

# *Reirradiation of brain tumors: why not?*

*G Minniti*

Ospedale Sant'Andrea, Università Sapienza Roma



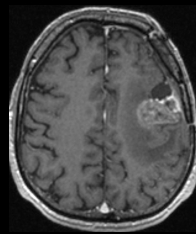
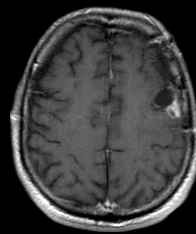
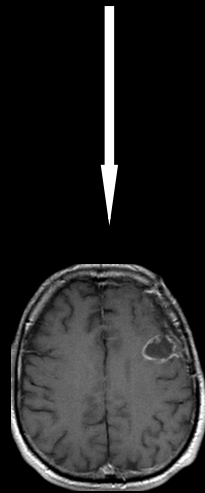
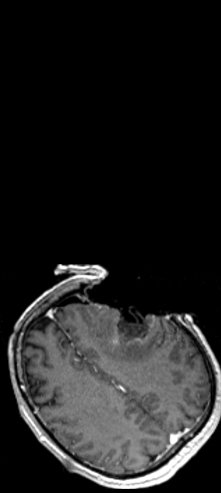
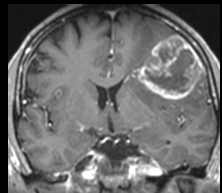
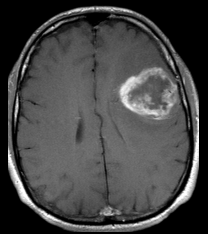
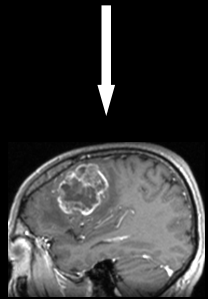
I declare no conflict of interest

man 47 years old, GBM

Diagnosis  
2/2010

IMRT + TMZ  
4/2010

Recurrent GBM  
3/2011



Surgery  
3/2010

Adjuvant TMZ  
6 cycles

✓ *Efficacy of reirradiation for progressive gliomas*

➤ *PFS and OS*

➤ *Toxicity*

➤ *Alternative treatments*

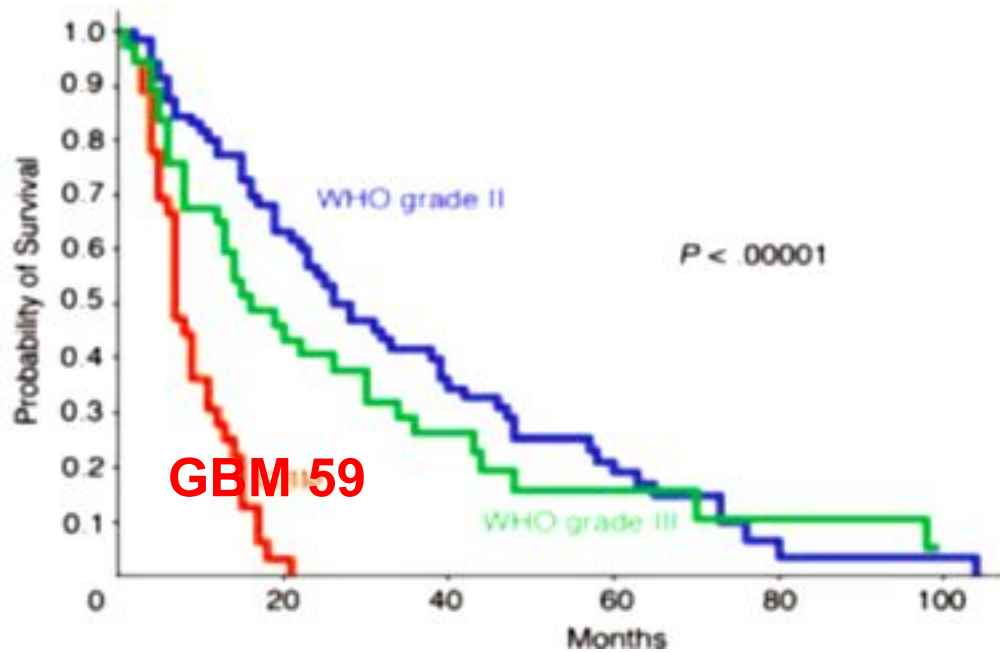


## ✓ *Reirradiation of malignant gliomas*

- *Conventional radiotherapy*
- *Stereotactic conformal fractionated radiotherapy*
- *Radiosurgery*



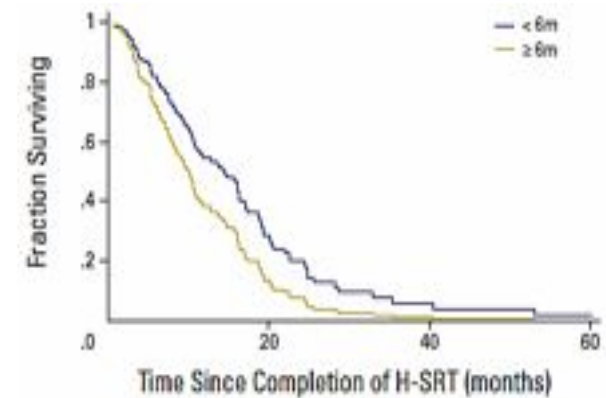
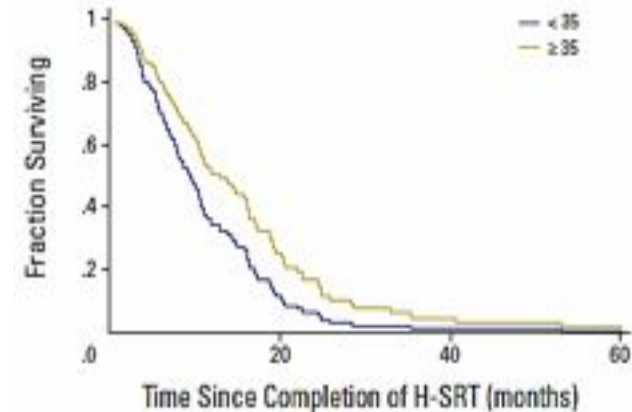
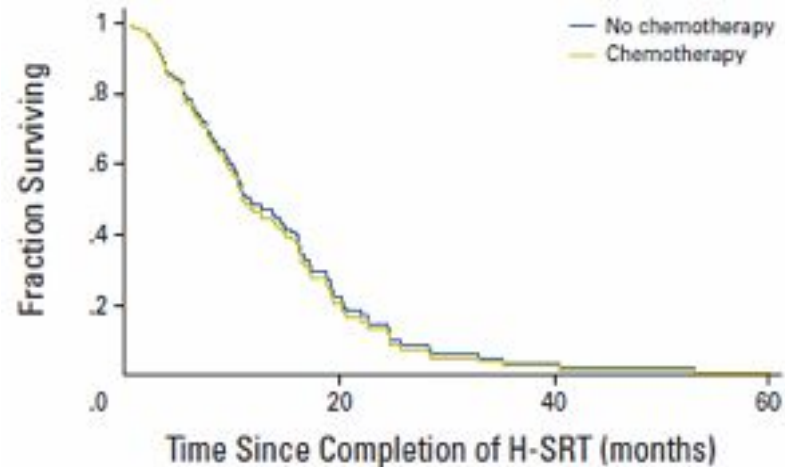
✓ *Reirradiation of 172 patients treated with FSRT*



Histology	Median (months)	1-Year Survival	2-Year Survival
GBM	8	23%	2%
WHO grade III	12	65%	41%
WHO grade II	22	77%	55%

# Hypofractionated Stereotactic Radiation Therapy: An Effective Therapy for Recurrent High-Grade Gliomas

Shannon E. Fogh, David W. Andrews, Jon Glass, Walter Curran, Charles Glass, Colin Champ, James J. Evans, Terry Hyslop, Edward Pequignot, Beverly Downes, Eileen Comber, Mitchell Maltenfort, Adam P. Dicker, and Maria Werner-Wasik



147 pts  
35 Gy in 10 fractions

✓ *Efficacy of reirradiation for progressive gliomas*

➤ *PFS and OS*

➤ *Toxicity*

➤ *Alternative treatments*

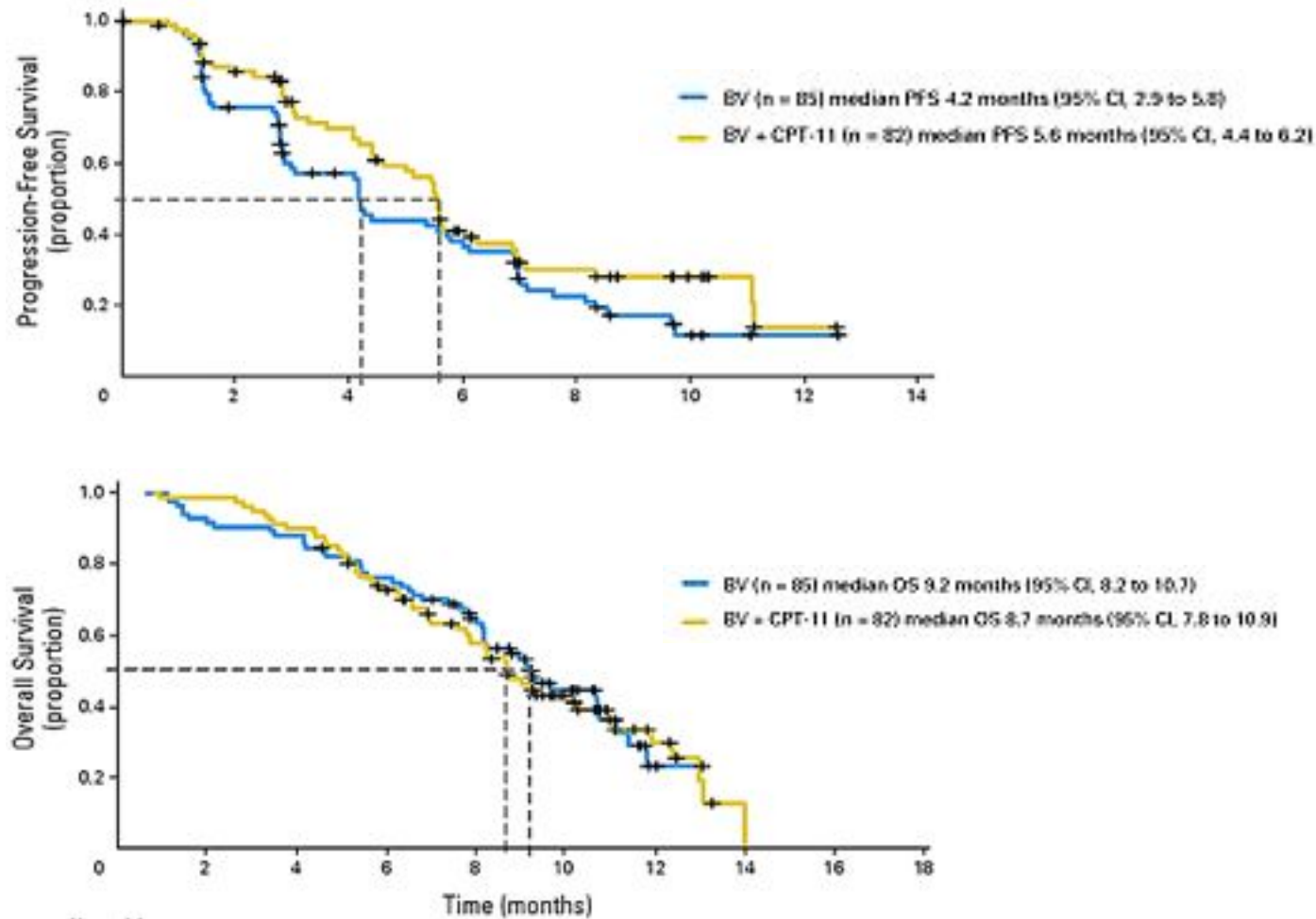


✓ *Recent published series on chemotherapy for recurrent gliomas*

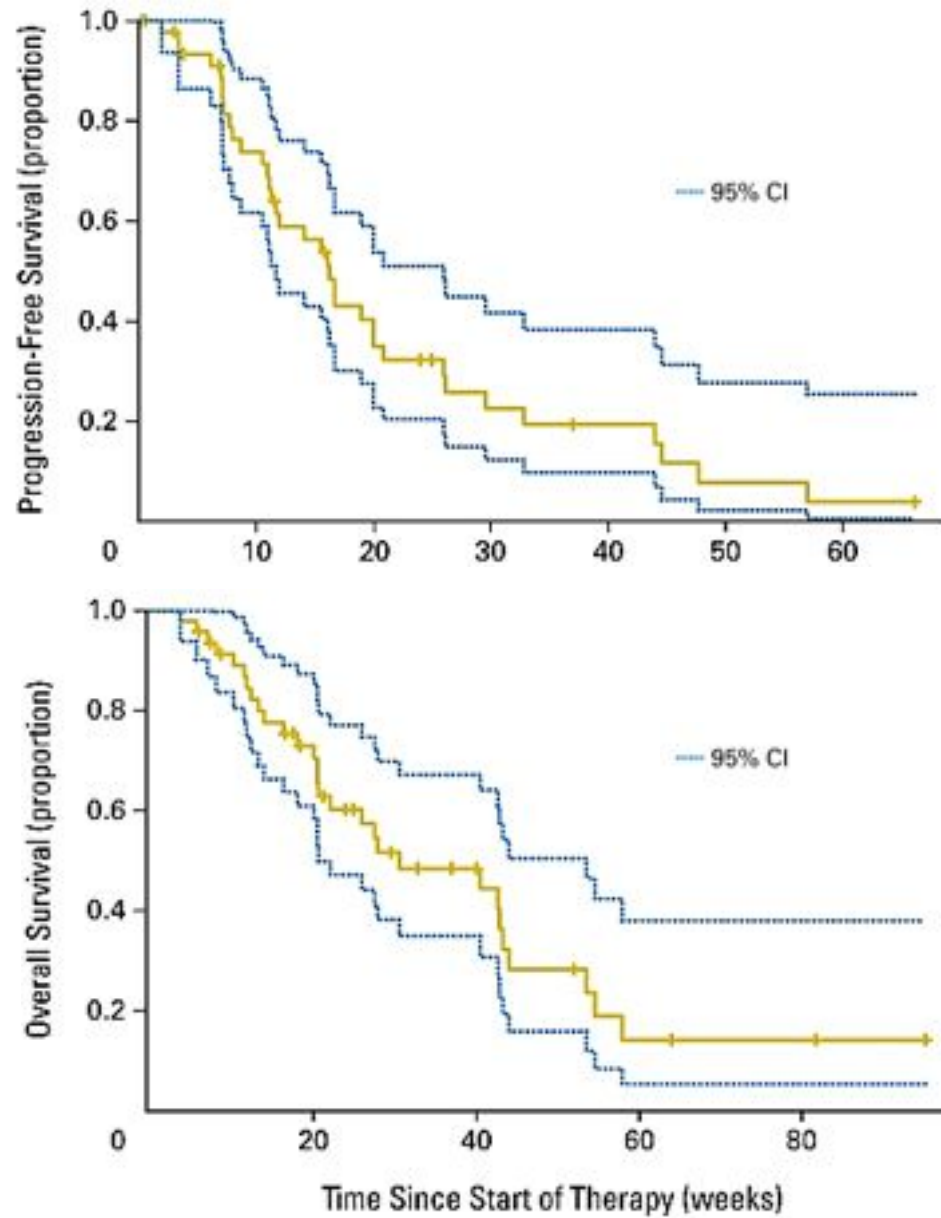
Authors	Pts	Type	CHT	PFS%	OS
Friedman et al., 2009	85	GBM	Beva	42.6 (6m)	9.2
	82		Beva + Irinotecan	50.3 (6m)	8.7
Kreisl et al., 2009	48	GBM	Beva	29 (6m)	7.9
Verhoeff et al., 2010	23	GBM	Beva + daily TMZ	17.4 (6m)	4.5
Reithmeier et al., 2010	35	GBM	BCNU	11 (wks)	22
Raizer et al., 2010	61	AA/GBM	Beva (3w)	25 (6m)	6.2
Desjardins et al., 2012	32	GBM	Beva + daily TMZ	18 (6m)	9
Kreisl et al., 2011	32	AA	Beva	20.9 (6m)	12
Omuro et al., 2013	15	GBM	Daily TMZ	19 (6m)	7 (13 vs 4.3*)
Taal et al., 2014	154	GBM	Lom / bev vs both		43/38/59 (9m)
Soffietti et al., 2014	44	GBM	Fot + Bev	42.6 (6m)	9.1



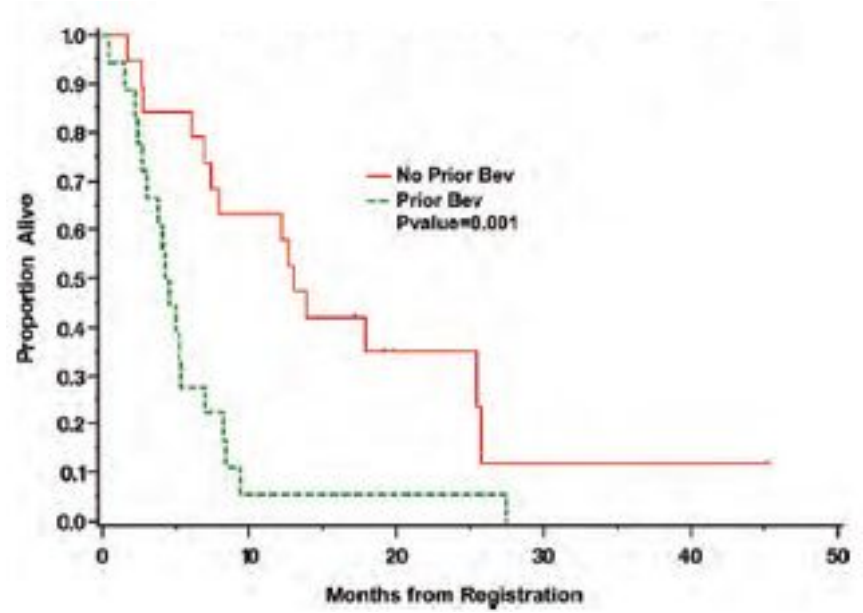
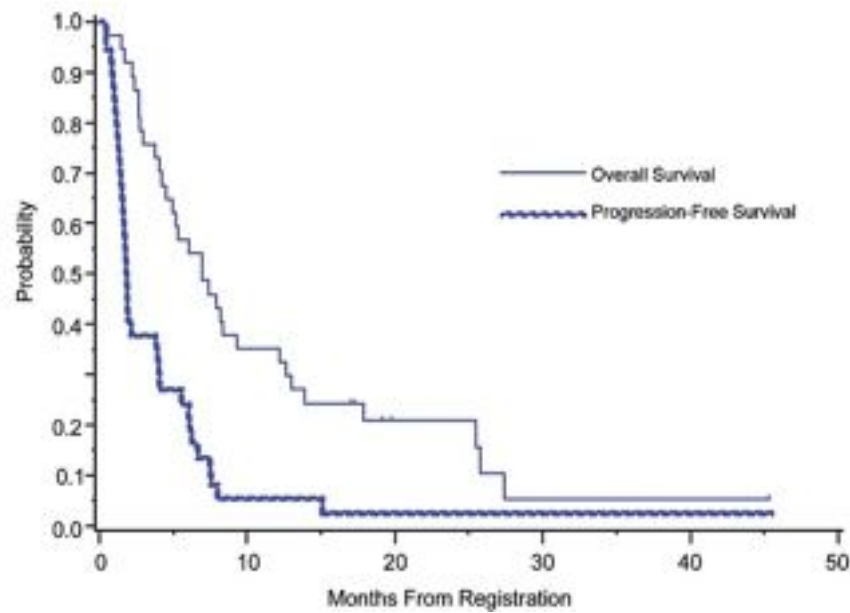
✓ *Bevacizumab Alone and in Combination With Irinotecan in Recurrent Glioblastoma*



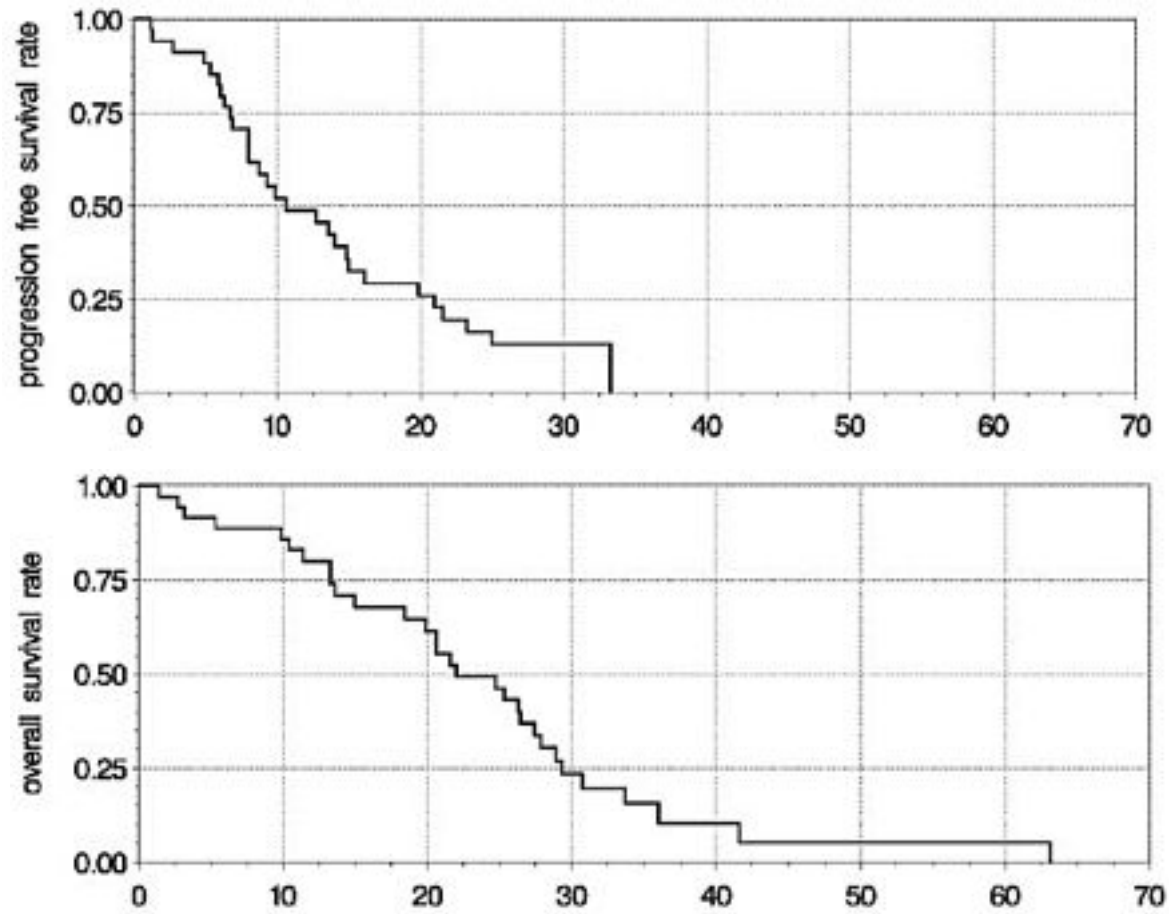
## ✓ Bevacizumab Alone in Recurrent Glioblastoma



✓ *Continuous low-dose temozolomide for patients with recurrent malignant glioma*

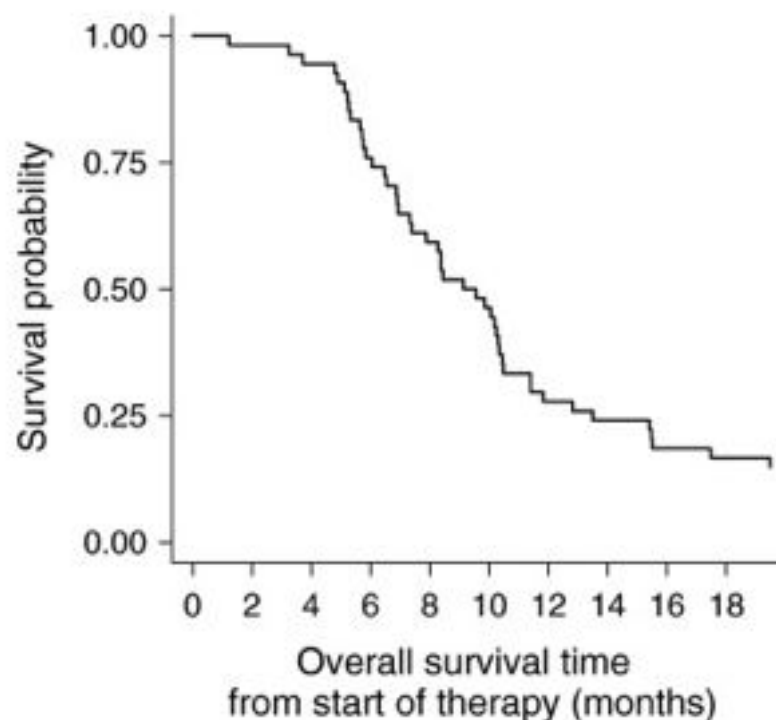
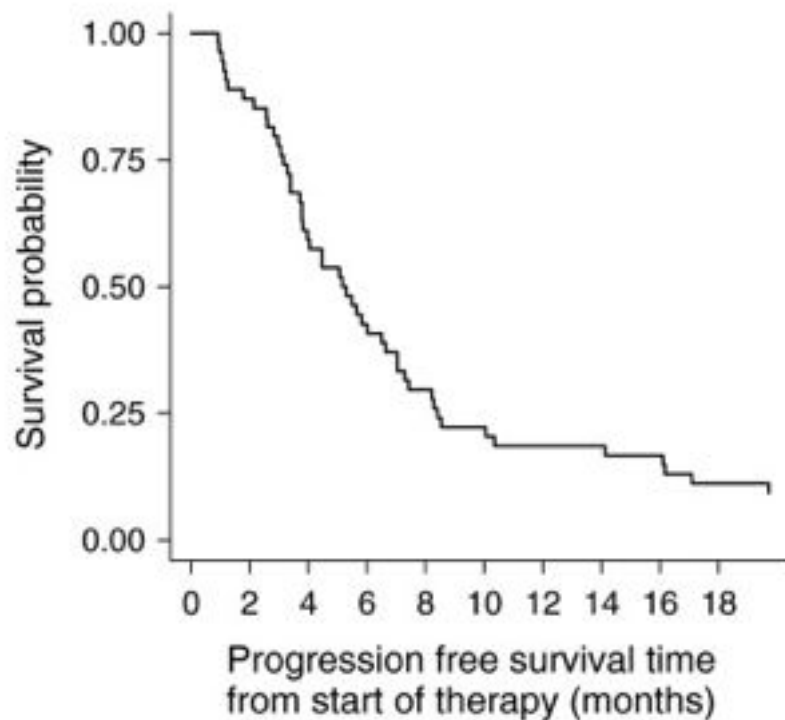


✓ BCNU for recurrent glioblastoma multiforme



## Bevacizumab and fotemustine for recurrent glioblastoma: a phase II study of AINO (Italian Association of Neuro-Oncology)

Riccardo Soffietti • Elisa Trevisan • Luca Bertero •  
Paola Cassoni • Isabella Morra • Maria Grazia Fabrinì •  
Francesco Pasqualetti • Ivan Lolli • Anna Castiglione •  
Giovannino Ciccone • Roberta Rudà



✓ *Efficacy of reirradiation for progressive gliomas*

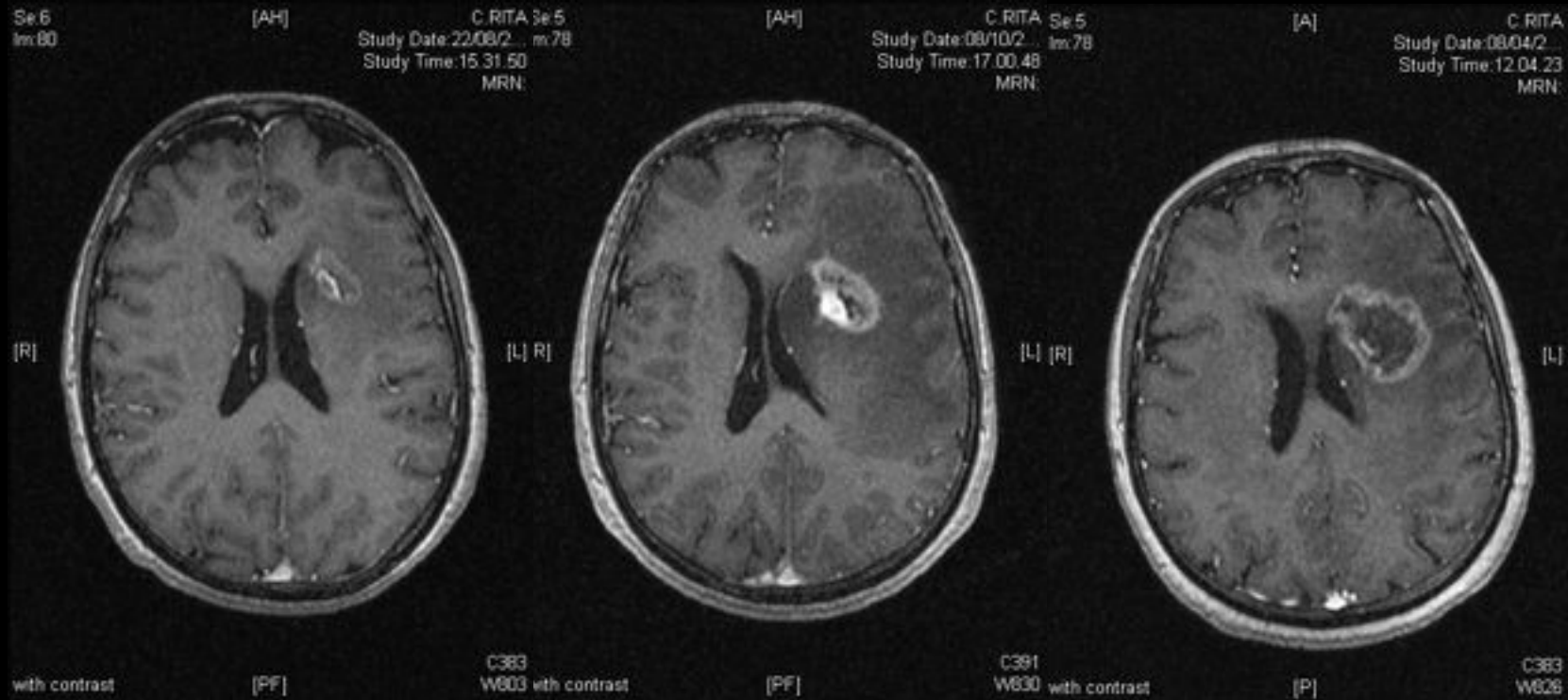
➤ *PFS and OS*

➤ *Toxicity*

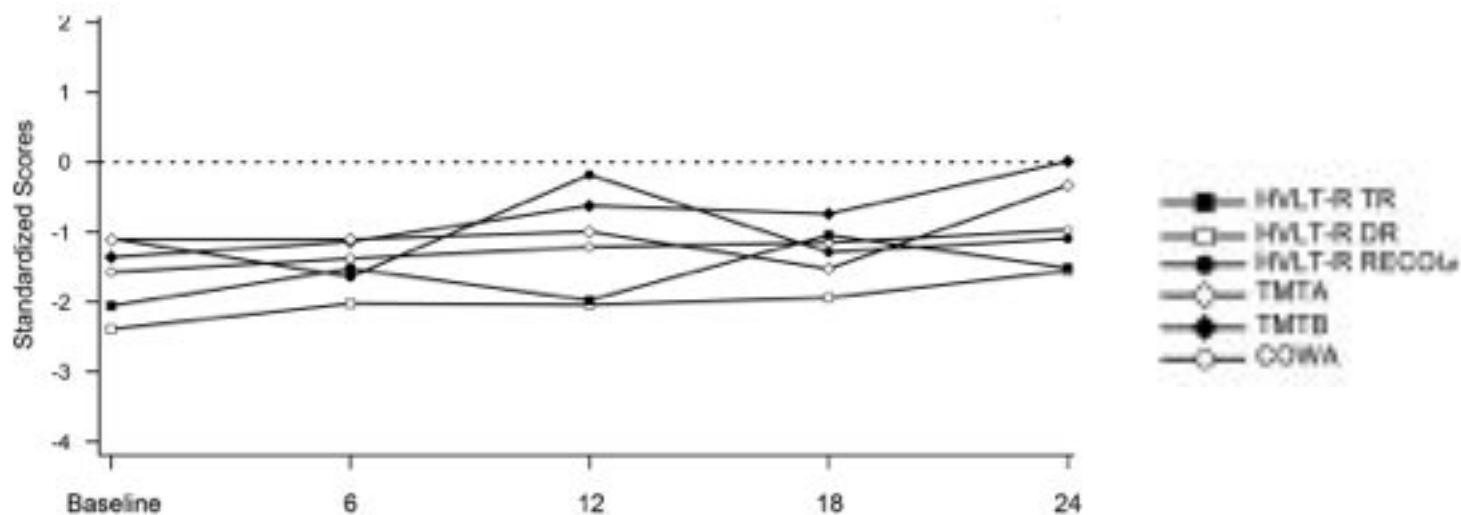
➤ *Alternative treatments*



✓ *Radionecrosis after SRS in a GBM patient*



## ✓ Neurocognitive Outcomes in the BRAIN Study



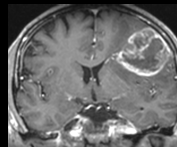
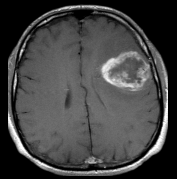
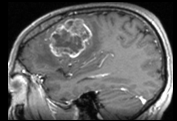
	Stable or improved on all tests	Declined on at least one test
Patients with an IRF-determined OR (at time of response) <sup>a</sup>	18/24 (75.0%)	6/24 (25.0%)
Patients with IRF-determined PFS >6 months (at Week 24 assessment) <sup>b</sup>	19/27 (70.4%)	8/27 (29.6%)
Patients with investigator-determined disease progression (at time of progression) <sup>c</sup>	15/49 (30.6%)	34/49 (69.4%)



✓ May we improve the clinical outcome with combined chemoradiotherapeutic regimens?

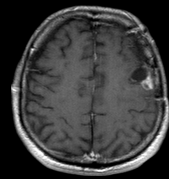
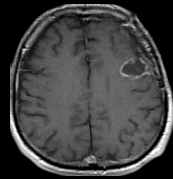
man 47 years old, GBM

Diagnosis  
2/2010



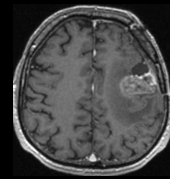
Surgery  
3/2010

IMRT + TMZ  
4/2010

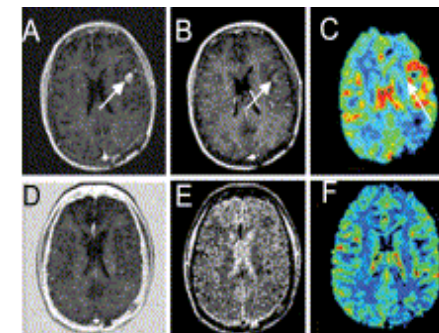
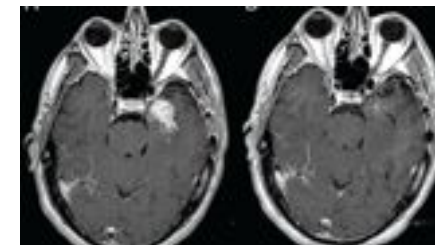
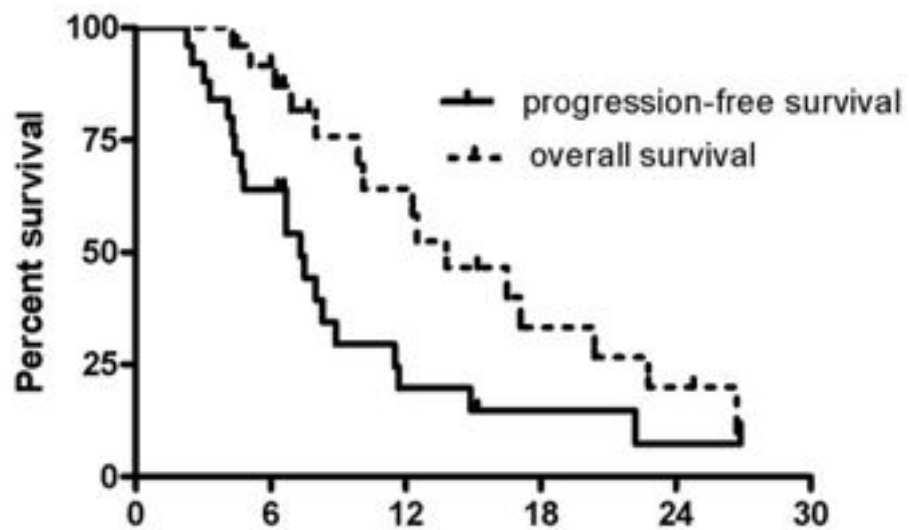


Adjuvant TMZ  
6 cycles

Recurrent GBM  
3/2011





✓ *Bevacizumab with Hypofractionated Stereotactic Irradiation for Recurrent Malignant Gliomas*

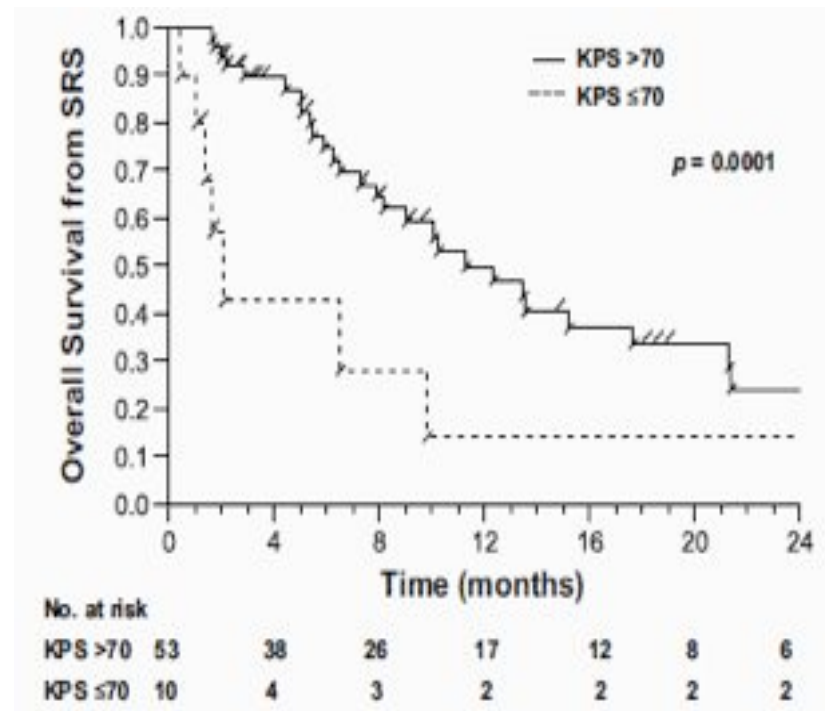
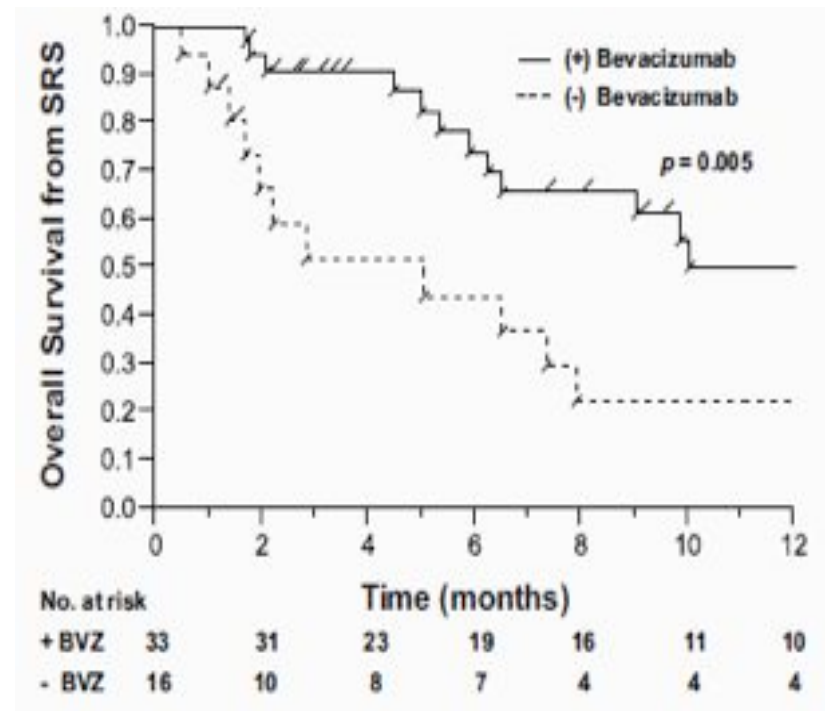


Clinical Investigation

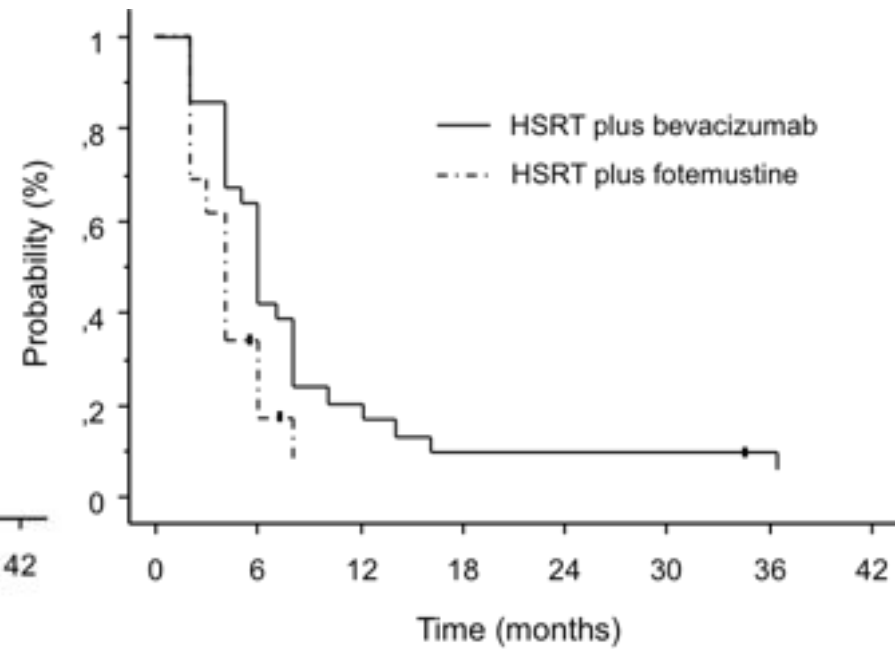
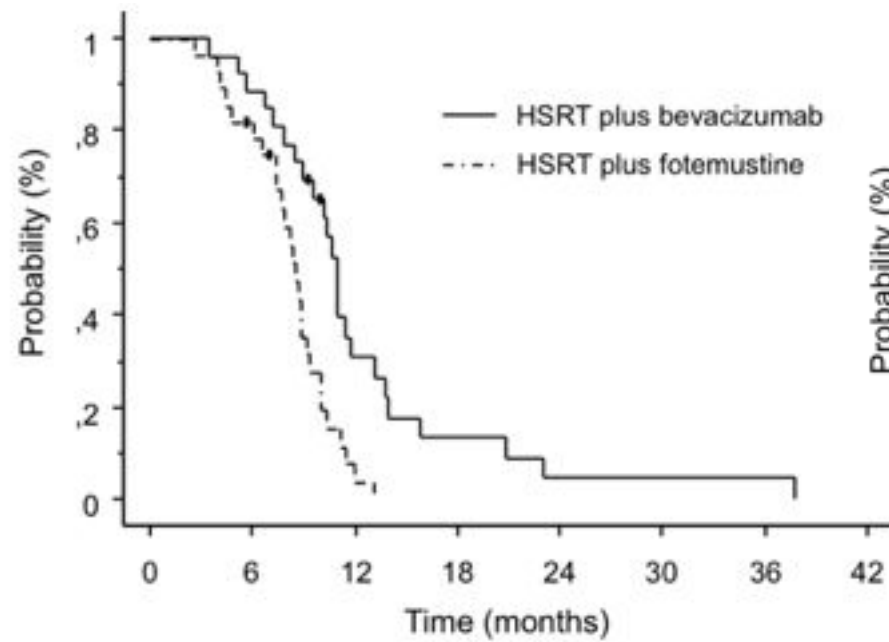
## Safety and Efficacy of Stereotactic Radiosurgery and Adjuvant Bevacizumab in Patients With Recurrent Malignant Gliomas

Presented at the 51st Annual Meeting of the American Society for Radiation Oncology, Chicago, IL, November 1–5, 2009.

Kyle C. Curcio, M.D.<sup>1</sup>, James J. Vredenburg, M.D.<sup>1,2</sup>, John H. Sampson, M.D., Ph.D.<sup>1,2</sup>, David A. Reardon, M.D.<sup>1,2</sup>, Annick Desjardins, M.D.<sup>1,2</sup>, Katherine B. Peters, M.D., Ph.D.<sup>1,2</sup>, Henry S. Friedman, M.D.<sup>1,2</sup>, Christopher G. Willett, M.D.<sup>1</sup>, John P. Kirkpatrick, M.D., Ph.D.<sup>1,2</sup>  

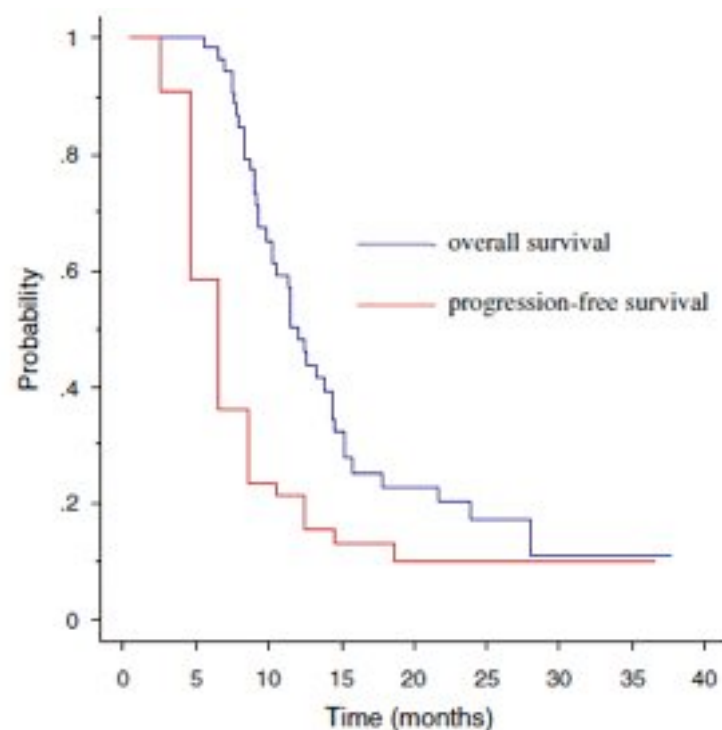


- ✓ *Hypofractionated stereotactic radiotherapy in combination with bevacizumab or fotemustine for patients with progressive malignant gliomas*



## Hypofractionated stereotactic radiotherapy and continuous low-dose temozolomide in patients with recurrent or progressive malignant gliomas

Giuseppe Minniti · Claudia Scaringi · Vitaliana De Sanctis · Gaetano Lanzetta · Teresa Falco · Domenica Di Stefano · Vincenzo esposito · Riccardo Maurizi Enrici



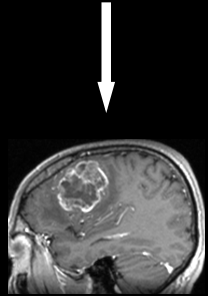
Factor	Hazard ratio (95 % CI)	P value
Risk of death		
KPS >70	0.42 (0.22–0.78)	0.01
Grade 3	0.18 (0.07–0.45)	0.0002
MGMT methylation status	0.61 (0.35–1.09)	0.08
Interval from initial treatment	0.97 (0.93–1.02)	0.4
Risk of progression		
Grade 3	0.32 (0.15–0.68)	0.003
MGMT methylation status	0.64 (0.34–1.18)	0.15

## ✓ *Summary*



- *Although reirradiation is a feasible option for patients with high grade gliomas, results are similar those observed with chemotherapy alone; better results are obtained with chemoradiation (bevacizumab, temozolomide?)*
- *Toxicity and neurocognitive decline remain of concern.*

Diagnosis  
2/2010



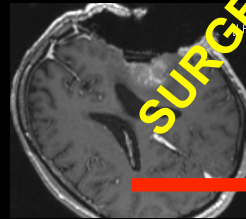
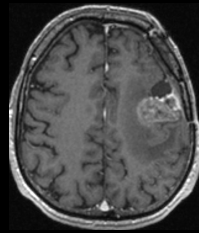
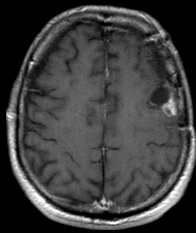
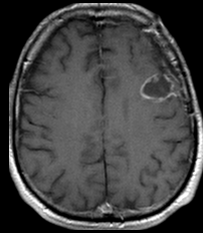
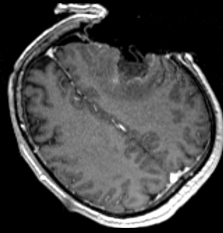
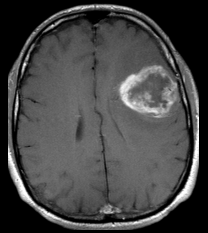
IMRT + TMZ  
4/2010



Recurrent GBM  
3/2011



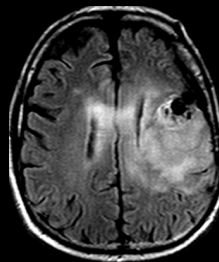
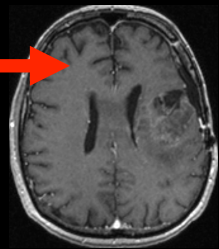
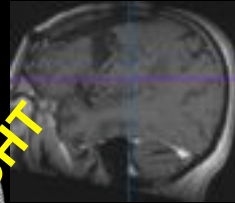
SRT + Beva  
6/2011



SURGERY

SRS/SRT

CHT



Surgery  
3/2010

Adjuvant TMZ  
6 cycles

2° Surgery  
4/2011

12/2011

(†1/2012)

man 47 years old, GBM



*...Grazie per l'attenzione*

Padova 10-11-2014