Efficacy and safety of olanzapine for the prophylaxis of chemotherapy-induced nausea and vomiting (CINV) as reported in phase I and II studies: a systematic review

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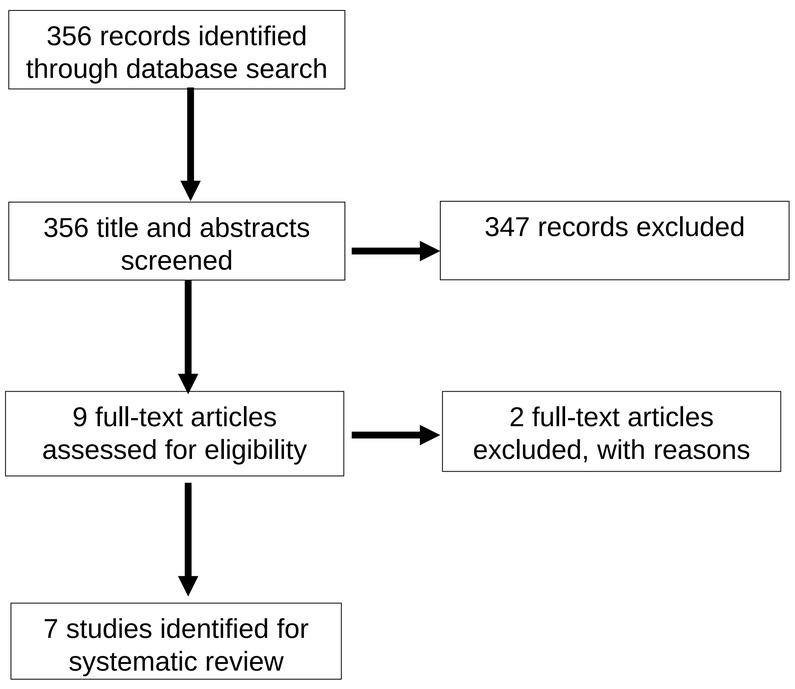
Objective

- Summarize all phase I and II trials that used olanzapine for the prophylaxis of CINV

Methods

- A literature search was conducted in Ovid MEDLINE from 1946 to July Week 1 2015, EMBASE and EMBASE Classic from 1947 to 2015 Week 28, and Cochrane Central Register of Controlled Trials up until 2015
- Phase I and II trials reporting on olanzapine for prophylaxis were included if they reported on at least one endpoint: complete response (CR), complete control (CC), no nausea, no emesis
- Primary endpoints were the percentage of patients achieving CR, CC, no nausea or no emesis in the acute (0-24 hr), delayed (24-120 hr) and overall phases (0-120 hr)

Results



Study	Patients (n)	Chemotherapy emetogenicity	Tumor Type
Passik et al 2002	15	CHEMO and RAD therapy	Breast (26.7%), lung (26.7%), ovary (13.3%), lymphoma (6.7%), myeloma (6.7%), pancreas (6.7%), bladder (6.7%), unknown (6.7%)
Passik et al 2003	28	Highly emetogenic chemotherapy (HEC) and moderately emetogenic chemotherapy (MEC)	Lung (25%), breast (17.9%), prostate (14.3%), colon (7.1%), rectum (7.1%), ovarian (7.1%), esophagus (3.6%), pancreas (3.6%), cervical (3.6%), lymphoma (3.6%), bowel (3.6%), stomach (3.6%)
Passik et al 2004	3	HEC and MEC	Lung (26.7%), breast (26.7%), rectal/perianal (13.3%), lymphoma (13.3%), prostate (6.7%), multiple myeloma (6.7%)
	3		
	8		
	2		
Navari et al 2005	10	HEC	Breast (53.3%), Hodgkin's lymphoma (10%), bladder (3.3%), colon (1%), endometrium (3.3%)
	20	MEC	
Navari et al 2007	8	HEC	Lung (42.5%), breast (30.0%), colon (17.5%), bladder (5.0%), malignant lymphoma (5.0%)
	32	MEC	
Abe et al 2015	40	HEC	Cervical (50.0%), endometrial (47.5%), vulval (2.5%)
Park et al 2015	32	MEC	Breast (100%)

Study	Intervention	Patients (n)	Chemo emetogenicity	Complete Response			Complete Control		
				Acute	Delayed	Overall	Acute	Delayed	Overall
Passik et al 2002	OLN (2.5mg)	15	CHEMO and RAD therapy	n/a	n/a	15 (100%)	n/a	n/a	n/a
	OLN (5mg)			n/a	n/a	15 (100%)	n/a	n/a	n/a
	OLN (10mg)			n/a	n/a	15 (100%)	n/a	n/a	n/a
Passik et al 2003	OLN (2.5mg or 5mg) bid	28	HEC and MEC	n/a	n/a	n/a	n/a	n/a	n/a
Passik et al 2004	OLN (5mg qam) d -2 to 7	3	HEC and MEC	n/a	n/a	n/a	n/a	n/a	n/a
	OLN (5mg qam) d -2 to 1, OLN (10mg qam) d 1-7	3		n/a	n/a	n/a	n/a	n/a	n/a
	OLN (5mg qam) d -2 to 1, OLN (15mg qam) d 1-7	8		n/a	n/a	n/a	n/a	n/a	n/a
	OLN (10mg qam) d -2 to 1, OLN (15mg qam) d 1-7	2		n/a	n/a	n/a	n/a	n/a	n/a
Navari et al 2005	OLN (5mg PO) d -2 to -1, OLN (10mg PO) d 1-4, GRAN (10mcg/kg IV) d1, DEX (20mg IV) d1, DEX (8mg PO bid) d2-3, DEX (4mg PO BID) d4	10	HEC	10 (100%)	8 (80%)	8 (80%)	n/a	n/a	n/a
		20	MEC	20 (100%)	17 (85%)	17 (85%)	n/a	n/a	n/a
Navari et al 2007	DEX (20mg PO or IV) before chemo, PALO (0.25mg IV) before chemo, OLN (10mg PO) d1-4	8	HEC	8 (100%)	6 (75%)	6 (75%)	n/a	n/a	n/a
	DEX (8mg PO or IV) before chemo, PALO (0.25mg IV) before chemo, OLN (10mg PO) d1-4	32	MEC	31 (97%)	24 (75%)	23 (72%)	n/a	n/a	n/a
Abe et al 2015	PALO (0.75mg IV) before chemo, APR (125mg PO) before chemo and APR (80mg PO) d2-3, DEX (9.9mg IV) before chemo and DEX (8mg PO or 6.6mg IV) d2-4, OLN (5mg) d-1-5	40	HEC	39 (97.5%)	38 (95.0%)	37 (92.5%)	37 (92.5%)	35 (87.5%)	33 (82.5%)
Park et al 2015	PALO and OLN	32	MEC	30 (94%)	25 (78%)	24 (75%)	n/a	n/a	n/a
HEC Outcomes				57/58 (98.3%)	52/58 (89.7%)	51/58 (87.9%)	37/40 (92.5%)	35/40 (87.5%)	33/40 (82.5%)
MEC Outcomes				81/84 (96.4%)	66/84 (70.6%)	64/84 (76.2%)	n/a	n/a	n/a
TOTAL				138/142 (97.2%)	118/142 (83.1%)	130/157 (82.8%)	37/40 (92.5%)	35/40 (87.5%)	33/40 (82.5%)

Study	Intervention	Patients (n)	Chemo emetogenicity	No Nausea			No Emesis		
				Acute	Delayed	Overall	Acute	Delayed	Overall
Passik et al 2002	OLN (2.5mg)	15	CHEMO and RAD therapy	n/a	n/a	9 (60%)	n/a	n/a	15 (100%)
	OLN (5mg)			n/a	n/a	14 (93.3%)	n/a	n/a	15 (100%)
	OLN (10mg)			n/a	n/a	14 (93.3%)	n/a	n/a	15 (100%)
Passik et al 2003	OLN (2.5mg or 5mg) bid	28	HEC and MEC	n/a	n/a	17 (60.7%)	n/a	n/a	21 (75%)
Passik et al 2004	OLN (5mg qam) d -2 to 7	3	HEC and MEC	n/a	n/a	n/a	n/a	HEC: 4 of 6 (66.7%)	n/a
	OLN (5mg qam) d -2 to 1, OLN (10mg qam) d 1-7	3		n/a	n/a	n/a	n/a		n/a
	OLN (5mg qam) d -2 to 1, OLN (15mg qam) d 1-7	8		n/a	n/a	n/a	n/a		n/a
	OLN (10mg qam) d -2 to 1, OLN (15mg qam) d 1-7	2		n/a	n/a	n/a	n/a	MEC: 9 of 9 (100%)	n/a
Navari et al 2005	OLN (5mg PO) d -2 to -1, OLN (10mg PO) d 1-4, GRAN (10mcg/kg IV) d1, DEX (20mg IV) d1, DEX (8mg PO bid) d2-3, DEX (4mg PO BID) d4	10	HEC	10 (100%)	10 (100%)	10 (100%)	n/a	n/a	n/a
		20	MEC	17 (85%)	13 (65%)	13 (65%)	n/a	n/a	n/a
Navari et al 2007	DEX (20mg PO or IV) before chemo, PALO (0.25mg IV) before chemo, OLN (10mg PO) d1-4	8	HEC	8 (100%)	4 (50%)	4 (50%)	n/a	n/a	n/a
	DEX (8mg PO or IV) before chemo, PALO (0.25mg IV) before chemo, OLN (10mg PO) d1-4	32	MEC	32 (100%)	25 (78%)	25 (78%)	n/a	n/a	n/a
Abe et al 2015 (5)	PALO (0.75mg IV) before chemo, APR (125mg PO) before chemo and APR (80mg PO) d2-3, DEX (9.9mg IV) before chemo and DEX (8mg PO or 6.6mg IV) d2-4, OLN (5mg) d-1-5	40	HEC	35 (87.5%)	27 (67.5%)	27 (67.5%)	40 (100%)	39 (97.5%)	39 (97.5%)
Park et al 2015 (6)	PALO and OLN	32	MEC	n/a	n/a	n/a	n/a	n/a	n/a
HEC Outcomes				53/58 (91.4%)	41/58 (70.7%)	41/58 (70.7%)	40/40 (100%)	43/46 (93.5%)	39/40 (97.5%)
MEC Outcomes				49/52 (94.2%)	38/52 (73.1%)	38/52 (73.1%)	n/a	9/9 (100%)	n/a
TOTAL				102/110 (92.7%)	79/110 (71.8%)	108/153 (70.6%)	40/40 (100%)	52/55 (94.5%)	75/83 (90.4%)

Conclusions

- Olanzapine is efficacious and safe when used as a prophylaxis
- Olanzapine achieved higher rates of CC and no emesis endpoints and lower rates of CR in patients receiving MEC

We thank the generous support of Bratty Family Fund, Michael and Karyn Goldstein Cancer Research Fund, Joey and Mary Furfari Cancer Research Fund, Pulenzas Cancer Research Fund, Joseph and Silvana Melara Cancer Research Fund, and Ofelia Cancer Research Fund.