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Safety and pharmacokinetics of recombinant human hepatocyte growth factor (rh-HGF) in patients with fulminant hepatitis: a phase I/II clinical trial, following preclinical studies to ensure safety

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Patient No.	1	2	3	4
Age/Gender	67/M	71/F	64/F	40/M
Diagnosis/Etiology	FHSA/HEV	FHSA/unknown	LOHF/unknown	FHSA/drug
Reason for not receiving LT	donor[1]	age[2]	donor[1]	donor[1]
Before rh-HGF administration				
Grade of HE	II	II	V	0
Prothrombin time INR (%)	2.07 (33)	1.55 (49)	1.78 (37)	1.62 (43)
Albumin (g/dl)	2.9	3.7	2.9	2.9
T-Bil (mg/dL)	11.2	6.9	11.7	27.6
Direct/total bilirubin ratio	0.58	0.41	0.44	0.71
ALT (IU/L)	32	131	260	253
Serum HGF (ng/ml)	0.77	1.94	1.07	1.88
AFP (ng/ml)	20	22.9	3.9	39.7
Liver volume (mL)	1055	595	640	1110
Days between HE and rh-HGF administration (days)	7	5	5	5
Duration of rh-HGF dosing (days)	13	14	12	14
Outcome				
during the study period	alive	alive	dead	alive
during the follow-up period	dead	alive	-	alive

FHSA, fulminant hepatitis subacute type; LOHF, late onset hepatic failure; HEV, hepatitis E virus; LT, liver transplantation; HE, hepatic encephalopathy. [1]lack of an appropriate donor; [2]age 70 or over.

Figure 8. HGF 第 I/II 相臨床試験のまとめ（文献 25 より改変）.

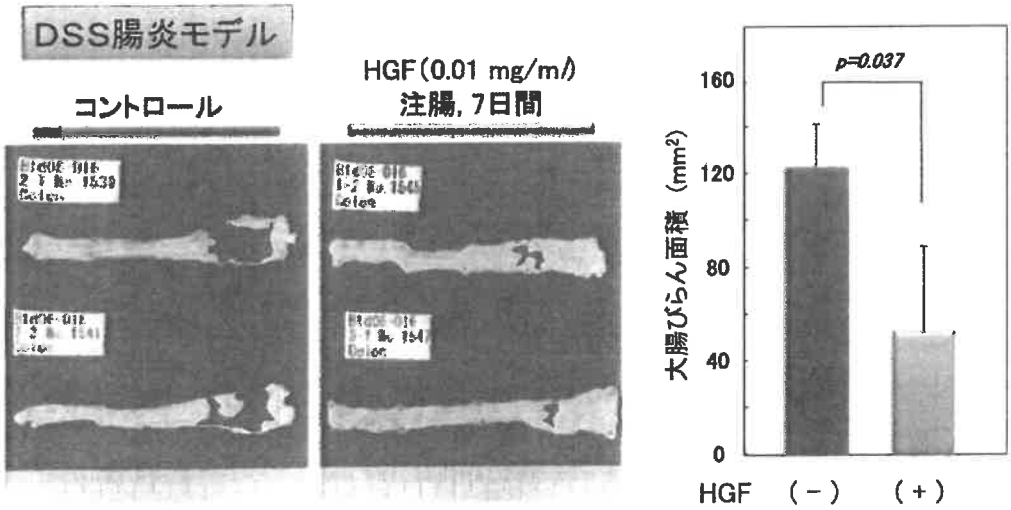

Figure 9. HGF の注腸投与による消化管粘膜障害の修復・再生促進作用（文献 28 より）.

細胞増殖因子を用いた急性肝不全治療薬”という研究課題で，平成 23 年度科学技術振興機構研究成果最適展開支援プログラム（A-STEP）本格研究開発ステージ実用化挑戦タイプ（創薬分野）に応募し，採択された．2011 年 10 月より 7 年間で約 20 億円の支援を受けて，HGF の創薬に取り組んでいる．

また，HGF は筋萎縮性側索硬化症や脊髄損傷

の治療薬としても開発が進んでいる．HGFを発見したものとして，HGFが多くの難治性疾患に対する治療薬となることを期待している．

本論文内容に関連する著者の利益相反
：坪内博仁（MSD株式会社，田辺三菱製薬株式会社，エーザイ株式会社，中外製薬株式会社，株式会社カン研究所，第一三共株式会社，株式会社ミノファーゲン製薬）

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