A phase I study of capecitabine and concurrent radiotherapy (RT) for patients with newly diagnosed glioblastoma multiforme (GBM).

Sub-category: CNS Tumors

Category: Central Nervous System Tumors

Meeting: 2004 ASCO Annual Meeting

Session Type and Session Title: General Poster Session, Central Nervous System Tumors

Abstract No: 1537


Abstract:

Background: Capecitabine, an oral fluoropyrimidine, has efficacy in many solid tumors, and has proven to be safe and effective when combined with RT for rectal cancer. Studies suggest correlation of response with tumor thymidine phosphorylase (TP) and dihydropyrimidine dehydrogenase (DPD) expression (TP/DPD ratio). TP/DPD is increased in GBM and RT improves this ratio.

Methods: Patients were enrolled in 2 cohorts based on anti-convulsant (AED) use (P450 inducing or non-P450) and received 60 Gy RT in 30 fractions over 6 weeks and concurrent BID capecitabine starting at 625 mg/m² BID (1250 mg/m²/day). Capecitabine was escalated by 25% in consecutive groups of 3 pts per cohort. Pts received daily capecitabine during RT and for 4 weeks after (induction). After a 1-week break, pts received maintenance capecitabine: 1250 mg/m² BID (2500 mg/m²/day), days 1-14 every 3 weeks until progression or unacceptable toxicity. Primary endpoint: maximum tolerated dose (MTD) of capecitabine during induction. Secondary endpoints: safety, disease free and overall survival. Laboratory correlates: tumor TP/DPD by Q-RT-PCR, correlation of toxicity/efficacy with DPD promoter polymorphisms, and effects of P450 inducing AEDs on capecitabine pharmacokinetics.

Results: From March to December 2003, 15 evaluable pts were enrolled [13 male, 2 female; mean age 52.1 years (range 19-70); mean KPS 88.67% (range 60-100%)]. A dose limiting toxicity (DLT) occurred in both arms at dose level 1 resulting in expansion to 6 pts. No further DLTs occurred. The non-P450 AED arm at level 2 (750mg/m² BID) had 2 DLTs (diarrhea) in the first 3 pts. The MTD for this arm was defined as 625mg/m² BID. Enrollment continues for dose level 2 P450 AED arm. Conclusions: Capecitabine and concurrent RT for newly diagnosed GBM appears safe and well tolerated without unexpected toxicities. This combination is an exciting new approach to the treatment of GBM and merits further evaluation.

Associated Presentation(s):

1. A phase I study of capecitabine and concurrent radiotherapy (RT) for patients with newly diagnosed glioblastoma multiforme (GBM).

Meeting: 2004 ASCO Annual Meeting
Presenter: Alfred J. Newman
Session: Central Nervous System Tumors (General Poster Session)

Other Abstracts in this Sub-Category:

1. Concomitant and adjuvant temozolomide (TMZ) and radiotherapy (RT) for newly