Phase II study summary of safusidenib erbumine

Findings of: Arakawa Y, Saito R, Kanemura Y, Mishima K, Koriyama S, Narita Y, Kumabe T,
Motomura K, Sugiyama K, Yamasaki F, Mukasa A, Kanamori M, Kuga D, Nagane M, Kakurai Y, Isobe K, Nakamura H. Phase II study of safusidenib erbumine in patients with chemotherapy- and radiotherapy-naïve isocitrate dehydrogenase 1-mutated WHO grade 2 gliomas. Neuro Oncol. 2025 Nov 8:noaf258. doi: 10.1093/neuonc/noaf258. Epub ahead of print. PMID: 41206766.

Here is the annotated summary of the trial:

Bibliographic citation

Arakawa Y, Saito R, Kanemura Y, Mishima K, Koriyama S, Narita Y, Kumabe T, Motomura K, Sugiyama K, Yamasaki F, Mukasa A, Kanamori M, Kuga D, Nagane M, Kakurai Y, Isobe K, Nakamura H. Phase II study of safusidenib erbumine in patients with chemotherapy- and radiotherapy-naïve isocitrate dehydrogenase 1-mutated WHO grade 2 gliomas. *NeuroOncol.* 2025 Nov 8; noaf258. doi:10.1093/neuonc/noaf258. PMID: 41206766. PubMed +1

Study design

- Multicentre, open-label, single-arm phase II study of Safusidenib erbumine (a selective mutant IDH1 inhibitor) in patients with **chemotherapy- and radiotherapy-naïve** WHO grade 2 gliomas harbouring an IDH1 mutation. PubMed +1
- 27 patients enrolled under protocol NCT04458272. OUP Academic +1
- Eligibility: grade 2 gliomas with confirmed IDH1 mutation, no prior chemo or radiotherapy. The rationale: grade 2 gliomas are infiltrative, complete resection often not feasible, and IDH1 mutation is frequent in this subgroup. OUP Academic +1
- Primary endpoint: confirmed objective response rate (ORR) per the Response Assessment in Neuro-Oncology (RANO) criteria for WHO grade 2 gliomas. Secondary / exploratory endpoints included progression-free survival (PFS), safety/tolerability. OUP Academic +1

Key findings

- The confirmed ORR was **44.4 %**. PubMed
- Median PFS was *not reached* at time of report; the 24-month event-free probability (i.e., remaining free of progression or event) was **87.9 %**. PubMed

- Safety: The most frequent treatment-emergent adverse events (TEAEs) (occurring in ≥ 40 %) included:
    - Alopecia: 59.3%
    - Arthralgia: 55.6%
    - Skin hyper-pigmentation: 48.1%
    - Alanine aminotransferase (ALT) increased: 40.7% PubMed
- Most TEAEs were grade 1-2. The incidence of treatment-related grade ≥ 3 TEAEs was 18.5%. PubMed

Interpretation and implications

- The ORR of ~44% in a previously untreated (no chemo/radio) grade 2 IDH1-mutant glioma cohort is a promising signal for a targeted molecular therapy in this setting, especially given the historical difficulty of treating these infiltrative tumours while preserving neurological function.
- The fact that median PFS was not yet reached and 24-month event-free rate was ~88% suggests potential durability of response, although longer follow-up will be needed.
- The safety profile appears manageable: while alopecia, arthralgia and hyperpigmentation were common, high-grade toxicities were relatively limited (≈18.5%).
- If confirmed in larger, randomized trials, safusidenib erbumine could represent a new therapeutic option in IDH1-mutated WHO grade 2 gliomas, potentially allowing deferral of or sparing of cytotoxic therapies (chemo/radiotherapy) and their associated toxicities.
- For pediatric neuro-oncology and blood-brain barrier (BBB) delivery contexts: The drug is described as having “substantial blood-brain barrier penetration” in the background of the paper. OUP Academic +1 This is particularly relevant to your interest in pediatric BBB/drug-delivery topics.

Limitations / caveats

- Single-arm design, no comparator/control arm: outcomes must be interpreted with caution relative to historical controls.
- Relatively small sample size (n = 27) and relatively short follow-up so far (median PFS not reached).
- This is in adult patients (presumably) – extrapolation to pediatric populations requires caution.

- Long-term outcomes such as overall survival (OS), quality of life, neurocognitive outcomes, and impact on delaying/avoiding radiotherapy need further data.

Relevance to your interests

- The strong BBB penetration of the agent aligns with your interest in pediatric BBB and drug delivery — this trial provides an example of a small-molecule IDH1 inhibitor being used in a CNS tumour setting.
- The setting of chemo- and radiotherapy-naïve grade 2 glioma is interesting as treatment paradigms evolve from “watch & wait / surgery” towards molecular-targeted therapy for IDH-mutant gliomas.
- Though this trial is adult and grade 2, the concept of targeting IDH1 mutation and leveraging BBB-penetrant molecules may inform pediatric applications (e.g., IDH1-mutated low-grade gliomas in children) and translational strategies.