Niacin glioblastoma study summary

> *Summary and findings of: Roldan Urgoiti G, de Robles P, Tsang RY, Willson M, Ghosh S, Faruqi M, Lim G, Loewen S, Nordal R, Cairncross G, Leckie C, Poon CC, Yong VW. A phase I-II study of niacin in patients with newly diagnosed glioblastoma: safety and interim phase II analysis. J Neurooncol. 2025 Nov 28;176(1):101. doi: 10.1007/s11060-025-05351-z. PMID: 41313494.*

Here's a **summary of the Phase I–II niacin (vitamin B3) glioblastoma study** by **Roldan Urgoiti et al.** (J Neurooncol. 2025 Nov 28;176(1):101. doi:10.1007/s11060-025-05351-z; PMID: 41313494), including key findings from the **interim Phase II analysis**: Sciety +1

📌 Study Overview

Title: A phase I–II study of niacin in patients with newly diagnosed glioblastoma: safety and interim phase II analysis. PubMed

Population:

- Adults (18–75 yrs) with **newly diagnosed IDH-wild-type glioblastoma (GBM)**.
- All received **standard of care (SOC)**: maximal safe resection + radiotherapy with concomitant and adjuvant temozolomide (Stupp regimen). Sciety

Intervention:

- Oral **controlled-release niacin (NiacinCRT™)** added to SOC.
- Dose-escalation in Phase I (500–3000 mg/day) to determine safety, **maximum tolerated dose (MTD)**, and **recommended Phase II dose (RP2D)**. Sciety

Phase II aim:

> Determine whether adding niacin improves **6-month progression-free survival (PFS-6M)** compared with historical controls (~54% PFS-6M). Sciety

🧪 Phase I Results – Safety & Tolerability

- **15 patients** in Phase I (median age ~57 yrs, ~40% female; ~47% MGMT-methylated). ResearchGate
- **MTD / RP2D:** 2000 mg niacin daily. ResearchGate

- **Common side effects:**
  - **Flushing** (10/15; mostly grade 1).
  - Other toxicities included fatigue, nausea, pruritus. ResearchGate
- **Dose-limiting toxicities (DLTs):**

  Occurred at 2500 mg/day: grade 3 **thrombocytopenia** and **hyperbilirubinemia**. ResearchGate
- Some hematologic and liver abnormalities required monitoring, consistent with overlapping toxicities of niacin and temozolomide. ResearchGate

📈 Interim Phase II Analysis – Efficacy Signals

- **Interim futility analysis** performed per protocol after enough patients were evaluable for 6-month outcomes. ResearchGate
- **PFS-6M (central review): ~82.3%**, representing ~28% absolute increase over historical benchmarks (~54%). ResearchGate
- Median **progression-free survival** ~10 months; median **overall survival (OS)** ~17 months; 1-year OS ~77.5%. ResearchGate
- Sub-analysis (small numbers):

  MGMT-methylated subgroup had numerically higher PFS-6M (~85.7%) vs **unmethylated** (~77.9%). ResearchGate
- Based on these interim results, the **Data Safety Monitoring Committee (DSMC)** recommended continuing the study. ResearchGate

📊 Key Takeaways

✅ Safety

- Niacin at ≤2000 mg/day appears tolerable when added to SOC in newly diagnosed GBM.
- Flushing and mild AEs were common; serious toxicities were manageable with monitoring. ResearchGate

📈 Efficacy (Interim)

- An **encouraging signal in PFS-6M** suggests niacin might improve early disease control compared with historical data. ResearchGate
- While these data are interim and unrandomized, the ~82% PFS-6M is higher than typical benchmarks (~54%). Sciety

🔬 Mechanistic Rationale

Preclinical work indicates niacin modulates immune cells (e.g., reactivating myeloid antitumor function) that may help overcome GBM-associated immunosuppression. science.org

🧠 Clinical Context

- Standard SOC yields ~15 months median OS and ~50–55% PFS-6M. Improvements beyond this have been challenging in GBM trials. PubMed
- The study shows feasibility for repurposing niacin as an adjunct therapeutic, although **randomized evidence** is needed to conclusively establish benefit.

📌 Summary Conclusion

This first-in-human Phase I–II trial suggests controlled-release niacin, when added to standard radiochemotherapy, is **feasible and safe** up to 2000 mg/day and shows an **encouraging preliminary increase in 6-month PFS** compared with historical controls. Ongoing accrual and eventual randomized analysis will be important to confirm clinical benefit. ResearchGate