Impact of Dysgeusia on Transplant Recipients With Refractory Cytomegalovirus With/Without Resistance Receiving Maribavir: Post-hoc Analyses from a Phase 3 Randomized Trial

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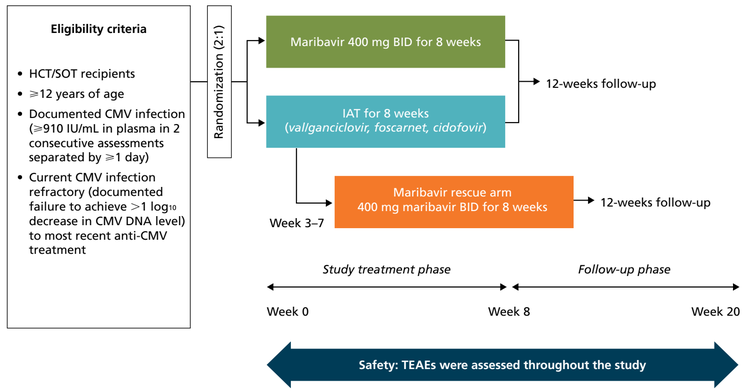
INTRODUCTION

- In the Phase 3 SOLSTICE study (NCT02931539), maribavir was superior to investigator-assigned therapies (IAT; val/ganciclovir, foscarnet, and cidofovir) for cytomegalovirus (CMV) viremia clearance at Week 8 in transplant recipients with refractory CMV with/without resistance (primary endpoint: 55.7% vs 23.9%, respectively).[1]
- In SOLSTICE, dysgeusia, an altered sense of taste, was the most common treatment-emergent adverse event (TEAE) in patients receiving maribavir.[1]
- The objective of these analyses was to assess the impact of dysgeusia on patients treated with maribavir in SOLSTICE.

METHODS

Figure 1. Study design of SOLSTICE



Post-hoc analyses by dysgeusia AESI:
- Confirmed CMV viremia clearance (plasma CMV DNA concentration <137 IU/mL in 2 consecutive post-baseline samples, separated by ≥5 days) at Week 8 (primary endpoint from the pre-specified analysis)
- Median change in body weight from baseline to Week 8

AESI, adverse event of special interest; BID, twice daily; HCT, hematopoietic cell transplant; SOT, solid organ transplant.

- Dysgeusia (which included preferred terms ageusia, dysgeusia, hypogeusia, and/or taste disorder) was an AESI.

RESULTS

- Overall, 352 patients were randomized; of these 234 received study-assigned maribavir and 116 received IAT and were included in the safety set (n=350).
- 46.2% of patients who received maribavir had dysgeusia on-treatment and this was considered treatment-related in 44.0% of patients (**Table 1**).

Table 1. Incidence of treatment-emergent[a] AESI of dysgeusia during the on-treatment observation period[b] by treatment

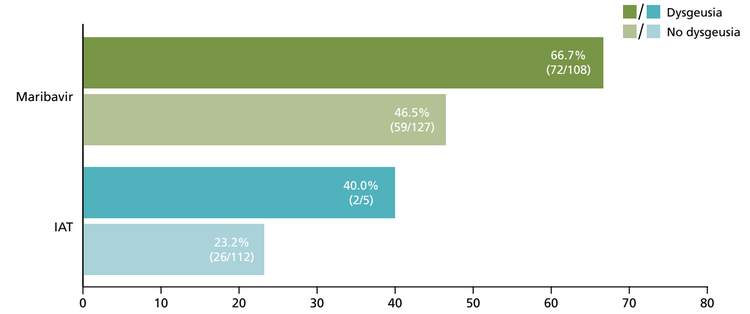
	Maribavir n=234	IAT n=116
Any dysgeusia AESI	108 (46.2)	5 (4.3)
Dysgeusia[c]	87 (37.2)	4 (3.4)
Taste disorder[c]	21 (9.0)	1 (0.9)
Ageusia[c]	1 (0.4)	0
Hypogeusia[c]	1 (0.4)	0
Severity of dysgeusia AESI[d]		
Grade 1 (mild)	86 (36.8)	4 (3.4)
Grade 2 (moderate)	17 (7.3)	1 (0.9)
Grade 3 or above	0	0
Missing	5 (2.1)	0
Any dysgeusia treatment-related AESI[d]	103 (44.0)	2 (1.7)
Any dysgeusia serious AESI[d]	0	0
Dysgeusia leading to treatment discontinuation	2 (0.9)	0

Data are n (%).
[a]An adverse event that starts on or after the first dose of study treatment or that has a start date before the first dose, but increases in severity after the first dose will be considered treatment-emergent. [b]On-treatment observation period started at study treatment initiation through 7 days (21 days for cidofovir) after the last dose of study treatment, or until the maribavir rescue treatment initiation, whichever was earlier. [c]AESI class preferred term. Patients were counted once per AESI and once per preferred term. [d]Includes preferred terms dysgeusia, taste disorder, ageusia, and hypogeusia.

Confirmed CMV viremia clearance at Week 8 analyses by dysgeusia

- In patients who received maribavir, confirmed CMV viremia clearance at Week 8 was achieved in 66.7% of patients with dysgeusia and 46.5% of patients without dysgeusia (**Figure 2**); adjusted difference, –21.7 (95% CI: –34.24, –9.25).

Figure 2. Proportion of patients achieving CMV viremia clearance at Week 8 (SOLSTICE pre-specified primary endpoint) with or without treatment-emergent AESI dysgeusia during the on-treatment observation period[a]

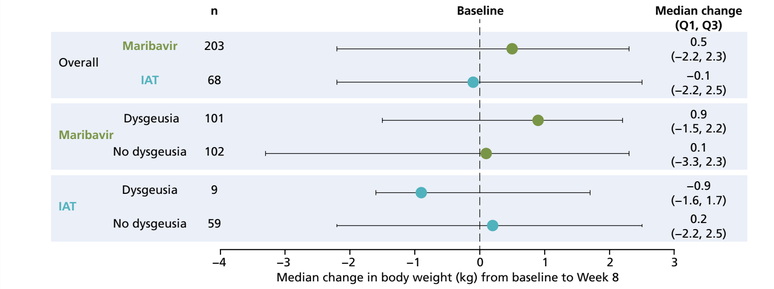


[a]On-treatment observation period started at study treatment initiation through 7 days (21 days for cidofovir) after the last dose of study treatment, or until the maribavir rescue treatment initiation, whichever was earlier.

Change in body weight by dysgeusia

- In patients who received maribavir, median change in body weight from baseline to Week 8 was similar with and without dysgeusia (**Figure 3**).
- In patients with dysgeusia, median change in body weight was similar between treatment groups (**Figure 3**).

Figure 3. Median change in body weight from baseline to Week 8 in patients with and without dysgeusia AESI



Included all reported adverse events for AESI dysgeusia regardless of treatment emergence according to the original study assignment.

Resolution of dysgeusia

- For patients who received either maribavir as study-assigned or rescue treatment (n=256), median treatment duration was 57 days (range, 2–64) and 57 days (range, 22–60), respectively.
- In patients who received maribavir and had dysgeusia, 37% had resolution while still on treatment for a median of 43 days.
- Median duration of dysgeusia while off treatment was 6 days (**Table 2**).

Table 2. Dysgeusia frequency and resolution in patients who received maribavir (study-assigned or rescue treatment)

	Maribavir or maribavir rescue n=256
At least 1 dysgeusia episode during treatment, n (%)	119 (46.5)
Dysgeusia resolution during treatment, n (%)[a]	44 (37.0)
Median duration of dysgeusia resolved on treatment, days (min, max)	43 (7, 59)
Ongoing dysgeusia at last treatment date, n (%)[a]	75 (63.0)
Dysgeusia resolution off treatment, n (%)[b]	67 (89.3)
Dysgeusia ongoing at the last study follow-up date, n (%)[b]	8 (10.7)
Median duration of dysgeusia resolved off treatment, days (min, max)	6 (2, 85)

[a]Denominator based on patients with at least 1 dysgeusia episode during treatment (n=119). [b]Denominator based on patients with ongoing dysgeusia at last treatment date (n=75).

CONCLUSIONS

- In SOLSTICE, dysgeusia was common in the maribavir arm but was generally mild/moderate in severity and rarely associated with treatment discontinuation.
- In these post-hoc analyses, the proportion of patients treated with maribavir who achieved CMV clearance at Week 8 was higher in patients with dysgeusia than those without. This was not likely due to better absorbance with dysgeusia, as a slight negative correlation was noted between pharmacokinetics and dysgeusia.
- The proportion of patients who achieved CMV clearance at Week 8 was higher in patients who received maribavir than IAT irrespective of dysgeusia, reflecting the SOLSTICE primary endpoint analysis.
- There were no clinically meaningful changes in body weight in patients with or without dysgeusia.
- For the majority of patients treated with maribavir who experienced dysgeusia, resolution of dysgeusia occurred off-treatment.

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REFERENCE:

1. Avery RK, et al. *Clin Infect Dis* 2021; ciab988.

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This poster is intended for healthcare providers.