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HUMAN MMP-1 TRANSGENE PROTECTS EXPERIMENTALLY INDUCED HEPATIC FIBROSIS IN MICE

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Hepatic fibrosis is characterized by excessive synthesis and deposition of fibrillar collagens in the liver with impaired turnover. Since the major collagenolytic enzyme, matrix metalloproteinase-1 (MMP-1) is absent in mice, MMP-13 is mainly responsible for collagen remodeling during fibrogenesis. In the present study, we examined whether transgenic expression of human MMP-1 could protect the N-nitrosodimethylamine (NDMA) induced hepatic fibrosis in mice. Hepatic fibrosis was induced in wild-type and MMP-1 transgenic mice through intraperitoneal injections of NDMA in doses of 1 mg/100 g body weight on 3 consecutive days of every week over a period of 4 weeks. NDMA administrations resulted in marked elevation of serum AST, ALT, hyaluronic acid (HA), transforming growth factor-β1 (TGF-β1) and procollagen-III peptide in wild-type mice. There was marked activation of hepatic stellate cells, deposition of collagen-1 and HA in the liver. However, these processes were markedly decreased in NDMA administered MMP-1 transgenic mice. qRT-PCR and Western blotting for collagen I, α-smooth muscle actin (α-SMA), and TGF-β1 demonstrated marked upregulation of mRNA and protein levels respectively, in NDMA treated wild-type mice but not in similarly treated transgenic mice. Our study demonstrated that transgenic expression of MMP-1 protects the liver from NDMA induced hepatic fibrosis in mice by preventing excessive deposition of collagens in the liver. Our results further indicate that methods to upregulate the activity of MMP-1 could provide an option for therapeutic intervention of human hepatic fibrosis.

Disclosures:

The following people have nothing to disclose: Joseph George, Jeanine D'Armiento, Mikihiro Tsutsumi

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COMPARISON OF ENHANCED LIVER FIBROSIS TEST AND TRANSIENT ELASTOGRAPHY FOR THE NON-INVASIVE ASSESSMENT OF LIVER FIBROSIS IN CHRONIC HEPATITIS B

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Background The enhanced liver fibrosis (ELF) test accurately assesses fibrosis and predicts clinical outcomes in chronic liver disease. This is the first study of performance of ELF in chronic hepatitis B (CHB) using a single aetiology cohort, and we compare its performance with an alternative method of assessing fibrosis, transient elastography (TE). **Methods** 188 patients with CHB were recruited consecutively at a single Italian centre. TE, serum sampling and liver biopsy were performed on the same day. ELF tests were performed in one batch at a central laboratory using thawed samples previously stored at -20°C. Biopsies were assessed by one pathologist using the Ishak staging system. Diagnostic performance of ELF and TE for detection of histological stages of liver fibrosis was assessed and area under receiver operator characteristic curves (AUROC) calculated. Only those in whom TE was successfully performed were included. Different fibrosis levels were assessed, from any fibrosis (0 vs 1-6) to cirrhosis (0-4 vs 5,6 and 0-5 vs 6). **Results** Patients were treatment-naïve, median age was 47 years. 78% were e-antigen negative. Biopsies reported mild/moderate fibrosis (Ishak 0-1) in 21%, moderate fibrosis (2-3) 41% and severe fibrosis/cirrhosis (4-6) 38%. ELF and TE demonstrated good performance in identifying fibrosis (Table - representative fibrosis stages are shown, further data available). Both modalities showed similar performance in identifying any fibrosis and minimal fibrosis, with TE performing better in identifying moderate and severe fibrosis, and cirrhosis. **Conclusion** In untreated patients with CHB with moderate and severe fibrosis or cirrhosis, TE correlated more closely with histological staging than ELF. The relatively modest performance of ELF in detecting severe fibrosis compared to previous studies may be attributable to disease aetiology or prolonged sample storage at -20°C. Further validation of TE and ELF in CHB should include analysis at the time of sampling and evaluation of the prognostic performance for clinical outcomes as well as histology. **Note** PT & PL contributed equally to this abstract

Table. ELF & TE results for selected fibrosis stages

Fibrosis stage	ELF score		TE (kPa)		p-value+
	Median (IQR)	AUROC (95% CI)	Median (IQR)	AUROC (95% CI)	
0 vs 1-6	8.1 (0.8) vs 9.3 (1.8)	0.812 (0.695-0.930)	5.6 (3.1) vs 8.4 (5.4)	0.798 (0.640-0.957)	0.826
0-2 vs 3-6	8.4 (1.1) vs 9.9 (1.5)	0.831 (0.771-0.890)	6.5 (2.6) vs 10.1 (6.7)	0.865 (0.814-0.916)	0.306
0-4 vs 5,6	9.0 (1.4) vs 10.6 (2.0)	0.844 (0.777-0.912)	7.3 (2.8) vs 15.4 (11.7)	0.946 (0.911-0.982)	0.003

CI, confidence interval; IQR, interquartile range +Significance of comparison of ELF & TE AUROC

Disclosures:

Pietro Lampertico - Advisory Committees or Review Panels: Bayer; Speaking and Teaching: Bristol-Myers Squibb, Roche, GlaxoSmithKline, Novartis, Gilead

Julie Parkes - Stock Shareholder: iQur (spouse is shareholder)

Massimo Colombo - Advisory Committees or Review Panels: BRISTOL-MEYERS-SQUIBB, SCHERING-PLOUGH, ROCHE, GILEAD; Grant/Research Support: BRISTOL-MEYERS-SQUIBB, ROCHE, GILEAD; Speaking and Teaching: Glaxo Smith-Kline, BRISTOL-MEYERS-SQUIBB, SCHERING-PLOUGH, ROCHE, NOVARTIS, GILEAD, VERTEX

William M. Rosenberg - Advisory Committees or Review Panels: Merk, Gilead; Board Membership: iQur Limited; Speaking and Teaching: siemens, Roche

The following people have nothing to disclose: Paul M. Trembling, Sudeep Tanwar, Mauro Viganò, Floriana Facchetti

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THE ROLE OF TRANSIENT ELASTOGRAPHY IN THE ASSESSMENT OF LIVER FIBROSIS IN PATIENTS WITH MYELODYSPLASTIC SYNDROMES

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BACKGROUND: Myelodysplastic syndromes (MDS) are hematopoietic stem cell malignancies characterized by ineffective blood cell production. Most MDS patients eventually become red blood cell (RBC) transfusion dependent, risking iron overload, which may lead to cardiac and hepatic failure. Due to increase risk of complications, hematologists do not recommend liver biopsy to assess liver iron concentration and use other non-invasive methods such as serum ferritin level. Liver