Long-term survival from a Phase II trial (JG002) using Cyclotron Neutron Source and Boronophenylalanine.

Summarize the Key findings of the following article:
Kawabata S, Goto H, Narita Y, Furuse M, Nonoguchi N, Shidoh-Kazuki R, Eza K, Hirose K, Ohno M, Kondo N, Suzuki M, Tanaka H, Ono K, Nihei K, Wanibuchi M, Miyatake SI. Extended follow-up of recurrent glioblastoma patients treated with boron neutron capture therapy (BNCT): Long-term survival from a Phase II trial (JG002) using Cyclotron Neutron Source and Boronophenylalanine. Appl Radiat Isot. 2025 Aug 22;226:112118. doi: 10.1016/j.apradiso.2025.112118. PMID: 40865370.

Study overview

Phase II trial JG002 evaluated accelerator-based boron neutron capture therapy using a cyclotron neutron source (BNCT30) combined with boronophenylalanine (SPM-011) in patients with recurrent malignant glioma, predominantly glioblastoma.

Patients and treatment

- **Population:** 27 patients with recurrent malignant glioma, of whom 24 had glioblastoma.
- **Key eligibility:** relapsed after standard radiotherapy and temozolomide, not previously treated with bevacizumab.
- **Primary endpoint:** one-year survival from BNCT treatment.

Efficacy — survival outcomes

- **One-year survival:** 79.2% for relapsed glioblastoma patients.
- **Median overall survival (mOS):** initial report 18.7 months; extended long-term follow-up mOS 19.2 months (95% CI 13.1–24.8).
- **Longer-term survival rates:** 2-year survival 33.3% and 3-year survival 20.8%.

Safety and subsequent management

- **Major treatment-related toxicity:** cerebral edema in the irradiated field with associated contrast enhancement on imaging.
- **Post-progression therapy:** 21 of 27 patients received bevacizumab after imaging-defined progression.

Authors' conclusions

Accelerator-based BNCT with cyclotron neutrons and boronophenylalanine demonstrated an acceptable safety profile and a meaningful long-term survival benefit for patients with recurrent malignant gliomas, predominantly glioblastoma.

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What are the implications of these findings for treatment?

Clinical significance for treatment selection

- **BNCT offers a promising salvage option** for patients with recurrent glioblastoma who previously received standard radiotherapy and temozolomide and are bevacizumab-naïve, showing substantially higher 1-year and median overall survival versus historic bevacizumab trial controls.
- **Best candidates:** patients with good performance status (KPS ≥60), limited alternatives after standard care, and tumors amenable to boron delivery and neutron irradiation.

How BNCT fits into the treatment pathway

- **Use as re-irradiation strategy:** BNCT functions as a tumor-selective re-irradiation modality that can be offered when conventional radiotherapy options are exhausted.
- **Sequence with systemic therapy:** many patients in the trial received bevacizumab after imaging-defined progression; combining BNCT with timely anti-VEGF therapy to manage radiation-related edema is a practical pathway observed in the study.

Management of expected toxicities

- **Risk of cerebral edema and contrast enhancement in the irradiated field is high; proactive monitoring and early use of bevacizumab is effective for control** and was employed in most treated patients.
- **Clinical implication:** establish protocols for close neuroimaging follow-up, corticosteroid stewardship, and rapid access to anti-angiogenic therapy post-BNCT.

Efficacy profile to counsel patients about

- **Overall survival benefit despite short PFS:** BNCT produced prolonged median overall survival but relatively short median progression-free survival, suggesting imaging changes and edema can mimic early progression and that survival benefit may persist despite early radiographic events.
- **Counseling point:** patients should be informed about the likelihood of early post-treatment imaging changes and the potential need for interventions to control edema.

Operational and system implications

- **Facility and logistics:** delivering BNCT requires an accelerator-based neutron source (cyclotron BNCT30 or equivalent), approved boron agent, specialized dosimetry, and multidisciplinary teams experienced in BNCT planning and toxicity management.
- **Access and capacity:** adoption will need investment in equipment, training, and referral networks; centers should develop patient selection criteria and standardized care pathways.

Research and guideline implications

- **Need for confirmatory randomized studies:** findings justify phase III or comparative trials against best available care to define magnitude of benefit and optimal combination strategies.
- **Questions for future research:** optimal boron agent dosing/scheduling, timing and role of concurrent or sequential bevacizumab, biomarkers predictive of response, long-term neurocognitive outcomes, and health-economic analyses.

Practical recommendations for teams considering BNCT

- **Establish multidisciplinary BNCT program** with neuro-oncology, radiation oncology, neurosurgery, medical physics, neuroradiology, and neuro-critical care.
- **Adopt clear monitoring and management protocols** for early post-treatment cerebral edema and radiographic changes, including thresholds for initiating bevacizumab.
- **Inform patients clearly** about realistic goals (salvage therapy with potential OS benefit), likely imaging changes, and the need for close follow-up.

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