

## Disposition of temozolomide in a patient with glioblastoma multiforme after gastric bypass surgery

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Received: 25 September 2008 / Accepted: 15 December 2008  
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**Abstract** Temozolomide, used for anaplastic gliomas and glioblastoma multiforme, is an oral drug that is stable under acidic, but labile under neutral and basic conditions. Although the bioavailability of temozolomide is approximately 100%, pathology or anatomical changes of the gastrointestinal tract may adversely affect absorption, and consequently therapeutic response. HPLC-UV was used to evaluate temozolomide plasma pharmacokinetics in a

patient with unresponsive glioblastoma multiforme who had previously undergone gastric bypass as part of a weight-loss strategy. Temozolomide plasma pharmacokinetics were comparable to values reported for patients with normal gastrointestinal anatomy. These data imply that progression of disease in this patient was not due to inadequate temozolomide concentrations. Physicians need to become aware of the rapidly increasing population of patients who have had a gastric bypass and require oral therapy, of which our case is representative. The effect of gastric bypass on pharmacokinetics will need to be evaluated on a drug-by-drug basis.

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**Keywords** Temozolomide · Gastric bypass ·  
Pharmacokinetics

### Introduction

Temozolomide (Temodar<sup>®</sup>) is an alkylating agent approved for the treatment of newly diagnosed glioblastoma multiforme and anaplastic astrocytoma after progression on nitrosourea and procarbazine [1–3]. Off-label use of temozolomide includes treatment of advanced metastatic malignant melanoma [4]. Temozolomide is converted to its active metabolite MTIC by non-enzymatic hydrolysis, which occurs under physiological conditions, as opposed to the production of MTIC from dacarbazine (DTIC), which requires metabolic conversion [5], see Fig. 1. MTIC is a reactive intermediate, and exerts antitumor activity by specific methylation of O<sup>6</sup> and N<sup>7</sup> positions of guanine in DNA [6].

Temozolomide displays linear pharmacokinetics over a dose range of 50–1,200 mg/m<sup>2</sup> with an oral bioavailability of approximately 100% [5, 7]. Temozolomide is cleared