

Abstract

A phase II trial of thalidomide (Thal) and procarbazine (Pro) in adults with recurrent or progressive malignant gliomas (MG)

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Background: Thal and Pro are among the few agents with demonstrated activity against MG. A two-stage, phase II trial was initiated within the WFURB to establish the response rate of combination Thal-Pro in patients (pts) with recurrent or progressive MG. **Methods:** Eligibility included pt age = 18 with measurable tumor on contrast enhanced brain scans; KPS = 60; normal liver, kidney and hematologic function; and treatment with = 2 prior regimens. Pts were required to participate in the S.T.E.P.S. Program and mandated to comply with agreed upon measures to avoid conception. Protocol therapy included Pro 250mg/m²/d x 5d q 28days and Thal 200mg/day continuously. Inpatient dose escalation of Thal was attempted (increase by 100mg/day weekly as tolerated) to a maximum of 800mg/day. All pts received daily pyridoxine(100mg), warfarin(1mg) and stool softeners/laxatives. MRI/CT scans were performed prior to each odd cycle (every 8 weeks) to assess response based upon changes in the products of the largest bidimensional tumor diameters. Quality of life questionnaires including the FACT-Br were performed at baseline and prior to each odd cycle in all treated pts. **Results:** 18 pts (11 male) were enrolled (median age 50, range 27–63). One pt refused any therapy and is excluded from the analysis. The 17 treated pts received 36 cycles (median 2) of therapy. The median maximum Thal dose achieved was 400mg (range 200–800). No complete or partial responses were seen; 1 pt (6%) experienced stable disease, 14 (82%) progressed as best response and 2 (12%) were not evaluable for response. Median time to progression was 2.1 months (95% CI, 1.5–2.5). 14 pts have died; median survival was 7.6 months (95% CI, 3.5–9.4). Grade 3/4 drug related toxicity was minimal. **Conclusions:** Despite modest individual response rates in multiple prior phase II and III trials, the combination of Pro and Thal demonstrated no efficacy in this trial and this combination is unworthy of further investigation in pts with MG. Supported by NCI 1 U10 CA81851 and Celgene.

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