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### Phase II NCCTG trial of RT + irinotecan and adjuvant BCNU plus irinotecan for newly diagnosed GBM.

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#### Abstract

Irinotecan has radiosensitizing effects and shows synergism with nitrosoureas. We performed a Phase II study of RT and irinotecan, followed by BCNU plus irinotecan in newly-diagnosed GBM. The MTD for patients receiving enzyme-inducing anticonvulsants (EIAC) was as follows: irinotecan 400 mg/m(2)/week on Days 1, 8, 22 and 29 during RT, followed by BCNU 100 mg/m(2) Day 1, and irinotecan, 400 mg/m(2) on Days 1, 8, 22 and 29, every 6 weeks. The MTD for non-EIAC patients was as follows: irinotecan 125 mg/m(2)/week on Days 1, 8, 22 and 29 during RT, followed by BCNU 100 mg/m(2) Day 1 and irinotecan 75 mg/m(2) Days 1, 8, 22 and 29, every 6 weeks. Median OS was 10.8 mos. (95% CI: 7.7-14.9); OS at 12 months was 44.6% (95% CI: 33.3-59.8) and PFS 6 was 28.6% (95% CI: 18.9-43.2). Patients went off treatment due to adverse events (7%), refusal (11%), progressive disease (48%), death (9%), and other (9%); 16% completed protocol treatment. Survival was similar in patients with variant (6/7 or 7/7) and wild-type (6/6) UGT1A1\*28 genotypic alleles. Grade 3-4 toxicity was more common in non-EIAC patients with variant alleles. SN-38 C(max) and AUC in EIAC patients receiving 400 mg/m(2) irinotecan were 20.9 ng/ml and 212 ng/ml h, and in non-EIAC patients receiving 125 mg/m(2), 15.5 ng/ml and 207 ng/ml h. SN-38 AUC varied by UGT1A1\*28 status in non-EIAC patients. This regimen was not significantly active and radiosensitization was not observed. Non-EIAC patients with UGT1A1\*28 variant alleles appear particularly sensitive to toxicity from irinotecan.

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