Transarterial VSV oncolytic therapy for hepatocellular carcinoma

Antifibrotic properties of vesicular stomatitis virus as novel treatment option for liver fibrosis

Reference Number
B70098

Background
Hepatocellular carcinoma (HCC) is the third leading cause of cancer-related death worldwide, with the majority of clinical cases arising as a result of the wound-healing response to chronic liver injury known as hepatic fibrosis. If left untreated, the condition progresses to the state of cirrhosis with severe complications of end-stage liver disease including HCC. When HCC arises under these conditions, it presents a major clinical challenge for treatment of the cancer as well as the underlying liver disease.

Based on the results of early clinical trials, oncolytic virotherapy holds promise as a safe and effective treatment strategy for advanced HCC. It has been demonstrated that recombinant vesicular stomatitis virus (VSV) vectors are particularly attractive oncolytic agents for the treatment of HCC, resulting in significant tumor responses and subsequent prolongation of survival.

Origin
Technische Universität München

Industrial Sector
Pharmaceutics & medicine

Key Words
VSV, liver fibrosis, oncolytic, liver carcinoma

Patent Status
EP (10/ 2010)

Offer
Cooperation, license, option, purchase, world-wide, exclusive

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Innovation
Over the last 25 years, much progress has been made in understanding the mechanism of liver fibrogenesis, and as a result, it is now believed that fibrosis and cirrhosis are reversible processes. Despite this growing body of evidence, the clinical management of cirrhosis has fallen behind, and the success of available therapies has yet to be demonstrated. The challenge for a successful and safe antifibrotic therapy is specific targeting of the responsible cell types involved in fibrotic progression, without the introduction of collateral toxicities. In a preclinical rodent model of HCC with underlying fibrosis it could be shown that VSV administered by hepatic arterial infusion does not only maintain its ability to efficiently and selectively kill tumor cells, but it also possesses antifibrotic properties which provides the unique benefit in concomitant reversal of fibrotic progression with a single agent. Therefore, this innovation represents a significant therapeutic advantage over the current state of the art.

Commercial Opportunities
The development of VSV as a clinical therapeutic agent for the simultaneous treatment of HCC and underlying hepatic fibrosis is an attractive novel treatment option. This innovation has significant commercial potential due to the fact that there is currently no approved agent for safe and effective treatment of this complex clinical condition.

Developmental Status
- In vivo data from thioacetamide-induced fibrosis rat model showed lower Ishak fibrosis staging scores.
- Morphometric analysis revealed a decrease in fibrotic liver content
- Co-localization of VSV with hepatic stellate cells shown by IHC of tumor sections.

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