

CRO services for Liver Cancer

Hepatocellular carcinoma (HCC) is one of the most prevalent human cancers, with a rising incidence worldwide. In humans, HCC most often arises in the presence of chronic liver inflammation and advanced liver fibrosis or cirrhosis.

DEN and CCl₄ model, a mouse model of fibrosis-associated liver cancer, is designed to emulate the development of HCC in cirrhotic liver by a single injection of a low-dose genotoxic agent diethylnitrosamine (DEN) followed by repeated administration of carbon tetrachloride (CCl₄). A dramatic potentiation of liver tumor incidence is observed in the model, with 100% of mice developing liver tumors at 30 weeks of age. This model can be utilized in studies of the molecular mechanisms of fibrogenesis and HCC development, and testing for drug candidates.

SMC, a Tokyo-based biotech company also known as the leading nonclinical CRO for NASH-HCC, has re-validated DEN and CCl₄ model as a model translating non-clinical program into clinical practice. Our expertise in cancer research is now experienced in Oncology R&D.

SMC's services in DEN and CCl₄ model

Animal:

- Male B6C3 mice

DEN and CCl₄ model:

- DEN: a single ip injection at 14 days of age
- CCl₄: 2 times/week ip starting at 8 weeks of age for 22 weeks

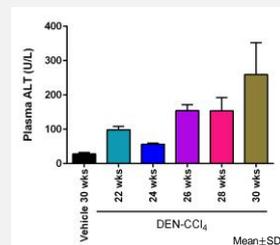
Major endpoints:

- Tumor number
- Tumor growth inhibition (Tumor size)
- Liver function (ALT, albumin etc.)
- Liver histology (Sirius red-staining followed by fibrosis area estimation)

Additional endpoints:

- Immunohistochemistry
- CT analysis

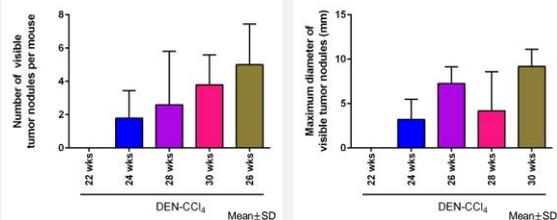
Biological analysis (plasma ALT level)



Vehicle: n=6
DEN and CCl₄: n=5

Plasma ALT levels were significantly increased in DEN-CCl₄ model (22 to 30 weeks) compared to vehicle treated mice.

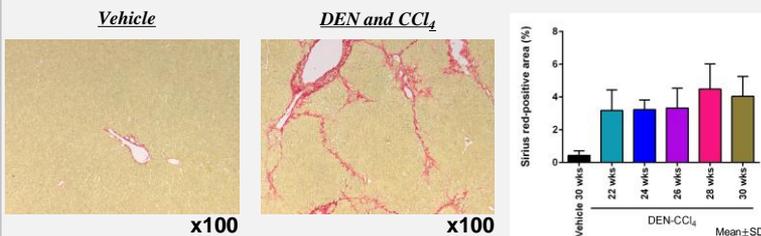
Macroscopic analyses of liver



Number and maximum diameter of visible tumor nodules were increased in DEN-CCl₄ model

Vehicle: n=6
DEN and CCl₄: n=5

Sirius-red staining and fibrosis area



Fibrosis area (Sirius red-positive area) was significantly increased in DEN-CCl₄ model compared to vehicle treated mice.

Vehicle: n=6
DEN and CCl₄: n=5

