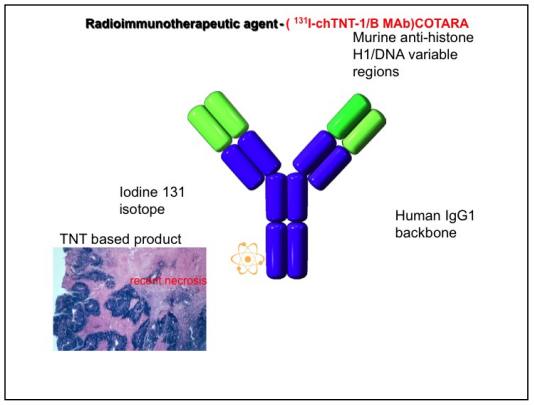
A Phase II Study of Intratumoral Radioimmunotherapy Treatment of Recurrent Glioblastoma Multiforme (GBM) and Review of Current Treatments of Recurrent Glioblastoma Multiform.

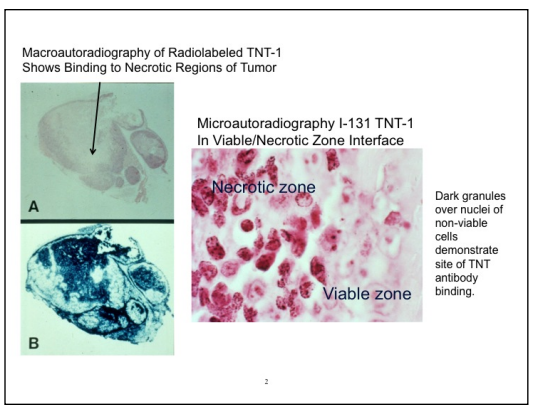
Deepak Kumar Gupta PhD

DEPARTMENT OF NEUROSURGERY AND NUCLEAR MEDICINE, ALL INDIA INSTITUTE OF MEDICAL SCIECNES, NEW



Introduction

Glioblastoma multiforme (GBM) is the most common /clinically aggressive of primary brain tumors. Prolongation of survival for recurrent GBM has not been convincingly demonstrated with any treatment strategy. 131I-chTNT-1/B MAb is a radioiodinated chimeric monoclonal antibody specific for DNA and histone H1 complex exposed in necrotic core of malignant gliomas.



Learning Objectives

This phase II study shows promising data results from this novel radioimmunotherapeutic compound in treatment of recurrent high grade gliomas.

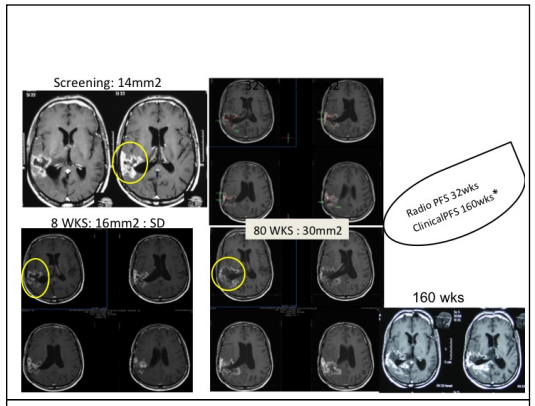
Methods

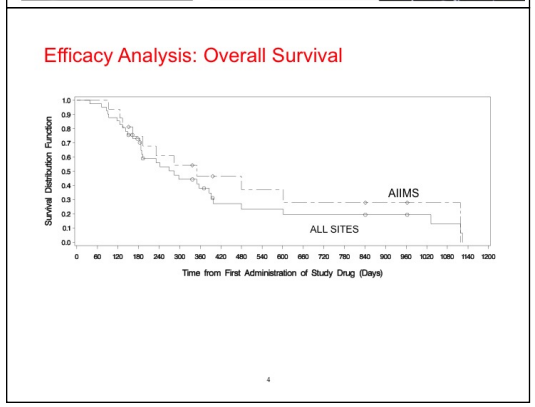
Phase II, open-label, dose confirmatory study. Patients aged 18 to 75 years with histologically confirmed GBM at first relapse, clinical target volume (CTV) of 5 to 60 cc, and Karnofsky Performance Status =70% were eligible. Drug adminstered by convection enhanced delivery via 2 catheters placed under stereotactic guidance, at a constant rate of 0.18 mL/h for 25 hours at dose of 2.5 mCi/cc of CTV. Additional endpoints included overall survival (OS), progression free survival (PFS), and proportion of patients alive at 6 months

Objectives :

Primary: To confirm the safety and tolerability of the maximum tolerated dose (MTD) of Cotara given as a single interstitial infusion

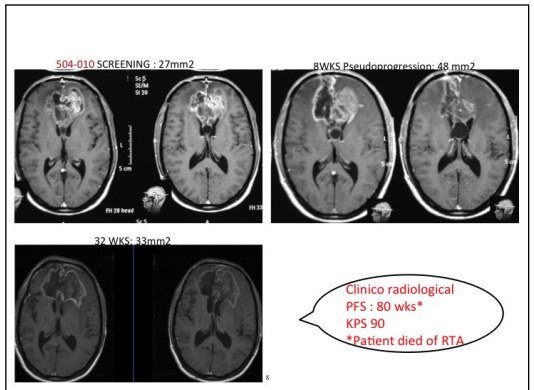
Secondary : To estimate overall survival, progression free survival and proportion of patients alive at 6 months after treatment.





Results

41 cases were enrolled and received study drug. Mean age was 52 years (24-74). Median CTV was 28.3 cc (1.6-65.8) and median KPS was 80 (70-100). The median administered therapeutic dose was 66.9 mCi (3.5 to 148) with most patients receiving >90% of planned therapy dose. The most common overall adverse events (AEs) (> 10%) were: brain edema (32%), headache (22%), convulsions (20%) and amnesia (12%).Interim median OS currently at 38 weeks and median PFS at 23 weeks



Literature review on therapies in Recurrent GBMs

Series(year)	n	median PFS	median OS	Tumor control rate	
EORTC BTSG26034 trial J Clin Oncol. 2009 Mar. Netherlands EGFR inhibitor(Erlotinib) vs TMZ	110	11.4% vs 24%			
Wich A , Germany J Neurology2009 May TMZ rechallenge	80	28.6%	Hematological toxicity (NCI-CTC grade 3-5) in 22 of 90 rechallenges		
Fabrini MG (Pisa, Italy) 2009 Aug Perioperative brachytherapy 18GY	21 HGG	42%	8months		Safe well tolerated
Br J cancer2009 Aug Grovas et al TMZ+ IFN vs TMZ+αIFN	34	31% vs 38%			
Oncologist2009 May, Cohen et al , FDA Bevacizumab	78	3.9 months		PR 26% (10-30%CI)	
J Neurooncol2008Zuniga et al, MI, USA Bevacizumab+ Irinotecan	37	7.6months PFS6mo: 43.7%	11.5months OSc:78%	CR+PR : 67%	
Neurology October 2009 Guzman et al,MSKCC, USA Bevacizumab with Irinotecan(42%) and Hypofractionated Reirradiation(58%)	37	4.5months		CR 8%,PR : 51% SD : 27%	
J Cl, Oncol Feb2009 Kreisel et al, Berkeda Phase II Bevacizumab with Irinotecan	48	4 months PFS6mo: 29%	7.2 months OSc:57%	CR+PR: 31% Irinotecan no extra benefit	
NS2005 Sunil Patel Cotara therapy	12		37wks	SD : 6cases PR : 1 case	
Present series 2011 Intratumoral I^{131}-chTNT-1/B Mab therapy	41 (16* AIIMS)		11.2 months(AIIMS) OSc:73% OS 1: 38%		

Conclusions Single interstitial administration of study drug at 2.5 mCi/cc was well-tolerated in this study of patients with recurrent GBM. I131-chTNT-1/B Mab is a novel radiolabeled monoclonal antibody with good safety profile when given as a single interstitial infusion at 2.5 mCi/cc CTV by convection enhanced delivery in patients with recurrent GBM.Encouraging interim survival data with 9.3 month (40.6 week) median, and 6-month, 1 year and 2 year survival of 73, 38 and 19%, respectively.