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Updated Efficacy and Safety Results From a Phase 2 Study of Safusidenib in Patients With Chemotherapy- and Radiotherapy-Naïve Grade 2 Isocitrate Dehydrogenase 1 (*IDH1*)-Mutant Glioma

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Background

- *IDH*-mutant gliomas are a distinct category of CNS tumors per WHO CNS 2021 criteria[1]
- Maximal safe resection is the standard initial treatment for Grade 2 *IDH1*-mutant gliomas, with subsequent treatment guided by perceived risk[2]
- Patients with higher-risk features may require early RT/CT, while those with lower-risk features may undergo watchful waiting or receive an IDH inhibitor to defer RT/CT and its detrimental effects[2,3]
- Safusidenib is an investigational mutant-IDH1 inhibitor with high potency, selectivity, and blood-brain barrier permeability[4]
- In a Phase 2 study (NCT04458272), safusidenib demonstrated encouraging antitumor activity in 27 Japanese patients with RT- and CT-naïve Grade 2 *IDH1*-mutant glioma[5]
- Here, we report updated efficacy and safety outcomes after 1 additional year of follow-up

Abbreviations

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BID, twice daily; BOR, best overall response; c, confirmed; CBR, clinical benefit rate; CI, confidence interval; CNS, central nervous system; COVID-19, coronavirus disease 2019; CR, complete response; CT, chemotherapy; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IDH1, isocitrate dehydrogenase 1; IERC, Independent Efficacy Review Committee; INV, investigator; KPS, Karnofsky performance status; MR, minor response; NR, not reached; ORR, objective response rate; PD, progressive disease; PFS, progression-free survival; PR, partial response; RANO-LGG, Response Assessment in Neuro-Oncology Low-Grade Glioma; RT, radiotherapy; SD, stable disease; SPD, sum of products of diameters; TEAE, treatment-emergent adverse event; TTR, time to response; WHO, World Health Organization.

References

1. Louis DN, et al. *Neuro Oncol* 2021;23:1231–1251
2. Weller M, et al. *Nat Rev Clin Oncol* 2021;18:170–186
3. Lanman TA, et al. *Cancers (Basel)* 2025;17:2630
4. Machida Y, et al. *Mol Cancer Ther* 2020;19:375–383
5. Arakawa Y, et al. *Neuro Oncol* 2026;28:717–727

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Methods

- The full study design has been previously reported[5]
- Patients with RT- and CT-naïve Grade 2 *IDH1*-mutant glioma received oral safusidenib 250 mg BID
- All patients treated with ≥1 dose of safusidenib were included in the efficacy and safety analyses
- Efficacy endpoints were assessed by IERC and INV

Efficacy

Patient Demographics and Baseline Characteristics

Baseline Characteristics	(N=27)[a]
Median age, years (range)	41 (24–58)
Sex, n (%)	
Male / Female	14 (51.9) / 13 (48.1)
ECOG PS, n (%)	
0 / 1	26 (96.3) / 1 (3.7)
KPS, n (%)	
80	1 (3.7)
90	7 (25.9)
100	19 (70.4)
Median time since most recent surgery, months (range)	24.2 (4–119)
Cancer types (latest diagnosis)[b]	
INV assessment, n (%)	
Oligodendroglioma	17 (63.0)
Diffuse astrocytoma	10 (37.0)
Central assessment, n (%)	
Oligodendroglioma	6 (22.2)
Anaplastic oligodendroglioma	9 (33.3)
Anaplastic astrocytoma	12 (44.4)

[a]All patients had measurable non-enhancing disease at baseline. [b]Cancer types were classified based on the 2016 WHO classification.

Safusidenib Demonstrated Durable Responses in Patients With RT- and CT-Naïve Grade 2 *IDH1*-Mutant Glioma

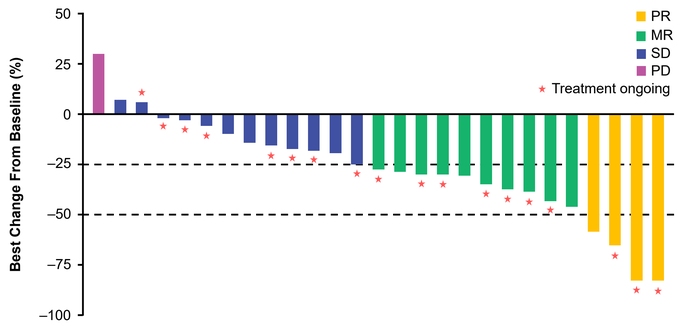
	IERC Assessed (N=27)[a]	INV Assessed (N=27)[a]
cORR, n (%)	14 (51.9)	14 (51.9)
95% CI	31.9–71.3	31.9–71.3
cBOR, n (%)		
CR	0	0
PR	4 (14.8)	6 (22.2)
MR	10 (37.0)	8 (29.6)
SD	12 (44.4)	13 (48.1)
PD	1 (3.7)	0
cCBR,[b] n (%)	22 (81.5)	24 (88.9)
95% CI	61.9–93.7	70.8–97.6

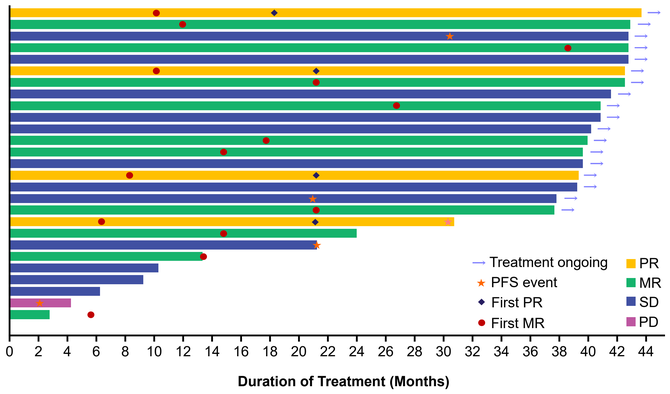
Data cutoff: March 14, 2024. [a]Assessed per RANO-LGG. [b]CR+PR+MR+SD with <0% of tumor size change from baseline.

- Responses were durable and, of the patients who responded, only one patient subsequently experienced PD per IERC at the time of data cutoff
- Median TTR per IERC was 14.1 months (range, 5.6–38.7)
- Median DOR per IERC was NR (95% CI, 24.0–NR)

Safusidenib Demonstrated Sustained Disease Control

- Among the 27 patients, the median best percent change in the SPD of the target lesions per IERC was –27.22% (range, –83.1, 30.2)



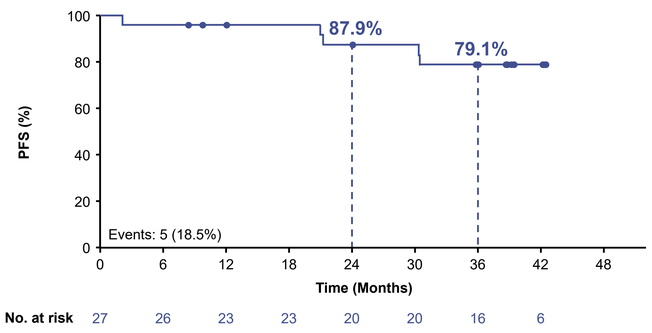


Data cutoff: March 14, 2024. Data shown per IERC.

- The majority of patients were on treatment for >36 months (3 years), with treatment still ongoing at the time of data cutoff

With Longer Follow-Up, Median PFS Was Not Reached

Median PFS follow-up: 38.8 months



	IERC Assessed (N=27)	INV Assessed (N=27)
Median PFS, months (95% CI)	NR (NR–NR)	NR (NR–NR)
24-month PFS rate, %	87.9	84.5
36-month PFS rate, %	79.1	80.5

Data cutoff: March 14, 2024. Kaplan–Meier curve shown per IERC.

Safety

- As of October 30, 2024, the median duration of safusidenib exposure was 46.7 months (range, 3–51)
- With longer follow-up, the safety profile of safusidenib remained consistent with previous reports,[5] with no new safety signals identified
- Safusidenib demonstrated a favorable risk-benefit profile in patients with *IDH1*-mutant glioma, with TEAEs being mostly low grade and managed with dose modifications
- The most common any-grade TEAEs were alopecia (59.3%), arthralgia (55.6%), skin hyperpigmentation (51.9%), increased ALT (40.7%), and rash (37.0%), which were mostly Grade 1 or 2
- TEAEs resulted in dose interruptions in 74.1% of patients, dose reductions in 37.0%, and treatment discontinuations in 11.1%[a]

Common TEAEs With Safusidenib

Most Frequent TEAEs (≥15% of Patients), n (%)	Any Grade	Grade ≥3
Alopecia	16 (59.3)	0
Arthralgia	15 (55.6)	1 (3.7)
Skin hyperpigmentation	14 (51.9)	0
ALT increased	11 (40.7)	2 (7.4)
Rash	10 (37.0)	0
AST increased	9 (33.3)	1 (3.7)
Back pain	9 (33.3)	0
Pruritus	9 (33.3)	0
Neutrophil count decreased	8 (29.6)	0
COVID-19	7 (25.9)	0
Diarrhea	7 (25.9)	0
Nausea	6 (22.2)	0
Upper respiratory tract infection	6 (22.2)	0
Headache	5 (18.5)	1 (3.7)
Nasopharyngitis	5 (18.5)	0

Data cutoff: October 30, 2024. [a]Three TEAEs (11.1%) led to treatment discontinuation: two events of hepatic dysfunction and one of amnesia. Amnesia was deemed not related to study drug. The two treatment-related events of abnormal hepatic function were both resolved after hospitalization and treatment discontinuation.

Conclusions

- With additional follow-up, safusidenib continued to demonstrate encouraging efficacy in patients with RT- and CT-naïve Grade 2 *IDH1*-mutant glioma, including durable responses and sustained disease control
- The safety profile of safusidenib was consistent with prior reports, with most TEAEs being mild to moderate in severity and effectively managed with dose modifications, allowing long-term administration
- These results suggest that safusidenib may represent a potential treatment option for patients with *IDH1*-mutant glioma who are not in need of immediate RT/CT

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