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Clinical Investigation

Prospective Randomized Phase 2 Trial of Hypofractionated Stereotactic Radiotherapy of 25 Gy in 5 fractions compared to 35 Gy in 5 fractions in the Reirradiation of Recurrent Glioblastoma

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INTRODUCTION

Glioblastoma (GBM) is the most common adult primary brain tumor. Despite optimal initial management, approximately 90% of patients will develop local progression, after which, median survival is 6.2 months[1,2].

Treatment options for recurrence include new resection, reirradiation, chemotherapy, antiangiogenic agents, immunotherapy, tumor treating fields or a combination of the above. Reirradiation is an option for selected cases of focal recurrent GBM, with 6 months and 1-year survival of…

Study design

This single center prospective randomized phase 2 trial compared the safety and efficacy of two regimens of HSRT in the treatment of recurrent or progressive GBM. The study was conducted at *Hospital das Clínicas da Faculdade de Medicina, University of São Paulo,* a tertiary public cancer center in São Paulo, Brazil.…

Eligibility Criteria

We enrolled patients 18 years of age or older who had recurrent or progressive GBM according to the 2007 and 2016 World Health Organization (WHO) Classification of Tumors of the…

RESULTS

From Oct 2011 through Aug 2019, 42 patients were enrolled. One patient withdrew consent before randomization; 41 patients were randomized, 20 to the 25Gy/5fx arm and 21 to 35Gy/5fx. One patient in the 35Gy/5fx arm rapidly progressed and died before initiation of RT and was excluded. Thus, 20 patients in each arm received at least one fraction of HSRT and were analyzed (CONSORT Diagram, Fig. 1). During follow-up, one patient moved to the northeast of the country and, being "too ill", did not…

DISCUSSION

Recurrent GBM is rapidly progressive and its overall prognosis remains dismal. Within this context, our prospective phase 2 randomized screening trial showed no signal that 35Gy in 5 fractions (BEDGy10 59.5; EQD2 49.6Gy) improves PFS compared to 25Gy in 5fx (BEDGy10 37.5; EQD2 31.3Gy). Even with a close follow-up that could potentially capture small differences (MRI every 2 months in the first 6 months and every 3 months after), the Kaplan-Meier curves during the first 6 months and throughout 1 …

CONCLUSION

Hypofractionated Stereotactic Radiotherapy alone with 35Gy/5fx was not superior to 25Gy/5fx in terms of PFS or OS. Due to a potential increase in the rate of clinically meaningful treatment-related necrosis, we suggest 25Gy/5fx as the standard dose in HSRT alone. During follow-up, attention should be given to differentiate tumor progression from potentially manageable complications. Future trials could study whether dose-escalated HSRT combined with antiangiogenic drugs can improve outcomes…

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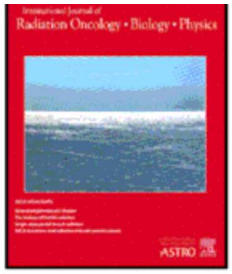

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Conflict of Interest: The following authors report potential conflicts of interest unrelated to this work: Dr. Helen Shih reports having received consulting fees from Servier Pharmaceuticals and Institutional financial support for RTOG 3508 by AbbVie;

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This trial is registered at ClinicalTrials.gov NCT01464177

Data Availability: De-identified data will be available upon request on a case-by-case basis to researchers who provide a methodologically sound proposal. Requests should be made to the corresponding author.

* Contributed to this study while at Hospital das Clínicas da FMUSP, São Paulo, Brazil

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