VYLOY®
Administration Manual

Hokkaido Cancer Center,
Sapporo, Hokkaido, Japan

Document created on November 1, 2024

Tips for Effectively Using Zolbetuximab (VYLOY®)

01

The combination regimen of **VYLOY®** plus chemotherapy (mFOLFOX6 or CAPOX) is appropriately classified as high emetic risk (HEC) .

02

The first episode of nausea and vomiting often occur within 1 hour of starting **VYLOY®** administration, so prophylactic antiemetics and early intervention are important.
Particular attention is needed for nausea and vomiting, especially in the initial treatment.

03

There is a correlation between the infusion rate of **VYLOY®** and its emetic potential, and adjusting the infusion rate may help reduce emesis.

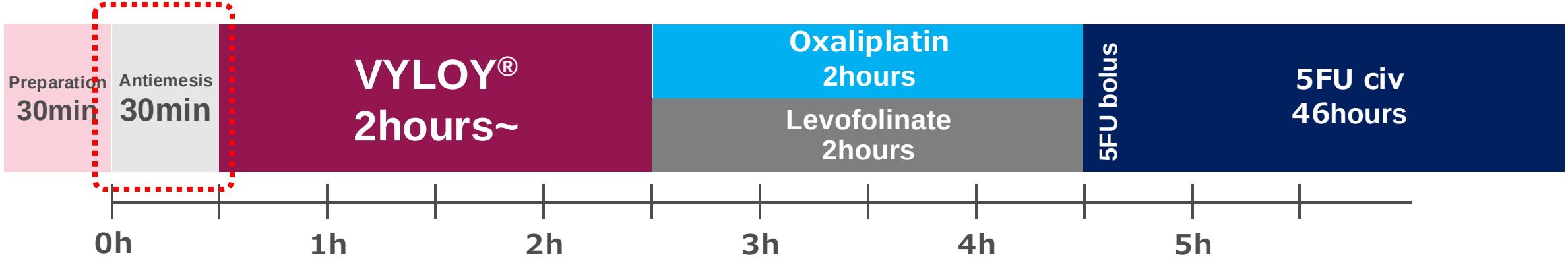
04

It's difficult to quickly assess the grade of nausea and vomiting.
We have decided to use **Face Rating Scale** to assess the grade of nausea and vomiting at our hospital.

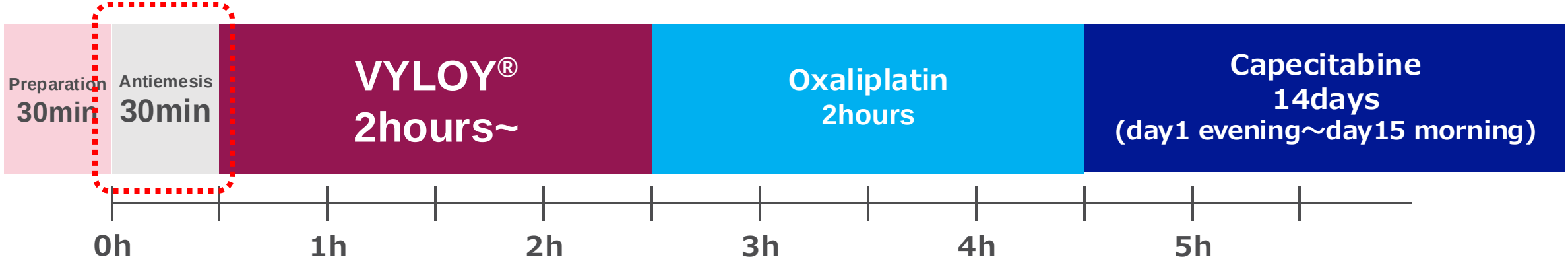
Antiemetic therapy

Chemotherapy containing Zolbetuximab (VYLOY®)

VYLOY®+mFOLFOX6

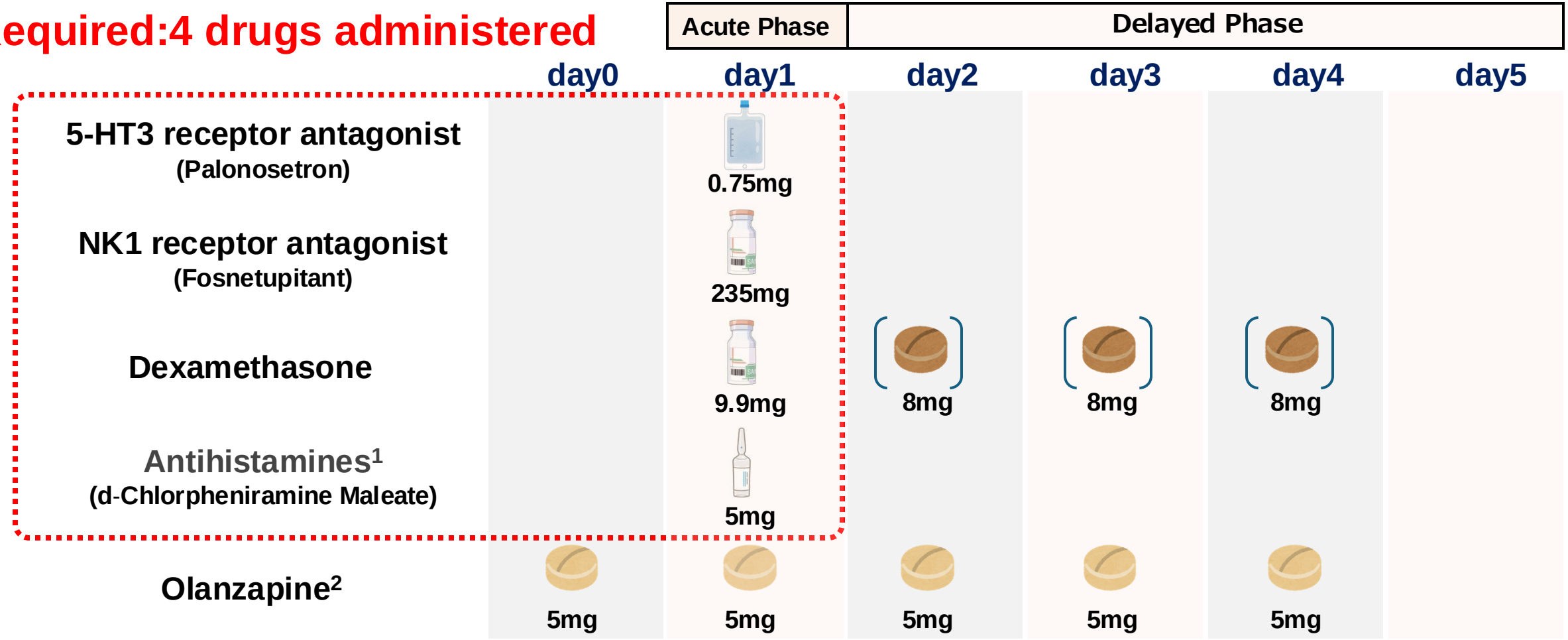


VYLOY®+CAPOX



Schematic diagram of antiemetic treatments for Zolbetuximab (VYLOY ®)

Required:4 drugs administered



Antihistamines[1]: In previous clinical trials of antiemetic therapy, the antiemetic effect of antihistamines has not been clearly established. However, according to the observations of the participating physicians, the drowsiness caused by antihistamines may have contributed to the antiemetic effect.

Olanzapine[2]: ① N/V caused by **VYLOY®** often occur early after administration, so administering olanzapine in the evening or before bedtime on the day of chemotherapy may be insufficient. It is necessary to consider additional doses of olanzapine the night before or in the morning on the day of administration.
② In case of the efficacy of this approach in the delayed phase was insufficient at the time of the first treatment cycle, consider administering olanzapine.

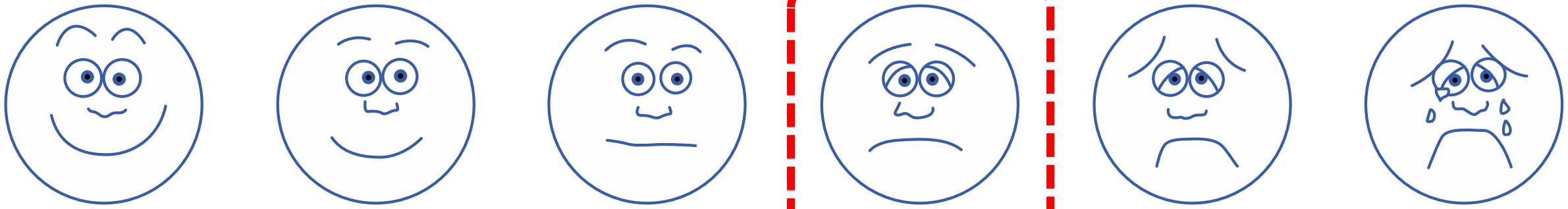
Other : For managing stomach pain, taking PPI orally from the day before, or administering H2 blocker (e.g., famotidine) 1A intravenously on the day of treatment.

Flexible modifications are necessary, depending on the specific condition of each patient.

Criteria for Nausea and Vomiting

For nurses

Wong-Baker FACES® Pain Rating Scale



0	1	2	3	4	5
No Nausea	Nausea Little Bit	Nausea Little More	Nausea Even More	Nausea Whole Lot	Nausea Worst

Nausea Grade 2 (CTCAE) equivalent

***Face Rating Scale（FRS）**

This is a method to judge the intensity of pain from the patient's facial expression.
It is mainly used in elderly people and children when it is difficult for them to answer questions using the Visual Analogue Scale (VAS) or Numerical Rating Scale (NRS).
The pain assessment method **Face Rating Scale** was applied to the criteria for judging nausea and vomiting.
The 6 participants who created this manual were asked to vote whether CTCAE Nausea G2 corresponds to Scale 0~5 of the **Face Rating Scale**.
Scale 3 was judged to be equivalent to Nausea G2 (6/6:100%)
There are 6-point scales (0-5) and 11-point scales (0-10), we use the simpler 6-point scale.

https://wongbakerfaces.org/wp-content/uploads/2015/02/FACES_Japanese_0-5_Blue.pdf

Appendix

Schematic diagram of antiemetic treatments for High emetic risk

5-HT3 receptor antagonist BQ2 BQ1

+

NK1 receptor antagonist

+

Dexamethasone CQ2

+

Olanzapin CQ1

Other adjunct medications

- **Lorazepam**
- **H2 block or Proton Pump Inhibitor**

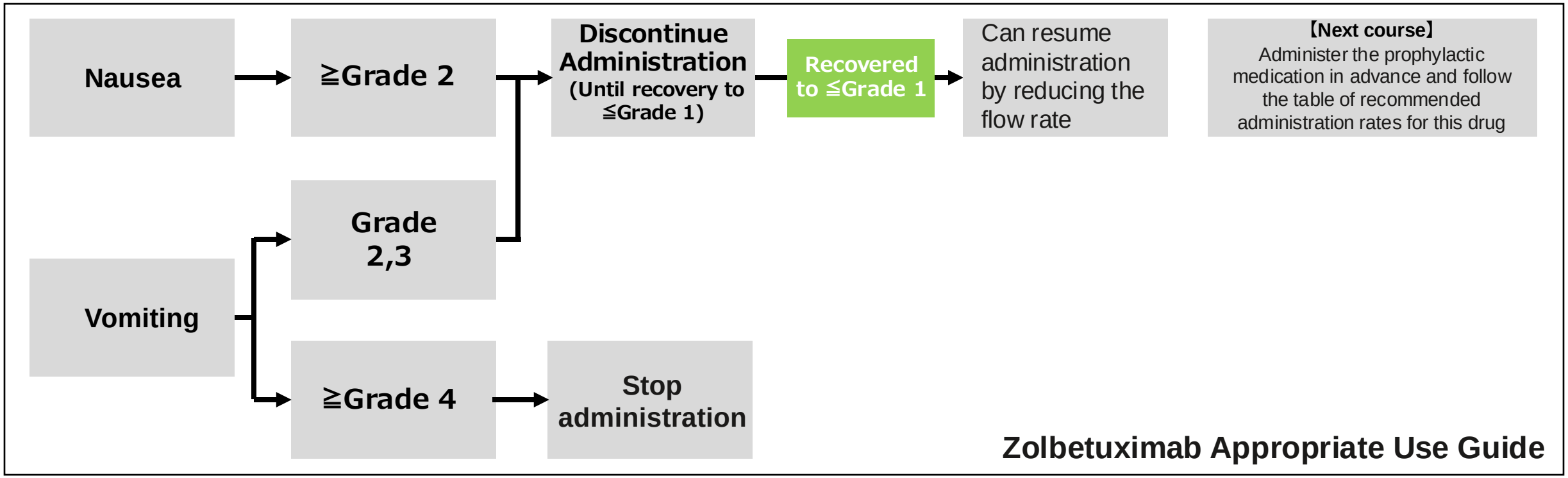
→ **Antiemetic therapy for breakthrough nausea and vomiting** CQ8

CQ1	We recommend the addition or concurrent use of **olanzapine** to a triplet antiemetic regimen to prevent nausea and vomiting associated with antineoplastic agents with high emetogenic risk.
CQ2	We suggest shortening the duration of **dexamethasone** administration to one day to prevent the nausea and vomiting associated with antineoplastic agents with a high emetogenic risk, especially in the case of AC regimens.
CQ8	We suggest the administration of **metoclopramide** for breakthrough nausea and vomiting.
BQ1	For highly emetogenic risk antineoplastic agents, a four-drug combination therapy using **olanzapine**, a **5-HT3 receptor antagonist**, an **NK1 receptor antagonist**, and **dexamethasone** is administered. In cases where the use of olanzapine is challenging, a three-drug combination therapy with a 5-HT3 receptor antagonist, an NK1 receptor antagonist, and dexamethasone is administered.
BQ2	For highly emetogenic risk antineoplastic agents, in the context of three-drug combination therapy, the acute antiemetic effect is nearly equivalent between first-generation (e.g., granisetron) and second-generation (e.g., palonosetron) agents. However, there is a tendency for palonosetron to exhibit a better delayed antiemetic effect. In cases of four-drug combination therapy, either first-generation or second-generation agents can be chosen. Yet, in situations where it is necessary to shorten the administration period of dexamethasone or when the use of olanzapine is challenging, palonosetron is prioritized

2023 Japan Society of clinical oncology clinical practice guidelines update for antiemesis

International Journal of Clinical Oncology (2024) 29:873–888

Guidelines for Interruption or Discontinuation of the Drug in Case of Adverse Effects



Nausea・Vomiting Grade classification (NCI-CTCAE ver. 5.0)

AE	Grade1	Grade2	Grade3	Grade4	Grade5	Definition
Nausea	Loss of appetite without alteration in eating habits	Oral intake decreased without significant weight loss, dehydration or malnutrition	Inadequate oral caloric or fluid intake; tube feeding, TPN, or hospitalization indicated	-	-	A disorder characterized by a queasy sensation and/or the urge to vomit.
Vomiting	Intervention not indicated	Outpatient IV hydration; medical intervention indicated	Tube feeding, TPN, or hospitalization indicated	Life-threatening consequences	Death	A disorder characterized by the reflexive act of ejecting the contents of the stomach through the mouth.

Nausea・Vomiting Grade classification (NCI-CTCAE)

Nausea・Vomiting Grade classification (NCI-CTCAE ver. 5.0)

AE	Grade1	Grade2	Grade3	Grade4	Grade5	Definition
Nausea	Loss of appetite without alteration in eating habits	Oral intake decreased without significant weight loss, dehydration or malnutrition	Inadequate oral caloric or fluid intake; tube feeding, TPN, or hospitalization indicated	-	-	A disorder characterized by a queasy sensation and/or the urge to vomit.
Vomiting	Intervention not indicated	Outpatient IV hydration; medical intervention indicated	Tube feeding, TPN, or hospitalization indicated	Life-threatening consequences	Death	A disorder characterized by the reflexive act of ejecting the contents of the stomach through the mouth.

Nausea・Vomiting Grade classification (NCI-CTCAE ver. 4.0)

AE	Grade1	Grade2	Grade3	Grade4	Grade5	Definition
Nausea	Loss of appetite without alteration in eating habits	Oral intake decreased without significant weight loss, dehydration or malnutrition	Inadequate oral caloric or fluid intake; tube feeding, TPN, or hospitalization indicated	-	-	A disorder characterized by a queasy sensation and/or the urge to vomit.
Vomiting	1 - 2 episodes (separated by 5 minutes) in 24 hrs	3 - 5 episodes (separated by 5 minutes) in 24 hrs	>=6 episodes (separated by 5minutes) in 24 hrs; tube feeding, TPN or hospitalization indicated	Life-threatening consequences; urgent intervention indicated	Death	A disorder characterized by the reflexive act of ejecting the contents of the stomach through the mouth.

List of antiemetics mentioned in the guidelines (Japan)

Classification	Drug name	Dosage form	Approved dosage in Japan
Corticosteroids	**Dexamethason**	injection	3.3～16.5 mg per day, divided into 1 to 2 doses, IV or DIV
		tablet	4～20 mg per day, divided into 1 to 2 doses, PO
	methylprednisolone	injection	250 mg, 2 times daily, DIV
5-HT3 receptor antagonist (1st generation)	**Azasetron**	injection	10 mg (as hydrochloride), , once daily, PO
		tablet	10～15 mg (as hydrochloride), once daily, PO
	Indisetron	tablet	8 mg (as hydrochloride) , once daily, PO
	Ondansetron	injection	4 mg, once daily, slowly IV
		tablet	4 mg, once daily, PO If the effect is insufficient, the same dose, IV
	Granisetron	injection	40 μg/kg, once daily, IV or DIV
		tablet	2 mg, once daily, PO
	Ramosetron	injection	0.3 mg (as hydrochloride), once daily, IV
		tablet	0.1 mg (as hydrochloride), once daily, PO
(2nd generation)	**Palonosetron**	injection	0.75 mg, once daily, IV or DIV
NK1 receptor antagonist	**Aprepitant**	capsule	125 mg on day1, 80 mg on day2&3, once daily, PO
	Fosaprepitant	injection	150 mg on day1, once daily, DIV
	Fosnetupitant (Arokaris®)	injection	235 mg on day1, once daily, DIV

http://www.jsco-cpg.jp/guideline/29.html

List of antiemetics mentioned in the guidelines (Japan)

Classification	Drug name	Dosage form	Approved dosage in Japan
Dopamine D2 receptor antagonist	**Domperidone** (Nauzelin®)	tablet	10 mg, 3 times daily before meals, PO
		Suppository	60 mg, 2 times daily, Rectal administration
	Metoclopramide (Primperan®)	injection	7.67 mg, 1~2 times daily, IM or IV
		tablet	7.67～23.04 mg per day, divided into 2 to 3 doses, before meals, PO
Benzodiazepine anxiolytic	**Alprazolam** (Solanax®)	tablet	0.4～0.8 mg, the night before the treatment and on the morning of the treatment (1 to 2 hours before the treatment) , PO
	Lorazepam (WYPAX®)	tablet	0.5～1.5 mg, the night before the treatment and on the morning of the treatment (1 to 2 hours before the treatment) , PO
Phenothiazine antipsychotics (Dopamine D2 receptor antagonistic action)	**Prochlorperazine** (Novamin®)	injection	5 mg, once daily, IM
		tablet	5～20 mg per day, divided into 1 to 4 doses, PO
	Chlorpromazine (Contomin®)	injection	10～50 mg (as hydrochloride), slowly IM
		tablet	25～75 mg (as hydrochloride) per day, divided into 2 to 3 doses, PO
Butyrophenone antipsychotics (Dopamine D2 receptor antagonistic action)	**Haloperidol** (Serenace®)	injection	0.5～2 mg, every 4 to 6 hours, IV
		tablet	0.5～2 mg, every 4 to 6 hours, PO
Benzisoxazole antipsychotics (Dopamine D2 receptor antagonistic action)	**Risperidone** (Risperdal®)	tablet liquid	1.0～1.5 mg, once daily, at bedtime, PO
Multireceptor acting antipsychotics (Dopamine D2, Histamine H1, and 5-HT3 receptor antagonistic action)	**Olanzapin (Zyprexa®)**	tablet	5～10 mg, once daily, PO
Propylamine antihistamines	**Chlorpheniramine** (Polaramine®)	injection	5 mg (as a maleate) , 3～4 times daily, IV or SC
		powder	2～6 mg (as a maleate), 2～4 times daily, PO

http://www.jsco-cpg.jp/guideline/29.html

Wong-Baker FACES® Pain Rating Scale

For Patients

0

No Nausea

1

Nausea Little Bit

2

Nausea Little More

3

Nausea Even More

4

Nausea Whole Lot

5

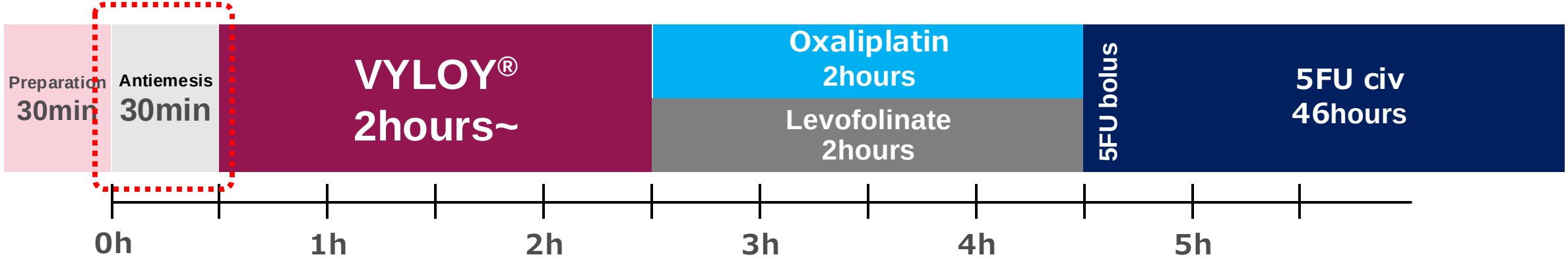
Nausea Worst

https://wongbakerfaces.org/wp-content/uploads/2015/02/FACES_Japanese_0-5_Blue.pdf

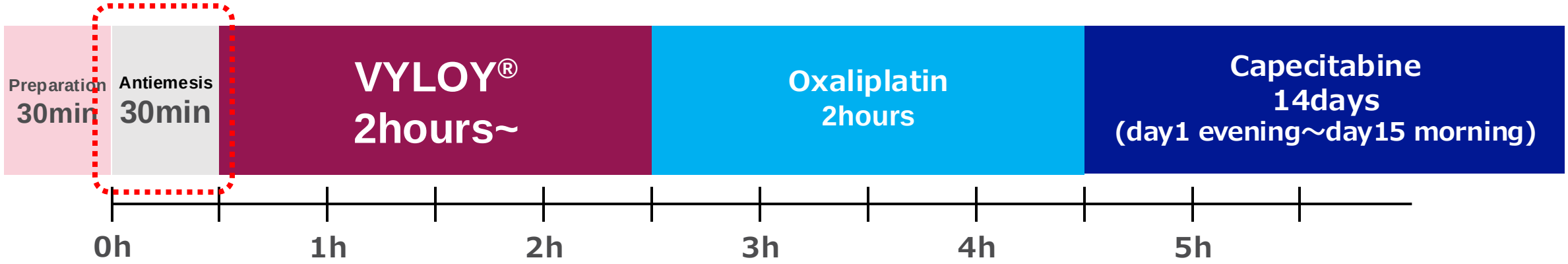
VYLOY®
Administration rate/ Infusion rate

Chemotherapy containing Zolbetuximab (VYLOY®)

VYLOY®+mFOLFOX6



VYLOY®+CAPOX



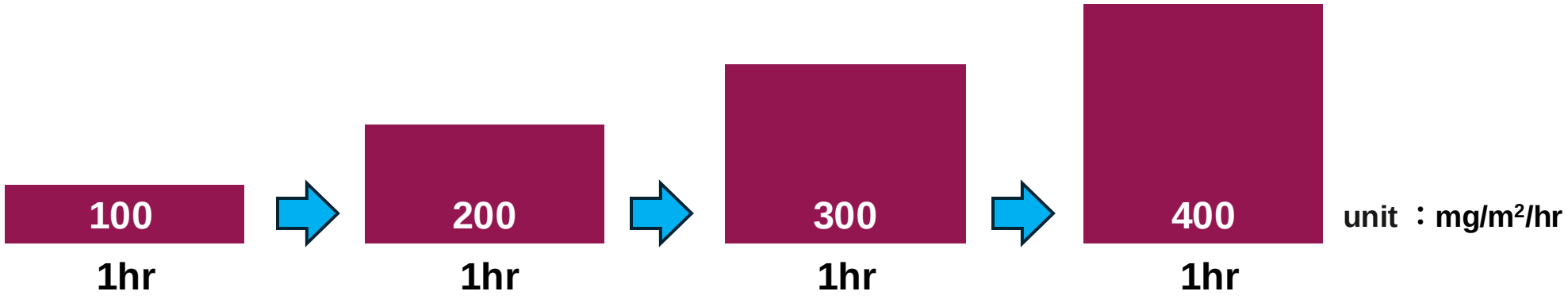
Zolbetuximab (VYLOY®) administration rate

Recommended administration rate of this drug

dosage		administration rate	
		from 30 to 60 minutes after the administration start	subsequently
1st cycle	800 mg/m²	100 mg/m²/hr	200~400 mg/m²/hr
2nd cycle~	600 mg/m² (every 3weeks)	75 mg/m²/hr	150~300 mg/m²/hr
	400 mg/m² (every 2weeks)	50 mg/m²/hr	100~200 mg/m²/hr

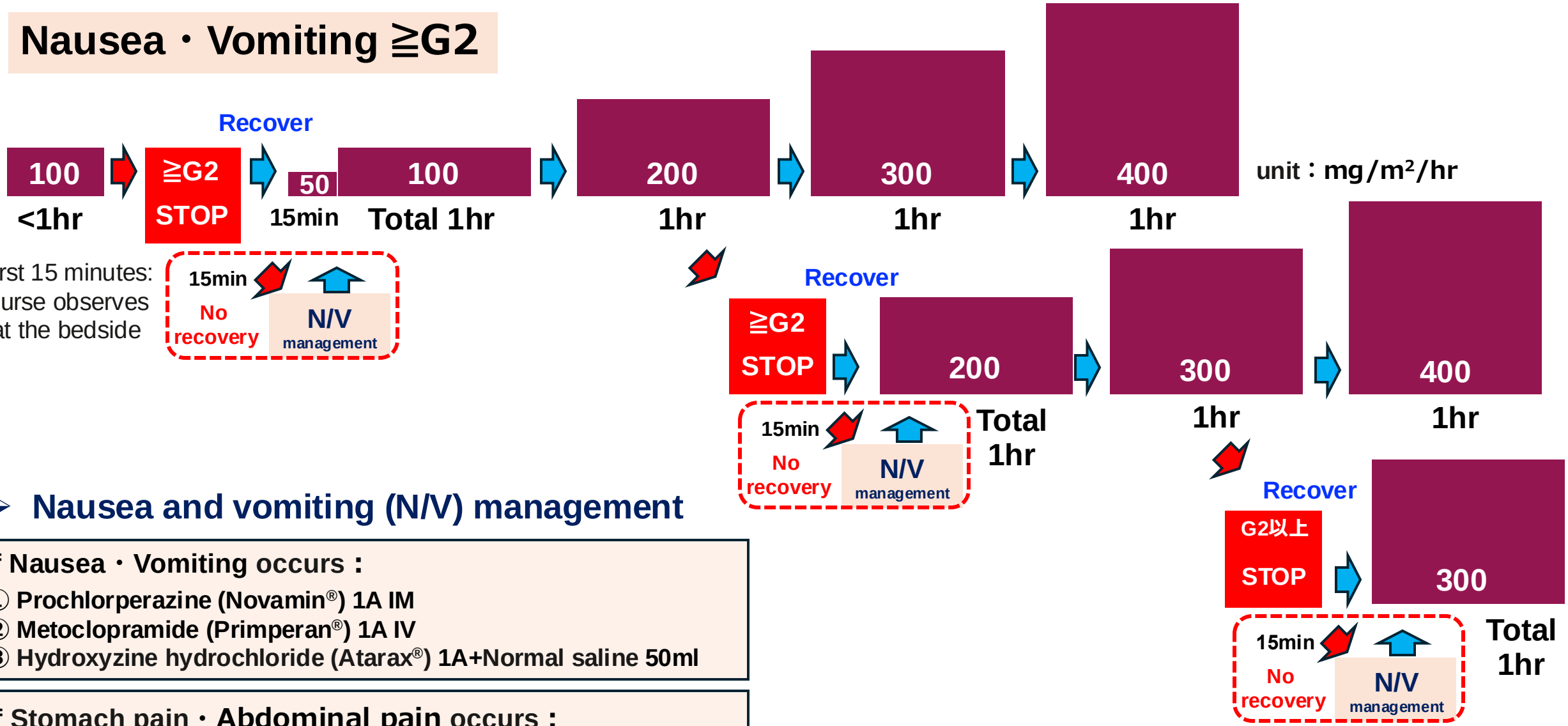
Zolbetuximab Appropriate Use Guide

Nausea・ Vomiting ≦G1



Administration rate of Zolbetuximab (VYLOY®) and Management of nausea and vomiting

Nausea・Vomiting ≧G2



➢ Nausea and vomiting (N/V) management

If Nausea・Vomiting occurs：

① Prochlorperazine (Novamin®) 1A IM
② Metoclopramide (Primperan®) 1A IV
③ Hydroxyzine hydrochloride (Atarax®) 1A+Normal saline 50ml

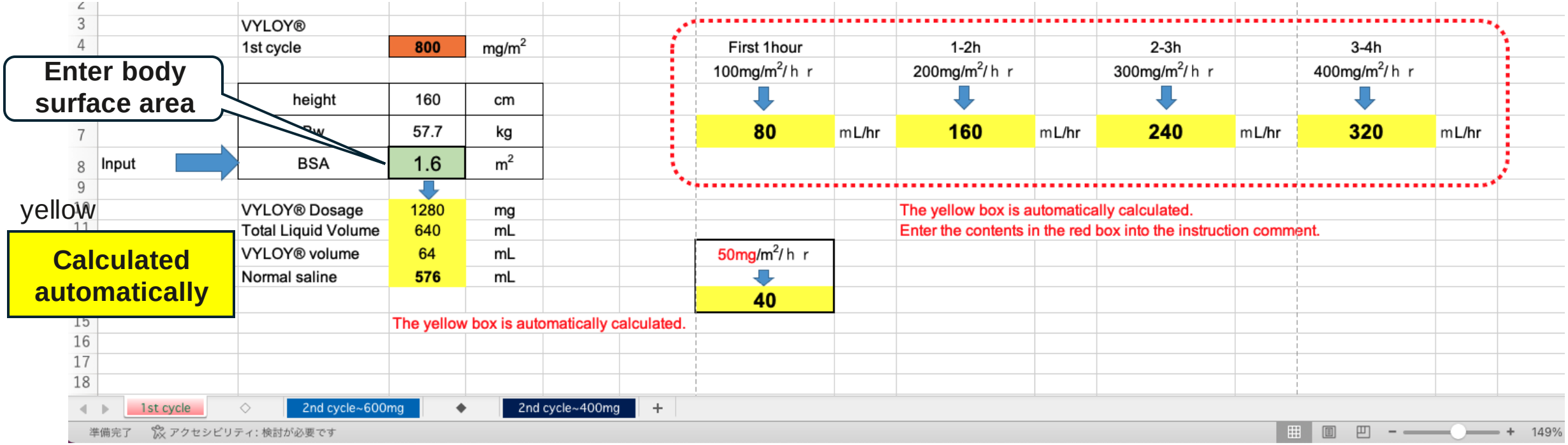
If Stomach pain・Abdominal pain occurs：

① Acetaminophen (acelio Bag for Intravenous Injection 1000mg®)
② Flurbiprofen Axetil (Lopion 50mg®) + Normal saline 50ml

We are actually operating “in ml/hr” :
please refer to the attached document.

Zolbetuximab (VYLOY®) Dosage Calculation Formula

Prepare the solution of Zolbetuximab (VYLOY®) to a concentration of 2.0 mg/mL

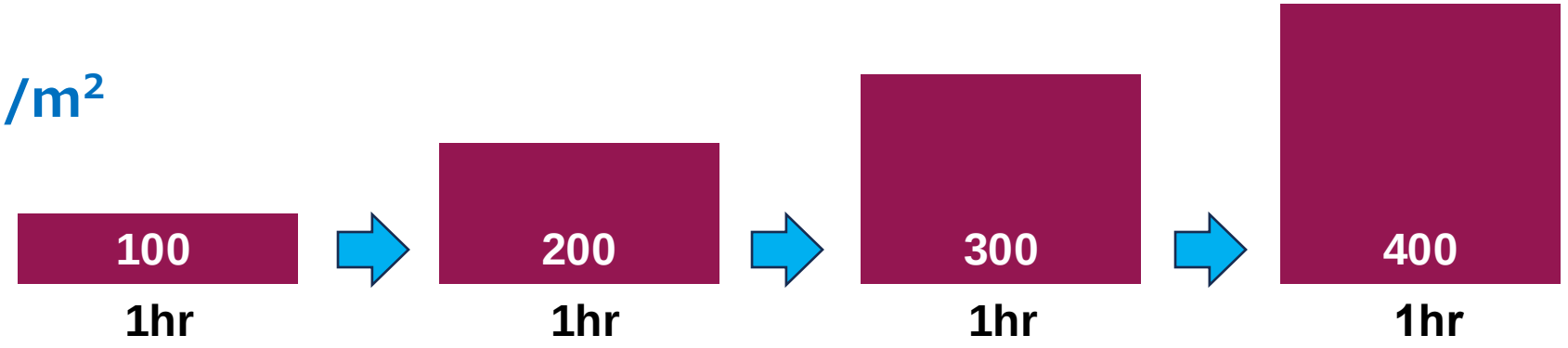


Created by ***Shinya Takada***, Ph.D., Department of Pharmacy, National Hospital Organization Hokkaido Cancer Center

Zolbetuximab (VYLOY®) administration rate

1st cycle

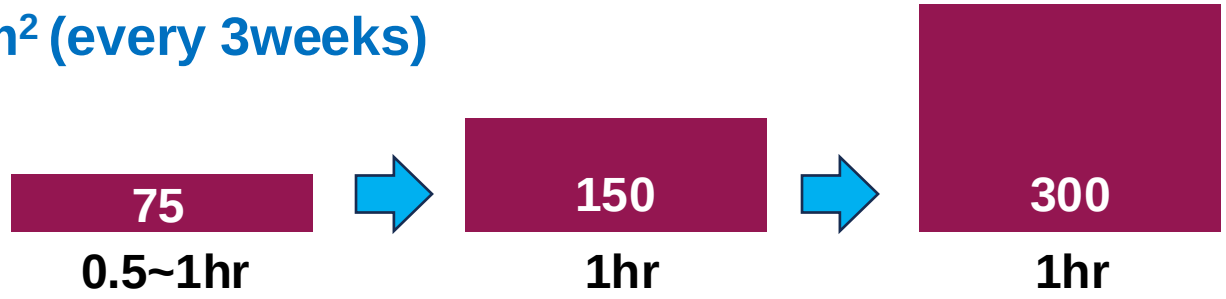
800 mg/m²



unit：mg/m²/hr

2nd cycle~

600 mg/m² (every 3weeks)



unit：mg/m²/hr

400 mg/m² (every 2weeks)

unit：mg/m²/hr

Zolbetuximab (VYLOY®) Infusion rate

simplified version

1st cycle 800mg : Quick Guide

BSA (m^2)	100mg/m^2/hr	200mg/m^2/hr	300mg/m^2/hr	400mg/m^2/hr
1.1	50	110	160	220
1.2	60	120	180	240
1.3	60	130	190	260
1.4	70	140	210	280
1.5	70	150	220	300
1.6	80	160	240	320
1.7	80	170	250	340
1.8	90	180	270	360
1.9	90	190	280	380
2.0	100	200	300	400

unit : ml/hr

Zolbetuximab (VYLOY®) Infusion rate

simplified version

Every 3weeks

2nd cycle~ 600mg : Quick Guide

BSA (m^2)	75mg/m^2/hr	150mg/m^2/hr	300mg/m^2/hr
1.1	40	80	160
1.2	40	90	180
1.3	40	90	190
1.4	50	100	210
1.5	50	110	220
1.6	60	120	240
1.7	60	120	250
1.8	60	130	270
1.9	70	140	280
2.0	70	150	300

unit : ml/hr

Every 2weeks

2nd cycle~ 400mg : Quick Guide

BSA (m^2)	50mg/m^2/hr	100mg/m^2/hr	200mg/m^2/hr
1.1	20	50	110
1.2	30	60	120
1.3	30	60	130
1.4	30	70	140
1.5	30	70	150
1.6	40	80	160
1.7	40	80	170
1.8	40	90	180
1.9	40	90	190
2.0	50	100	200

unit : ml/hr

Zolbetuximab (VYLOY®) N/V management flowchart (within 60 mins from the start)

100mg/m²/hr Start

★**First 15 minutes**: Nurse observes at the bedside

Primperan® : up to 3 times daily, at least 2 hours apart
(Up to 2 times while on VYLOY® treatment)
Novamin®, Atarax® : only once

For nurses

Vomitig or Severe Nausea

none

If the total administration time exceeds 1 hour at 100 mg/m²/hr, increase to 200 mg/m²/hr

Resume at 50 mg/m²/hr and increase to 100 mg/m²/hr after 15 minutes

Vomitig or Severe Nausea

To ①
If resumption is possible, restart at 100 mg/m²/hr

recover

recover

present

①

Discontinue administration and observe for 15 minutes

Symptoms persist

Novamin® 1A, IM or
Primperan® 1A, IV or
Atarax® 1A, DIV
Observe for 15 minutes

Symptoms persist

Dr. Call

Created by ***Yuika Noguchi***, Pharmacy Department, National Hospital Organization Hokkaido Cancer Center

Name	Affiliation	Qualifications	E-mail
Tamotsu Sagawa	Gastroenterology/ Oncology	Medical Oncologist and Supervisor Certified by the Japanese Society of Clinical Oncology Certified Oncologist by the Japan Cancer Treatment Certification Organization	stamotsu@jk9.so-net.ne.jp
Shinya Takada	Pharmaceutical Department	Certified Cancer Pharmacy Specialist by the Japanese Society of Pharmaceutical Health Care and Sciences Certified Oncology Pharmacist by the Japanese Society of Pharmaceutical Health Care and Sciences	takada.shinya.fa@mail.hosp.go.jp
Kengo Umehara	Pharmaceutical Department	Specialist in Pharmaceutical Care Specialist in Outpatient Cancer Treatment Pharmacy	umehara.kengo.ku@mail.hosp.go.jp
Yuika Noguchi	Pharmaceutical Department	Pharmacist	noguchi.yuika.bn@mail.hosp.go.jp
Miho Izumi	Nursing Department	Certified Nurse Specialist in Cancer Drug Therapy	izumi.miho.un@mail.hosp.go.jp
Tamaki Takase	Nursing Department	Certified Nurse Specialist in Cancer Chemotherapy	takase.tamaki.qc@mail.hosp.go.jp