


## Journal Article



## Fixed dose-rate gemcitabine as radiosensitizer for newly diagnosed glioblastoma: a dose-finding study

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**Abstract** In patients with newly diagnosed glioblastoma multiforme (GBM), concurrent chemo-radiotherapy with temozolomide is the new standard of care. In the present phase I study we investigated the association of gemcitabine, a cell-cycle antimetabolite with radiosensitizing properties, with radiotherapy (RT) in the first line treatment. Gemcitabine was delivered at a fixed dose-rate of 10 mg/m<sup>2</sup>/min weekly for 6 weeks starting 24–72 h prior to, and then concomitantly with RT (2.0 Gy per fraction, total dose 60 Gys). The primary end-point was the identification of dose-limiting toxicity (DLT), and maximum tolerated dose (MTD). Planned dose levels of gemcitabine started from 200 mg/m<sup>2</sup>/weekly (level 1), with sequential dose escalations of 25 mg/m<sup>2</sup>. Ten patients were enrolled, all with evaluable disease after surgery. Six patients were male, median age was 55 years (44–75), and median baseline Karnofsky performance status was 85 (70–100). Four patients entered level 1, one patient being excluded from the study because of early disease progression. At this level, two of three patients developed progressive neurological deterioration, potentially related to the experimental treatment. On this basis gemcitabine dose was prudentially reduced to 175 mg/m<sup>2</sup>/weekly in the subsequent step (level –1). No DLT was encountered in the six patients enrolled at this level. Interestingly, at this dose only two grade three toxicities (one neutropenia and one raise in serum transaminases) were reported. Thus, fixed dose-rate gemcitabine at

175 mg/m<sup>2</sup>/weekly is the recommended regimen for further evaluation in a phase II study that is presently in progress.

**Keywords** Glioblastoma multiforme - Gemcitabine - Chemo-radiotherapy - Phase I study

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References secured to subscribers.

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