THE EMETOGENECITY OF TRIFLURIDINE/TIPIRACIL (TAS-102) AND THE EFFICACY OF PROPHYLACTIC ANTIEMETICS: A PROSPECTIVE, OBSERVATIONAL, MULTICENTER STUDY

JASCC-CINV 2001

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ABSTRACT

Introduction:
Trifluridine tipiracil hydrochloride (TAS-102) is an oral anticancer agent with adequate efficacy in metastatic colorectal cancer (mCRC). We conducted a multicenter, prospective, observational study to investigate the incidence of chemotherapy-induced nausea and vomiting (CINV) and prophylactic antiemetic therapy in mCRC patients treated with TAS-102 (JASCC-CINV 2001).

Methods:
Patients with mCRC who received TAS-102 without dose reduction in the first course were included. The primary endpoint was the incidence of vomiting during the overall period. Secondary endpoints were the incidence of nausea, significant nausea, anorexia and patient satisfaction. Patient diaries were used to assess primary and secondary endpoints. All adverse events were assessed using PRO-CTCAE ver 1.0. and CTCAE ver 5.0.

Results:
Data were analyzed in 100 patients of the 119 patients enrolled. The incidence of vomiting, nausea, and significant nausea was 13%, 67%, and 36%, respectively. Prophylactic antiemetics were given to 24% of patients, of whom 70% received dopamine2 antagonists. The incidence of vomiting in patients with and without prophylactic antiemetic therapy were 20.8% and 10.5%, respectively. Patients who experienced CINV in previous treatment tended to be associated with frequent vomiting (hazard ratio: 7.13, 95% confidence interval: 0.87–58.5, P value= 0.067) in a multivariable analysis with cox proportional hazard model.

Conclusions:
Low incidence of vomiting and high patient satisfaction were observed in mCRC patients who received TAS-102 without prophylactic antiemetic therapy. On the other hand, patients who experienced CINV in previous treatment are at higher risk of developing vomiting.

INTRODUCTION

Trifluridine/tipiracil (TAS-102) is highly effective for metastatic unresectable colorectal cancer (mCRC) refractory to standard therapies such as fluoropyrimidine, irinotecan, and oxaliplatin. The emetic risk of TAS-102 varies among various guidelines, which means that ASCO and JSCO classify the risk as "moderate-to-severe (≥30%)" and "moderate (30-90%)", respectively, while both NCCN and MASCC/ESMO classify the risk as "minimal-to-low (<30%)" .

We conducted a multicenter prospective observational study to investigate the occurrence of nausea and vomiting and antiemetic therapy in patients with mCRC treated with TAS-102 by subjective evaluation using patient diaries.

METHODS AND MATERIALS

Study design and patient selection

- This study was a prospective observational study conducted at 10 centers in Japan
- We analyzed patients with mCRC receiving TAS-102 between January 2020 and March 2023.

【Key eligibility criteria】
1) Age ≥ 20 years
2) Ability to keep an accurate patient diary
3) Provided written informed consent

【Key exclusion criteria】
1) Starting on a reduced dose of TAS-102
2) Nausea and vomiting requiring antiemetic treatment at enrollment
3) Starting narcotic (strong opioid) medications within 48 hours of enrollment
4) Ascites fluid retention requiring therapeutic puncture
5) Presence of both symptomatic brain metastases and cancer meningitis
6) Gastrointestinal disorders such as bowel obstruction
7) Use of drugs affecting vomiting within 48 hours prior to treatment.

Primary endpoint

・The overall incidence of vomiting, including retching, during the entire evaluation period (0-28 days)

Secondary endpoints

・Incidence of nausea, significant nausea, anorexia, taste disturbance, fatigue, constipation, diarrhea, insomnia, and patient satisfaction. (Significant nausea was defined as the "moderate" and "severe" categories)
・Adverse events were evaluated according to PRO-CTCAE ver1.0. and CTCAE ver 5.0.

Statistical analysis

・Descriptive statistics: Patient characteristics, rate of CINV control, and treatment-related adverse events
・The impact of prophylactic antiemetics on vomiting, nausea, and significant nausea was assessed using a Cox proportional hazards regression model which incorporated age, sex, and experience with CINV as covariates.

RESULTS

Table 1. Patient characteristics

		n
Sex	Male	52
	Female	48
Median age (range)	64 (55 - 72)	
Chemotherapy	TAS-102	33
	BEV+TAS-102	67
Antiemetic prophylaxis	With	24
	Without	76
Performance Status	0	78
	1	19
	2	3
Motion sickness	No	77
	Yes	22
	Unknown	1
Morning sickness during pregnancy	No	20
	Yes	24
	No pregnancy	55
	Unknown	1
Habitual alcohol consumption	No	75
	Yes	24
	Unknown	1
Experience of CINV prior treatment	No	42
	Yes	57
	Unknown	1

Figure 1. Incidence of nausea and vomiting and other adverse events

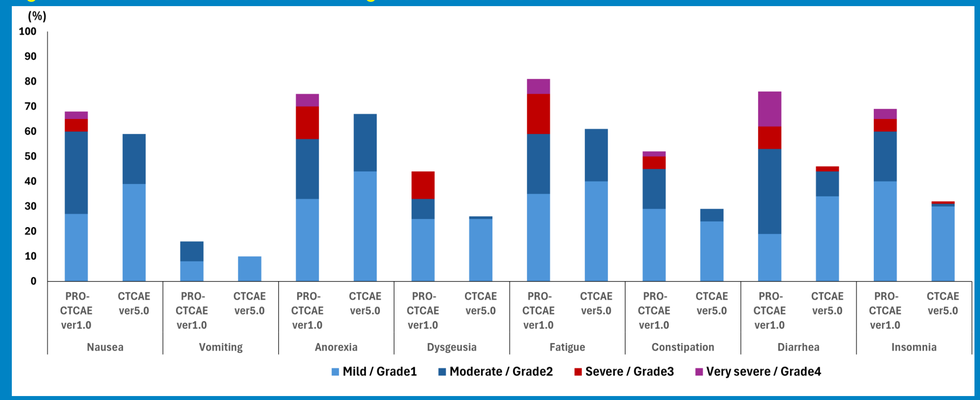

Figure 2. Patient satisfaction

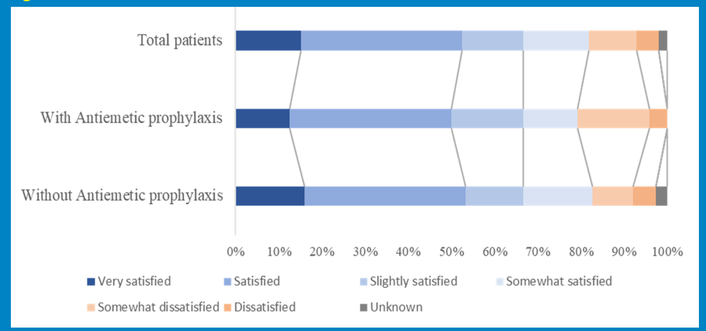

Figure 3. Prevalence of anorexia, nausea, and vomiting over time

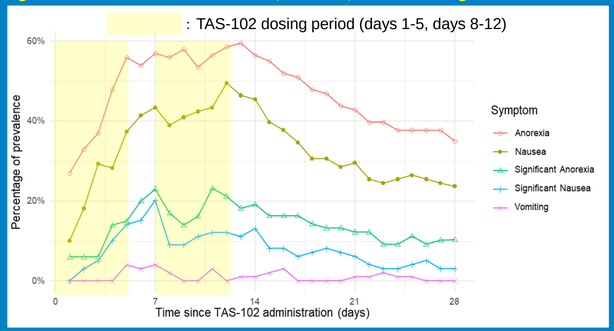

Table 2. Prognostic factors of vomiting, nausea and significant nausea

All	Multivariate					
	Vomiting		Nausea		Significant nausea	
	HR (95%CI)	*P* value	HR (95%CI)	*P* value	HR (95%CI)	*P* value
Antiemetics	1.61 (0.50 - 5.21)	0.43	2.27 (1.34 - 3.84)	<0.01	1.96 (0.94 - 4.08)	0.07
Female	2.92 (0.79 - 10.78)	0.11	1.02 (1.00 - 1.05)	0.12	1.04 (1.00 - 1.09)	0.03
Age	1.00 (0.94 - 1.06)	0.95	1.47 (0.90 - 2.42)	0.13	1.67 (0.83 - 0.15)	0.15
Experience of CINV	7.13 (0.87 - 58.5)	0.07	2.38 (1.36 - 4.16)	<0.01	3.28 (1.43 - 7.50)	<0.01

DISCUSSION AND CONCLUSIONS

The low incidence of vomiting and high patient satisfaction with TAS-102 suggest that antiemetic prophylaxis for all patients is not always necessary. However, antiemetic prophylaxis measures should be considered when initiating TAS-102 in patients who have experienced CINV with previous therapy.

Fujii H, et al. Support Care Cancer. 2024;32:291.