Local Delivery of Ribavirin as a Promising Therapeutic Option for Glioblastoma

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Disclosures

None
Introduction

Ribavirin is an FDA-approved anti-viral drug that has recently shown promise as a repurposed anti-tumor agent.

Our laboratory previously demonstrated therapeutic effects of ribavirin in cell and animal models of glioblastoma.

However, the impact of these findings is limited by the blood-brain barrier, which reduces intracranial drug bioavailability.

To build upon our previous findings and optimize the delivery of ribavirin to treat glioblastoma, we investigated the effects of ribavirin delivered locally via controlled release polymers placed at the site of tumor implantation.
10 mg wafers were formulated containing 50% ribavirin/50% poly[bis(p-carboxyphenoxy)propane] anhydride and sebacic acid polymer.

An *in vitro* release kinetics assay was performed to study the release profile of ribavirin from the polymer.

*In vivo* safety and efficacy experiments were conducted using wafers placed orthotopically into female F344 rats implanted with 9L glioma.
Results

Wafers with 50% ribavirin/50% pCPP:SA rapidly release their contents

In vitro Release Kinetics

The wafers rapidly released ribavirin, with a small amount of continued release over several days, at concentrations observably higher than can be achieved through systemic administration.
Results

Locally delivered ribavirin wafers are nontoxic in healthy rats

Wafers were well tolerated. All rats survived until sacrifice and demonstrated steady weight gain, normal behavior, and no signs of toxicity.
Local delivery of ribavirin wafers extends survival in a 9L rat model

Results

Local delivery of ribavirin in vivo led to a significant survival benefit in rats implanted with 9L glioma (p=0.0161) compared to untreated controls.
**Discussion**

Our findings demonstrate that locally delivered ribavirin is not only safe but also effective at improving survival in a glioma model.

We strengthen the case that ribavirin can be used as an anti-glioblastoma therapeutic using delivery methods known to be successful in treating malignant gliomas.

To expand upon these exciting findings, we are currently evaluating the effects of locally delivered ribavirin in combination with radiotherapy and chemotherapy (temozolomide).

Our work suggests a viable opportunity for ribavirin to be tested clinically as an anti-glioblastoma therapeutic.
Summary Points

Glioblastoma is the most common and aggressive malignant brain tumor in adults. Novel treatments are needed to improve current survival outcomes.

Our laboratory previously showed that ribavirin, an anti-viral drug FDA-approved for the treatment of chronic Hepatitis C, showed promise as an anti-tumor agent in glioblastoma.

To build upon these findings, we demonstrated that local delivery of ribavirin via controlled release polymers was safe and effective at improving survival in a 9L rat glioma model.