Abstract 476

Body weight loss as a prognostic/predictive factor in previously treated patients with metastatic gastric or gastroesophageal junction cancer: post hoc analyses of the phase III TAGS trial

Michele Ghidini,[1] Howard Hochster,[2] Toshihiko Doi,[3] Eric Van Cutsem,[4] Lukas Makris,[5] Karim A. Benhadji,[6] Wasat Mansoor[7]

[1]Azienda Ospedaliera di Cremona, Cremona, Italy; [2]Rutgers Cancer Institute, New Brunswick, NJ; [3]National Cancer Center Hospital East, Chiba, Japan; [4]University Hospitals Gasthuisberg, Leuven, Belgium; [5]Stathmi, Inc, New Hope, PA; [6]Taiho Oncology, Inc., Princeton, NJ; [7]The Christie NHS Foundation Trust, Manchester, UK

Introduction

- Nutritional status is closely linked to cancer mortality, particularly in patients with metastatic gastric or gastroesophageal cancer (mGC/GEJC)[1,2]
- Body weight loss (BWL) has been shown to be prognostic for survival in the curative, first-, and second-line settings in mGC/GEJC [1–4]
  - In patients with advanced GC receiving palliative chemotherapy, BWL during the first month of chemotherapy (early BWL) strongly correlated with poor overall survival (OS) outcomes[5]
- In the phase III TAGS trial, trifluridine/tipiracil (FTD/TPI) demonstrated survival benefit versus placebo and manageable safety in patients with mGC/GEJC who had received ≥2 prior chemotherapy regimens[6]
- In this retrospective post hoc analysis, we examined the association of early BWL with survival outcomes in the phase III TAGS trial

Methods

- The TAGS intent-to-treat (ITT) population was categorized into patients who experienced <3% or ≥3% BWL from the start of treatment until day 1 of cycle 2, each cycle being 28 days
  - The 3% threshold was chosen based on earlier correlative analyses in the mGC population[4]
- OS and progression-free survival (PFS) were compared between the BWL subgroups within each treatment arm because of significant imbalances in early BWL between the treatment arms
- The effect of early BWL on OS was assessed using a univariate Cox proportional hazards (PH) model and a multivariate Cox PH model that adjusted for baseline prognostic factors identified in the original ITT analysis[6]

Results

Patient population

- Body weight data were available for 451 of 507 (89%) patients overall (n=304, FTD/TPI; n=147, placebo)
- There was an imbalance in BWL between the 2 treatment arms: 35% of patients in the placebo arm experienced ≥3% BWL at the end of cycle 1 versus 26% in the FTD/TPI arm
- Although patient baseline characteristics were generally comparable between the <3% BWL and ≥3% BWL subgroups, the following differences were noted (**Table 1**):
  - Compared with patients with <3% BWL, a greater proportion of patients with ≥3% BWL had an Eastern Cooperative Oncology Group performance status of 1 and ≥3 metastatic sites

Table 1. Patient baseline characteristics

		<3% BWL		≥3% BWL	
		FTD/TPI (n=224)	Placebo (n=95)	FTD/TPI (n=80)	Placebo (n=52)
Age, years	Median (range)	64.0 (24–89)	64.0 (32–82)	61.0 (27–82)	58.5 (39–76)
Sex, %	Male	74	69	75	69
Geographic region, %	USA, Europe, or Australia	86	83	84	83
	Japan	14	17	16	17
Primary cancer type, %	Gastric	71	72	70	67
	GEJ	29	28	30	29
	Both	0	0	0	4
ECOG PS at baseline, %	0	42	48	26	35
	1	58	52	74	65
No. of metastatic sites, %	1–2	49	51	38	33
	≥3	51	49	62	67
No. of prior regimens, %	2	38	37	38	44
	3	37	38	37	27
	≥4	25	25	25	29
Baseline renal function, %	Normal (≥90 mL/min)	38	37	49	52
	Mild RI (60–89 mL/min)	42	48	40	31
	Moderate RI (30–59 mL/min)	19	15	11	15
	Severe RI (<30 mL/min)	1	0	0	2

BWL, body weight loss; ECOG PS, Eastern Cooperative Oncology Group performance status; FTD/TPI, trifluridine/tipiracil; GEJ, gastroesophageal junction; RI, renal impairment; USA, United States of America.

Efficacy

- Patients with <3% BWL experienced longer OS than those with ≥3% BWL in both the FTD/TPI and placebo arms (**Figure 1** and Supplementary Figure S1)
  - The effect of early BWL on OS was most pronounced in the placebo group
- Analyses using a univariate Cox PH model indicated a strong prognostic effect of early BWL on OS
  - The unadjusted HR in the pooled ITT population for <3% vs ≥3% BWL was 0.58 (95% confidence interval [CI], 0.46–0.73)
- Multivariate analyses were consistent with univariate analyses and indicated that BWL was both a prognostic (P<0.0001) and predictive factor (interaction P=0.0003) for OS (Supplementary Table S1)
- Early BWL was correlated with shorter PFS (Supplementary Figures S1 and S2)
  - Differences in PFS between the <3% and ≥3% BWL subgroups were greatest in the placebo arm

CONCLUSIONS

Early BWL was associated with unfavorable survival outcomes in patients with mGC/GEJC in the TAGS trial, regardless of FTD/TPI or placebo treatment

- Early BWL appeared to be a strong negative prognostic marker for OS, even in the third-or later-line setting in mGC/GEJC

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References

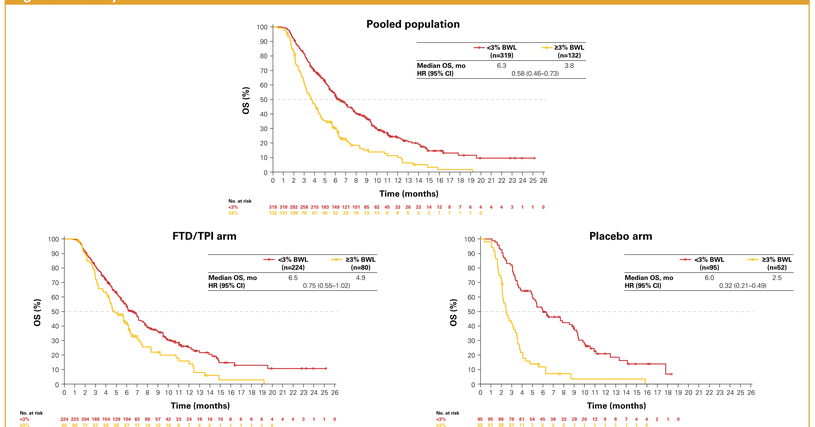
1. Liu X, et al. *Onco Targets Ther.* 2017;10:2107–14.
2. Sakurai K, et al. *Ann Surg Oncol.* 2016;23:525–33.
3. Parisi A, et al. *J Cancer Res Clin Oncol.* 2019;145:2365–73.
4. Mansoor W, et al. *J Clin Oncol.* 2020;38(4_suppl):348.
5. Ock C-Y, et al. *Gastric Cancer.* 2016;19:597–606.
6. Shitara K, et al. *Lancet Oncol.* 2018;19:1437–48.

Acknowledgments

- We thank the participating patients and their families, the clinical study teams who were involved in the TAGS trial, as well as the data and safety monitoring board members
- This study was sponsored by Taiho Oncology, Inc., and Taiho Pharmaceutical Co., Ltd.
- Professional medical writing and editorial assistance was provided by Vasupradha Vethantham, PhD, and Jennifer Robertson, PhD, at Ashfield Healthcare Communications, funded by Taiho Oncology, Inc.

Presented at the Virtual ASCO Gastrointestinal Cancers Symposium, January 15–17, 2021

Figure 1. OS by BWL

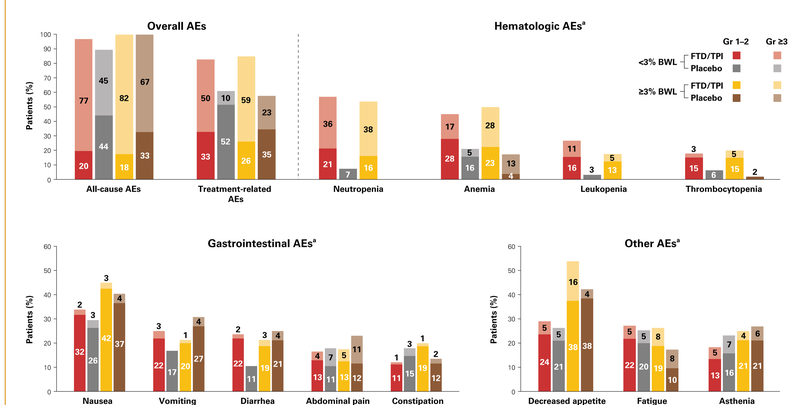


BWL, body weight loss; CI, confidence interval; FTD/TPI, trifluridine/tipiracil; HR, hazard ratio; mo, months; OS, overall survival.

Safety

- The overall incidences of adverse events were similar between FTD/TPI-treated patients in the 2 BWL subgroups; however, a trend toward higher rates of grade ≥3 toxicities was observed in placebo-treated patients with ≥3% BWL (**Figure 2**)
  - Rates of decreased appetite and nausea were higher in patients with ≥3% BWL than in those with <3% BWL

Figure 2. AEs by BWL



AE, adverse event; BWL, body weight loss; FTD/TPI, trifluridine/tipiracil; Gr, grade.
[a]Refer to AEs of any cause.