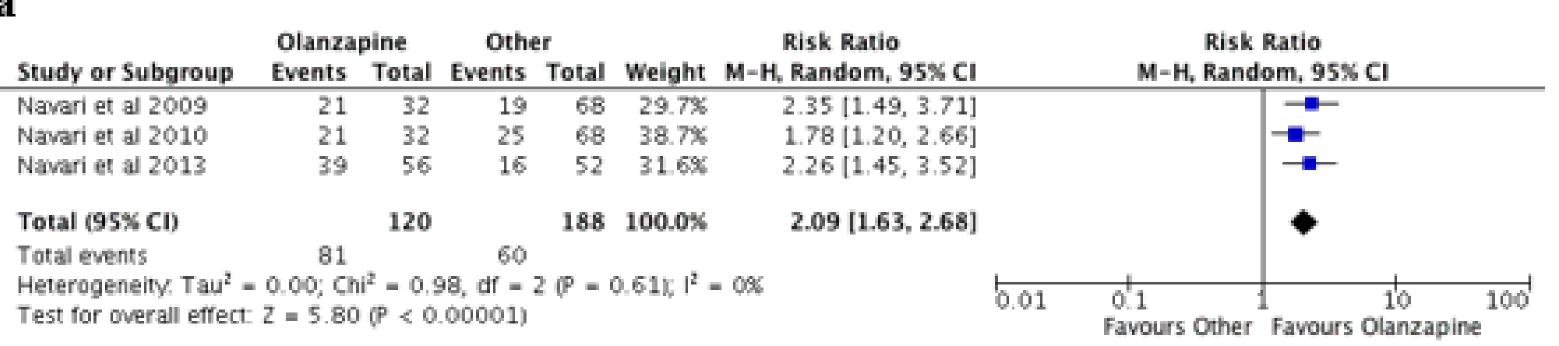


Fig. 2 a Efficacy of olanzapine compared with other standard antiemetics in the prophylaxis of chemotherapy-induced nausea and vomiting—no nausea in the acute phase b No nausea in the delayed phase c No nausea in the overall phase



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a Risk Ratio Olanzapine Other Risk Ratio Study or Subgroup Events Total Events Total Weight M-H, Random, 95% CI M-H, Random, 95% CI Mao et al 2011 1.18 [1.03, 1.36] 1.15 [0.96, 1.39] Mizukami et al 2014 1.04 [0.96, 1.13] 50 18.6% Mukhopadhyay et al 2015 1.12 [1.03, 1.21] Navari et al 2011 120 19.0% 1.05 [0.90, 1.24] Navari et al 2015 10.0% 1.69 [0.73, 3.88] Shumway et al 2009 0.6% 108 20.5% 1.01 [0.94, 1.08] Tan et al 2009 Wang et al 2012 1.48 [1.06, 2.06] Wang et al 2015 1.15 [0.96, 1.39] Total (95% CI) 1.10 [1.03, 1.17] 506 100.0% 521 Total events Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 16.53$, df = 8 (P = 0.04); $I^2 = 52\%$ 0.01 Test for overall effect: Z = 2.89 (P = 0.004) Favours Other Favours Olanzapine

	Olanzapine		Oth	Other		Risk Ratio	Risk Ratio	
Study or Subgroup	Events Total		Events Total		Weight	M-H, Random, 95% CI	M-H, Random, 95% CI	
Mao et al 2011	39	46	23	46	9.7%	1.70 [1.24, 2.32]	-	
Mizukami et al 2014	22	22	16	22	11.1%	1.36 [1.05, 1.77]	•	
Mukhopadhyay et al 2015	48	50	21	50	9.2%	2.29 [1.64, 3.18]		
Navari et al 2011	93	121	88	120	14.9%	1.05 [0.91, 1.21]	+	
Navari et al 2015	39	51	36	49	12.3%	1.04 [0.83, 1.31]	+	
Shumway et al 2009	5	8	5	9	2.8%	1.13 [0.51, 2.49]		
Tan et al 2009	102	121	73	108	14.8%	1.25 [1.07, 1.45]	•	
Wang et al 2012	46	60	32	60	10.8%	1.44 [1.09, 1.89]		
Wang et al 2015	40	42	34	42	14.4%	1.18 [1.00, 1.38]	-	
Total (95% CI)		521		506	100.0%	1.31 [1.14, 1.52]	•	
Total events	434		328					
Heterogeneity: Tau2 = 0.03	$Chi^2 = 2$	7.64, d	f = 8 (P	= 0.00	$05); I^2 = 3$	71%	0.1 1 10 10	
Test for overall effect: Z = 3				- 0.00	V21, 1	0.01	0.1 1 10 : Favours Other Favours Olanzapine	

С							
	Olanza	pine Other		Risk Ratio		Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Lu et al 2013	22	30	11	30	6.6%	2.00 [1.19, 3.36]	
Mao et al 2011	38	46	15	46	7.9%	2.53 [1.64, 3.92]	
Mizukami et al 2014	22	22	15	22	10.7%	1.45 [1.09, 1.94]	
Mukhopadhyay et al 2015	47	50	20	50	9.5%	2.35 [1.66, 3.32]	
Navari et al 2011	93	121	88	120	13.5%	1.05 [0.91, 1.21]	+
Navari et al 2015	39	51	36	49	12.0%	1.04 [0.83, 1.31]	+
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Tan et al 2009	102	121	73	108	13.4%	1.25 [1.07, 1.45]	•
Wang et al 2012	40	60	27	60	9.8%	1.48 [1.06, 2.06]	-
Wang et al 2015	38	42	33	42	12.8%	1.15 [0.96, 1.39]	+
Total (95% CI)		551		536	100.0%	1.41 [1.18, 1.68]	•
Total events	446		323				
Heterogeneity: Tau ² = 0.06;	$Chi^2 = 4$	0.47, d	f = 9 (P	< 0.00	001); l² =	78%	0.01 0.1 1 10 100
Test for overall effect: Z = 3.	.76 (P = 1	0.0002)				Favours Other Favours Olanzapine

Fig. 1 a Efficacy of olanzapine compared with other standard antiemetics in the prophylaxis of chemotherapy-induced nausea and vomiting—no emesis in the acute phase **b** No emesis in the delayed phase c No emesis in the overall phase

Fig. 3 a Efficacy of olanzapine compared with other standard antiemetics in the rescue of breakthrough chemotherapy-induced nausea and vomiting—no emesis.

Absolute risk difference between olanzapine and other antiemetic intervention arms for all included chemotherapy-induced nausea and vomiting endpoints

Endpoint	Absolute risk difference	95% confidence	Test for overall	Heterogeneity test	Satisfies MASCC/ESMO antiemetic guidelines
	(%)	interval (%)	effect		requirement
No emesis, acute phase (prevention)	9	4-14	p=0.0007	p=0.08	Approaching
No emesis, delayed phase (prevention)	21	10-33	p=0.0003	p<0.0001	Yes
No emesis, overall phase (prevention)	24	12-36	p=0.0001	p<0.0001	Yes
No nausea, acute phase (prevention)	4	0-9	p=0.06	p=0.64	No
No nausea, delayed phase (prevention)	24	13-35	p<0.0001	p=0.06	Yes
No nausea, overall phase (prevention)	24	14-35	p<0.0001	p=0.07	Yes
No emesis (breakthrough)	36	25-46	p<0.0001	p=0.74	Yes

No nausea, overall phase (prevention)	24	14-35	p<0.0001	p=0.07	Yes
No emesis (breakthrough)	36	25-46	p<0.0001	p=0.74	Yes
Endpoint	Absolute risk	95%	Test for	Heterogeneity	Satisfies MASCC/ESMO
	difference	confidence	overall	test	antiemetic guidelines
	(%)	interval (%)	effect		requirement
No emesis, overall phase (5 mg)	34	19-49	p<0.0001	p=0.75	Yes
No emesis, acute phase (10 mg)	7	3-14	p=0.002	p=0.07	No
No emesis, delayed phase (10 mg)	20	8-33	p=0.002	p<0.00001	Yes
No emesis, overall phase (10 mg)	22	8-36	p=0.003	p<0.00001	Yes
No nausea, acute phase (10 mg)	4	0-9	p=0.06	p=0.64	No
No nausea, delayed phase (10 mg)	24	13-35	p<0.0001	p=0.06	Yes
No nausea, overall phase (10 mg)	24	14-35	p<0.0001	p=0.07	Yes
No emesis, acute phase (Dex)	7	2-12	p=0.004	p=0.16	No
No emesis, delayed phase (Dex)	22	7-37	p=0.005	p<0.00001	Yes
No emesis, overall phase (Dex)	26	11-41	p=0.0009	p<0.00001	Yes
No nausea, acute phase (Dex)	4	-1-9	p=0.09	p=0.47	No
No nausea, delayed phase (Dex)	30	22-38	p<0.00001	p=0.73	Yes
No nausea, overall phase (Dex)	31	23-38	p<0.00001	p=0.71	Yes
No emesis, acute phase (No Dex)	16	5-28	p=0.006	p=0.39	Yes
No emesis, delayed phase (No Dex)	18	7-28	p=0.0008	p=0.37	Yes
No emesis, overall phase (No Dex)	16	5-28	p=0.006	p=0.39	Yes

Conclusions

- In regimens where dexamethasone was not included, olanzapine was not statistically superior to non-olanzapine regiments in two of the three analysed parameters – no emesis in the acute and overall phase
 - The observation that olanzapine is superior in all three parameters in the presence of dexamethasone may mean that some of the increased efficacy should be attributed to dexamethasone
- Olanzapine was found to be statistically and clinically superior to other breakthrough medications such as prochlorperazine and metochlopramide in the only assessable endpoint – no emesis
- Olanzapine is more efficacious than other standard antiemetics in the preventative and breakthrough setting
- We recommend the consideration of the use of a 5-mg dose of olanzapine in the prophylaxis of CINV as analysis shows that a 5-mg dose is equally efficacious to a 10-mg dose but may carry an added safety benefit

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