

Clinical Cancer Research



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Imaging, Diagnosis, Prognosis

Cancer Stem Cell Analysis and Clinical Outcome in Patients with Glioblastoma Multiforme

Roberto Pallini¹, Lucia Ricci-Vitiani³,
Giuseppe Luigi Banna⁴, Michele Signore³,
Dario Lombardi⁵, Matilde Todaro⁶, Giorgio Stassi⁶,
Maurizio Martini², Giulio Maira¹, Luigi Maria Larocca²
and Ruggero De Maria^{3,5}

Authors' Affiliations: ¹ Department of Neurosurgery and ² Institute of Pathological Anatomy, Catholic University of Rome; ³ Department of Hematology, Oncology and Molecular Medicine, Istituto Superiore di Sanità, Rome, Italy; ⁴ Unit of Medical Oncology, Vittorio Emanuele University Hospital; ⁵ Mediterranean Institute of Oncology, Catania, Italy; and ⁶ Department of Surgical and Oncological Sciences, University of Palermo, Palermo, Italy

Requests for reprints: Ruggero De Maria, Department of Hematology, Oncology and Molecular Medicine, Istituto Superiore di Sanità, Viale Regina Elena 299, 00161 Rome, Italy. Phone: 39-06-4990-3121; Fax: 39-06-4938-7087; E-mail: demaria@iss.it.

Purpose: Cancer stem cells (CSC) are thought to represent the population of tumorigenic cells responsible for tumor development. The stem cell antigen CD133 identifies such a tumorigenic population in a subset of glioblastoma patients. We conducted a prospective study to explore the prognostic potential of CSC analysis in glioblastoma patients.

Experimental Design: We investigated the relationship between the *in vitro* growth potential of glioblastoma CSCs and patient death or disease progression in tumors of 44 consecutive

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glioblastoma patients treated with complete or partial tumorectomy followed by radiotherapy combined with temozolomide treatment. Moreover, we evaluated by immunohistochemistry and immunofluorescence the prognostic value of the relative presence of CD133⁺ and CD133⁺/Ki67⁺ cells in patient tumors.

Results: *In vitro* CSC generation and the presence of $\geq 2\%$ CD133⁺ cells in tumor lesions negatively correlated with overall ($P = 0.0001$ and 0.02 , respectively) and progression-free ($P = 0.0002$ and 0.01 , respectively) survival of patients. A very poor overall ($P = 0.007$) and progression-free ($P = 0.001$) survival was observed among patients whose tumors contained CD133⁺ cells expressing Ki67. Taking into account symptom duration, surgery type, age, *O*⁶-methylguanine-DNA methyltransferase promoter methylation, and p53 status, generation of CSCs and CD133/Ki67 coexpression emerged as highly significant independent prognostic factors, with an adjusted hazard ratio of 2.92 (95% confidence interval, 1.37-6.2; $P = 0.005$) and 4.48 (95% confidence interval, 1.68-11.9; $P = 0.003$), respectively.

Conclusions: The analysis of CSCs may predict the survival of glioblastoma patients. *In vitro* CSC generation and presence of CD133⁺/Ki67⁺ cells are two considerable prognostic factors of disease progression and poor clinical outcome.

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