

Efficacy of Intracranial Microcapsule Delivery of Temozolomide compared to Systemic Therapy in a Model of Metastatic Breast Carcinoma

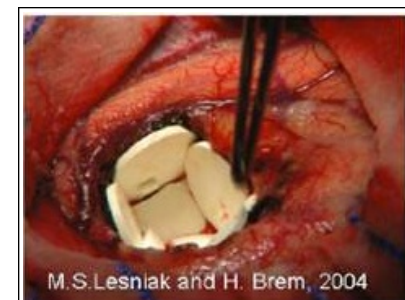
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Introduction

Temozolomide (TMZ) is an oral alkylating agent used clinically for the treatment of Grade IV astrocytoma. Systemic therapy is limited by dose-associated myelosuppression.[Ref. 1] We have previously shown that TMZ can be effectively released via an intracranially implanted multi-orifice, liquid crystal polymer (LCP) microcapsule. We now explore whether TMZ release via LCP microcapsule is superior to systemic TMZ administration in a rodent model of intracranial metastatic breast carcinoma.

Methods

Multi-orifice, LCP microcapsules were engineered and 11 mg of TMZ was placed within each device. Twenty-four F344 rats underwent intracranial implantation of CRL1666 rat breast adenocarcinoma cells and were randomized to three groups: 1) No treatment (n=8), 2) oral TMZ (50mg/kg) (n=8), or TMZ (11mg) microcapsule (n=8). Survival was the primary outcome.



Gliadel® Wafers

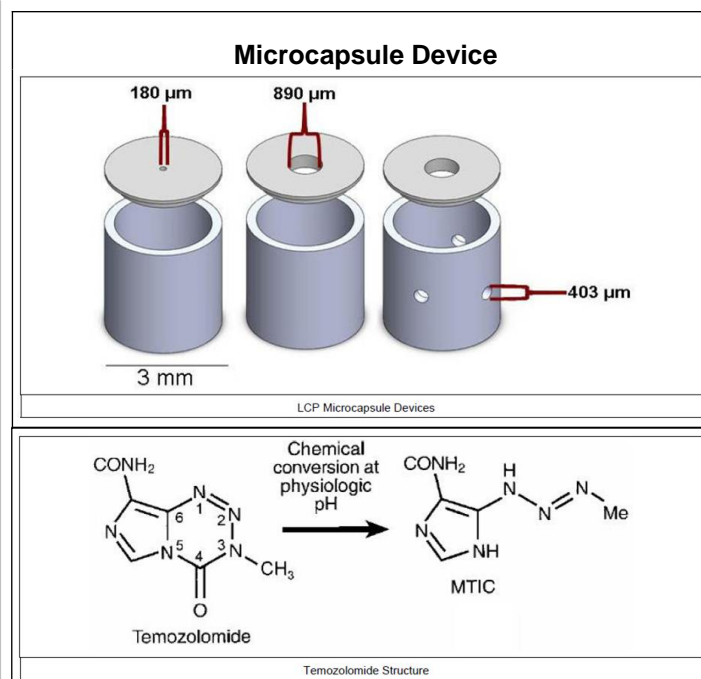
M.S.Lesniak and H. Brem, 2004



Microcapsule Device

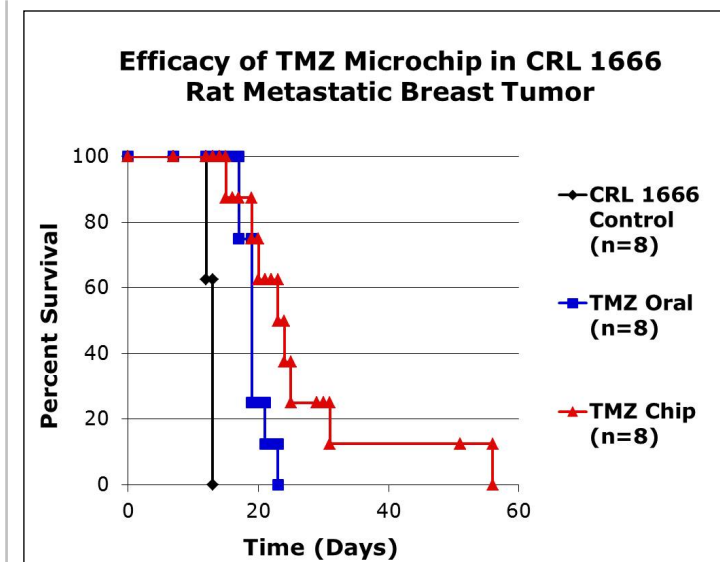
Y.Patta, MIT

Device Implantation: Gliadel(R) and Microcapsule Device



Results

Rats receiving no treatment had a median survival of 13 days. The oral TMZ group had significantly increased survival compared to control ($p=0.0001$) with a median survival of 19 days. Rats implanted with the intracranial TMZ microchip had a median survival of 23 days, a significant increase in comparison with both control ($p=0.0001$) and oral TMZ ($p=0.026$)(please see attached figure).



Conclusions

Intracranial delivery of TMZ via multi-orifice, LCP microcapsules was shown to be a safe and effective method of TMZ delivery to metastatic breast tumors that was superior to systemic TMZ treatment. LCP microcapsules should be further investigated as novel devices for local chemotherapeutic delivery to brain metastases.

Learning Objectives

- 1) Intracranial TMZ is safe and well tolerated.
- 2) Microcapsules should be further investigated as novel devices for local chemotherapeutic delivery to brain metastases.

References

- 1) Mutter N, Stupp R. Temozolomide: a milestone in neuro-oncology and beyond? Expert Rev Anticancer Ther. 2006 Aug;6(8):1187-204.