Table 1: Internet-Based-Survey of H/MEC for Standard Anti-Emetic

ClinRO Questionnaire for Current Antiemetics used in CINV		
This survey is conducted to assess the health status and HRQoL of patients who are allocated on current standard anti-emetics during administration of H/MEC in Egypt.		
Questions		Scoring format
Specify tumor type		
Mention standard anti-emetic regimen used in Egypt as a prophylaxis against CINV. (If Ondansetron is the standard, mention if is administered as a primary CINV prophylactic treatment or as a rescue medication)?		
Is standard anti-emetic administered with another antiemetic agents as NK1RA?		1. Yes 2. No 3. Other (please specify)
Primary outcome: QoL 1st domain (Performance of daily activities and being mentally and emotionally better	During complete response (CR), patients' functioning capability and ability to become emotionally better has which of the following assessment?	1. No limitation on patients' lives 2. Mild limitation on patients' lives 3. Moderate limitation on patients' lives 4. Severe limitation on patients' lives
	Evaluate effect of partial response on mental status of the patient (such as; depressed, afraid, discouraged, angry...)?	10-cm scale (0-10) (0 stands for badly affected mental health, 5 is mid-point average, 10 for nearly normal mental health).
Primary out-come: QoL 2nd domain (Appetite)	Assess psychological acceptance of patient toward meals during CR?	10-cm scale (0-10) (0 is no food acceptance, 5 is mid-point average, 10 stands for nearly normal appetite)
Primary out-come: QoL 3rd domain (Acceptance and trust toward anti-emetic)	During partial response, evaluate patients' confidence toward anti-emetic treatment?	10-cm scale (0-10) (0 is no confidence toward medication and desire to its discontinuation, 5 is mid-point average, 10 stands for medication acceptance).
Primary out-come: QoL 4th domain (Effect of antiemetic failure and discontinuation)	How hardship, suffering and pain due to antiemetic failure affect patients' lives?	1. Mild effect on patients' lives 2. Moderate effect on patients' lives 3. Severe effect on patients' lives 4. Very severe effect on patients' lives
	Mention number of events, in which patients could not take their medication due to emesis?	1. 2 or less 2. From 3 to 5 3. More than 5
	Estimate severity of N/V episode?	1. Mild severity, 2. Moderate severity 3. Extreme severity
	How did episodes of N/V affected patients' motivation to continue on medication?	1. No effect 2. Mild effect 3. Moderate effect 4. Severe effect

Secondary out-come: Improving adherence to chemotherapy	On a scale from 0 to 10, did medication improve the patients' adherence to chemotherapy?	10-cm scale (0-10) (0 stands for treatment discontinuation, 5 is mid-point average, 10 stands for adherence enhancement)
Secondary out-come: resources utilization	Did medication help in reduction of resources utilization?	1. Yes 2. No
Secondary out-come: good control from first cycle against delayed N/V and anticipatory N/V without rescue medications	Mention number of times that patient required to be allocated on rescue medications during a cycle of chemotherapy?	1. 2 or less 2. From 3 to 5 3. More than 5
	When is CINV mostly suspected to take place if preventative therapy fails?	1. Day 1 2. Day 2-3 3. Day 4-5 4. Further on
Secondary outcome: (factors that impact physicians to prescribe antiemetics)	What factors do you consider when prescribing CINV prophylactic treatment?	1. Patients' susceptibility to CINV 2. Emetogenicity of chemotherapy 3. Patients' socioeconomic status

ClinRO: clinician-reported outcome, CINV: chemotherapy induced nausea and vomiting, HRQoL: health related quality of life, H/MEC: highly and moderate emetogenic chemotherapy, NK-1RA: neurokinin-1 receptor antagonists, CR: complete response, N/V: nausea/vomiting

Table 2: Internet-Based-Survey of H/MEC for Palonosetron.

ClinRO Questionnaire for New Antiemetics used in CINV		
This survey is conducted to assess the health status and HRQoL of patients who are allocated on palonosetron during administration of H/MEC in Egypt.		
Questions		Scoring format
Specify tumor type		
Is palonosetron administered with another antiemetic agents as NK1RA?		1. Yes 2. No 3. Other (please specify)
Primary outcome: QoL 1st domain (Performance of daily activities and being mentally and emotionally better	During CR, patients' functioning capability and ability to become emotionally better has which of the following assessment?	1. No limitation on patients' lives 2. Mild limitation on patients' lives 3. Moderate limitation on patients' lives 4. Severe limitation on patients' lives
	Evaluate effect of partial response on mental status of the patient (such as; depressed, afraid, discouraged, angry...)?	10-cm scale (0-10) (0 stands for badly affected mental health, 5 is mid-point average, 10 for nearly normal mental health).
Primary out-come: QoL 2nd domain (Appetite)	Assess psychological acceptance of patient toward meals during CR?	10-cm scale (0-10) (0 is no food acceptance, 5 is mid-point average, 10 stands for nearly normal appetite)

Primary out-come: QoL 3rd domain (Acceptance and trust toward anti-emetic)	During partial response, evaluate patients' confidence toward anti-emetic treatment?	10-cm scale (0-10) (0 is no confidence toward medication and desire to its discontinuation, 5 is mid-point average, 10 stands for medication acceptance).
Primary out-come: QoL 4th domain (Effect of antiemetic failure and discontinuation)	How hardship, suffering and pain due to anti-emetic failure affect patients' lives?	1. Mild effect on patients' lives 2. Moderate effect on patients' lives 3. Severe effect on patients' lives 4. Very severe effect on patients' lives
	Mention number of events, in which patients could not take their medication due to emesis?	1. 2 or less 2. From 3 to 5 3. More than 5
	Estimate severity of N/V episode?	1. Mild severity 2. Moderate severity 3. Extreme severity
	How did episodes of N/V affected patients' motivation to continue on medication?	1. No effect 2. Mild effect 3. Moderate effect 4. Severe effect
Secondary out-come: Improving adherence to chemotherapy	On a scale from 0 to 10, did medication improve the patients' adherence to chemotherapy?	10-cm scale (0-10) (0 stands for treatment discontinuation, 5 is mid-point average, 10 stands for adherence enhancement)
Secondary out-come: resources utilization	Did medication help in reduction of resources utilization due to less cardiotoxicity events?	1. Yes 2. No
Secondary out-come: good control from first cycle against delayed N/V and anticipatory N/V without rescue medications	Mention number of times that patient required to be allocated on rescue medications during a cycle of chemotherapy?	1. 2 or less 2. From 3 to 5 3. More than 5
	When is CINV mostly suspected to take place if preventative therapy fails?	1. Day 1 2. Day 2-3 3. Day 4-5 4. Further on
Secondary out-come: (factors that motivates physicians to prescribe antiemetics)	What factors do you consider when prescribing CINV prophylactic treatment?	1. Patients' susceptibility to CINV 2. Emetogenicity of chemotherapy 3. Patients' socioeconomic status

ClinRO: clinician-reported outcome, CINV: chemotherapy induced nausea and vomiting, HRQoL: health related quality of life, H/MEC: highly and moderate emetogenic chemotherapy, NK-1RA: neurokinin-1 receptor antagonists, N/V: nausea/vomiting, CR: complete response

Results

The total number of responses are 42 for both HEC and MEC surveys in both treatment arms generated by 11 responders/experts; eleven responses for HEC in each treatment arm (22 responses) and ten responses for MEC in each treatment arm (20 responses). All institutions adopt HEC and MEC regimens except Breast Cancer Institute, New Cairo, did not adopt MEC regimen within the last six months.

Basic demographics

In MEC, the most common types of cancer presented in palonosetron arm were breast cancer (50%, 5 respondents), colon cancer (20%, 2 respondents), bronchogenic cancer (10%, 1 respondent), stage-three ovarian cancer (10%, 1 respondent) and lung cancer (10%, 1 respondent). The concomitant prophylactic anti-emetics used with palonosetron among MEC were aprepitant (40%), ondansetron (10%), aprepitant (10%) in some cases and the other 4 respondents (40%) did not report any concomitant anti-emetic.

In MEC, the most common types of cancer presented in SoC arm were breast cancer (27.2%), ovarian cancer (9.1%), bronchogenic cancer (9.1%), uterine cancer (9.1%), malignant lymphoma (9.1 %), colon cancer (9.1%), lung cancer (9.1%), Ewing sarcoma (9.1%) and head and neck cancer (9.1%). The concomitant prophylactic anti-emetics used with SoC among MEC were aprepitant (30%), NK1RA (10%) in some cases and 6 respondents (60%) did not report any concomitant anti-emetic. The standardized prophylactic anti-emetic medications received were ondansetron (45.45%), granisetron (27.27%), aprepitant (9.1%), and ondansetron or granisetron plus dexamethasone (18.18%).

In HEC, the most common types of cancer presented in palonosetron arm were breast cancer (54.5%), colon cancer (9.1%), bronchogenic cancer (9.1%), ovarian cancer (9.1%), lung cancer (9.1%), and head and neck cancer (9.1%). The concomitant prophylactic anti-emetics used with palonosetron among HEC were aprepitant (81.82%), aprepitant (9.09%) in some cases and 1 respondent (9.09%) did not report any concomitant anti-emetic.

In HEC, the most common types of cancer presented in SoC arm were breast cancer (45.4%), bronchogenic cancer (9.1%), non-Hodgkin lymphoma (NHL; 9.1%), larynx cancer (9.1%), stomach cancer (9.1%), lung cancer (9.1%), and head and neck cancer (9.1%). The concomitant prophylactic anti-emetics used with SoC among HEC were aprepitant (81.82%), and 2 respondents (18.18%) did not report any concomitant anti-emetic. The standardized prophylactic anti-emetic medications received were ondansetron (45.5%), granisetron (18.2%), aprepitant (9.1%), and ondansetron or granisetron plus dexamethasone (27.2%).

ClinRO Results for MEC in CINV

The total score of ClinRO (sum of primary outcome sub-scores) of palonosetron vs SoC in MEC were 21.4 vs 20 out of 27, respectively (Table 3). Palonosetron has a better response in functioning capability and emotionally wellbeing, significant food tolerance and less severe hardship after treatment failure due to less severe N/V episodes. Both treatments showed similar effect in mental status during partial response.

Palonosetron showed better adherence, less use of rescue medications and more protection against delayed CINV. Emetogenicity of chemotherapy was the most common factor reported when prescribing CINV prophylactic treatment during MEC regimen. These secondary outcomes align with the results of the primary outcomes.

Table 3: ClinRO Results for MEC in CINV (10 respondents)

Outcome	Palonosetron	SoC
(A) Primary Outcome		
1a-In CR, patients' functioning capability and ability to become emotionally better		
No impact on patients' lives	6 respondents (60%)	4 respondents (40%)
Mild impact on patients' lives	4 respondents (40%)	4 respondents (40%)
Moderate impact on patients' lives	0%	2 respondents (20%)
Severe impact on patients' lives	0%	0%
Mean Score	3.6 out of 4 (±0.52)	3.2 out of 4 (±0.79)
1b-Effect of partial response on mental status of the patient 0=deteriorated mental health, 10=normal mental health		
	7 (moderate deterioration)	7 (moderate deterioration)
Mean Score (*P value*=0.70394)	2	2
2-Psychological acceptance of patient toward meals in CR 0=no food acceptance, 10=normal appetite		
	9 (normal)	7 (moderate)
Mean Score (*P value*=0.02574)	3	2
3-In partial response, patients' confidence toward anti-emetic treatment		

0= discontinuation, 10=medication acceptance		
	7 (moderate)	8 (normal)
Mean Score (*P value*=0.9124)	2	3
4a-Suffering and pain due to anti-emetic failure affect patients' lives		
Mild effect on patients' lives	3 respondents (30%)	2 respondents (20%)
Moderate effect on patients' lives	3 respondents (30%)	3 respondents (30%)
Severe effect on patients' lives	4 respondents (40%)	5 respondents (50%)
Very severe effect on patients' lives	0%	0%
Mean Score	2.9 out of 4 (± 0.88)	2.7 out of 4 (± 0.82)
4b-Number of events, in which patients could not take their medication due to emesis		
2 events or less	7 respondents (70%)	3 respondents (30%)
3 – 5 events	3 respondents (30%)	5 respondents (50%)
> 5 events	0%	2 respondents (20%)
Mean Score	2.7 out of 3 (± 0.48)	2.1 out of 3 (± 0.74)
4c-Severity of N/V episode		
Mild severity	7 respondents (70%)	4 respondents (40%)
Moderate severity	3 respondents (30%)	5 respondents (50%)
Extreme severity	0%	1 respondent (10%)
Mean Score	2.7 out of 3 (± 0.48)	2.3 out of 3 (± 0.67)
4d-Episodes of N/V affected patients' motivation to continue on medication		
No effect	0%	1 respondent (10%)
Mild effect	5 respondents (50%)	5 respondents (50%)
Moderate effect	5 respondents (50%)	4 respondents (40%)
Severe effect	0%	0%
Mean Score	2.5 out of 4 (± 0.53)	2.7 out of 4 (SD ± 0.67)
(B) Secondary Outcome		
1-Improvement of the patients' adherence to chemotherapy (0 = discontinuation, 10 = adherence enhancement)		
	9	8
2-Reduction of resources utilization due to less cardiotoxicity events in Palonosetron only		
Yes	8 respondents (80%)	8 respondents (80%)
No	2 respondents (20%)	2 respondents (20%)
3-Frequency of patients allocated on rescue medications during chemotherapy		
2 events or less	9 respondents (90%)	3 respondents (30%)
3 – 5 events	1 respondent (10%)	6 respondents (60%)
> 5 events	0%	1 respondent (10%)
Time of CINV occurred upon failure of preventative therapy		
Day 1	2 respondents (20%)	1 respondent (10%)
Day 2-3	3 respondents (30%)	9 respondents (90%)
Day 4-5	2 respondents (20%)	
Further on	3 respondents (30%)	
4-Additional factors considered in prescribing CINV prophylactic treatment		
Patients' susceptibility to CINV	2 respondents (20%)	1 respondent (10%)
Emetogenicity of chemotherapy	8 respondents (80%)	9 respondents (90%)
Patients' socioeconomic status	0%	0%

ClinRO: clinician-reported outcome, CINV: chemotherapy induced nausea and vomiting, QoL: quality of life, MEC: moderate emetogenic chemotherapy, NK-1RA: neurokinin-1 receptor antagonists, CR: complete response, 5-HT3RA: 5-hydroxytryptamine receptor antagonist

ClinRO Results for HEC in CINV

In HEC, palonosetron as a prophylactic anti-emetic in CINV vs SoC generated a ClinRO score of 22.4 vs 20.1 out of 27, respectively (Table 4). Palonosetron has a better response in functioning

capability and emotionally wellbeing, patient continuity on their anti-emetic medications, and less severe hardship after treatment failure due to less N/V episodes. Both treatments showed similar effect in mental status, acceptance of anti-emetic during partial response, and food tolerance during CR.

Palonosetron showed better adherence, less use of rescue medications and more protection against delayed CINV. Emetogenicity of chemotherapy was the most common factor reported when prescribing CINV prophylactic treatment during HEC regimen. These secondary outcomes align with the results of the primary outcomes. Thus, palonosetron proved its HRQoL improvement in patients allocated on both M/HEC compared to standard of care.

Table 4: ClinRO Results for HEC in CINV (11 respondents)

Outcome	Palonosetron	SoC
(A) Primary Outcome		
1a-In CR, patients' functioning capability and ability to become emotionally better		
No impact on patients' lives	7 respondents (63.6%)	6 respondents (54.5%)
Mild impact on patients' lives	4 respondents (36.4%)	2 respondents (18.2%)
Moderate impact on patients' lives	0%	2 respondents (18.2%)
Severe impact on patients' lives	0%	1 respondent (9.1%)
Mean Score	3.6 out of 4 (±0.5)	3.2 out of 4 (±1.08)
1b-Effect of partial response on mental status of the patient 0=deteriorated mental health, 10=normal mental health		
	7 (moderate deterioration)	7 (moderate deterioration)
Mean Score (*p-value* = 0.7414)	2	2
2-Psychological acceptance of patient toward meals in CR 0=no food acceptance, 10=normal appetite		
	8 (normal)	8 (normal)
Mean Score (*P value* = 0.71884)	3	3
3-In partial response, patients' confidence toward anti-emetic treatment 0= discontinuation, 10=medication acceptance		
	7 (moderate)	7 (moderate)
Mean Score (*p-value* = 0.97606)	2	2
4a-Suffering and pain due to anti-emetic failure affect patients' lives		
Mild effect on patients' lives	5 respondents (45.5%)	4 respondents (36.4%)
Moderate effect on patients' lives	2 respondents (18.2%)	2 respondents (18.2%)
Severe effect on patients' lives	4 respondents (36.3%)	4 respondents (36.4%)
Very severe effect on patients' lives	0%	1 respondent (9%)
Mean Score	3.1 out of 4 (± 0.94)	2.8 out of 4 (± 1.08)
4b-Number of events, in which patients could not take their medication due to emesis		
2 events or less	10 respondents (90.9%)	6 respondents (54.5%)
3 – 5 events	1 respondent (9.1%)	2 respondents (18.2%)
> 5 events	0%	3 respondents (27.3%)
Mean Score	of 2.9 out of 3 (± 0.3)	2.3 out of 3 (± 0.9)
4c-Severity of N/V episode		

Mild severity	9 respondents (81.8%)	6 respondents (54.5%)
Moderate severity	2 respondents (18.2%)	2 respondents (18.2%)
Extreme severity	0%	3 respondents (27.3%)
Mean Score	2.8 out of 3 (± 0.40)	2.3 out of 3 (± 0.90)
4d-Episodes of N/V affected patients' motivation to continue on medication		
No effect	5 respondents (45.5%)	3 respondents (27.3%)
Mild effect	1 respondent (9%)	2 respondents (18.2%)
Moderate effect	5 respondents (45.5%)	4 respondents (36.3%)
Severe effect	0%	2 respondents (18.2%)
Mean Score	3 out of 4 (± 1)	2.5 out of 4 (± 1.13)
(B) Secondary Outcome		
1-Improvement of the patients' adherence to chemotherapy (0 = discontinuation, 10 = adherence enhancement)		
	9	7
2-Reduction of resources utilization due to less cardiotoxicity events in Palonosetron only		
Yes	10 respondents (90.9%)	9 respondents (81.8%)
No	1 respondent (9.1%)	2 respondents (18.2%)
3-Frequency of patients allocated on rescue medications during chemotherapy		
2 events or less	9 respondents (81.8%)	4 respondents (36.4%)
3 – 5 events	1 respondent (9.1%)	3 respondents (27.2%)
> 5 events	1 respondent (9.1%)	4 respondents (36.4%)
Time of CINV occurred upon failure of preventative therapy		
Day 1	4 respondents (36.4%)	3 respondents (27.3%)
Day 2-3	3 respondents (27.3%)	3 respondents (27.3%)
Day 4-5	3 respondents (27.3%)	4 respondents (36.4%)
Further on	1 respondent (9%)	1 respondent (9%)
4-Additional factors considered in prescribing CINV prophylactic treatment		
Patients' susceptibility to CINV	4 respondents (36.4%)	3 respondents (27.3%)
Emetogenicity of chemotherapy	7 respondents (63.6%)	8 respondents (72.7%)
Patients' socioeconomic status	0%	0%

ClinRO: clinician-reported outcome, CINV: chemotherapy induced nausea and vomiting, HEC: highly emetogenic chemotherapy, CR: complete response, N/V: nausea/vomiting, SoC: standard of care