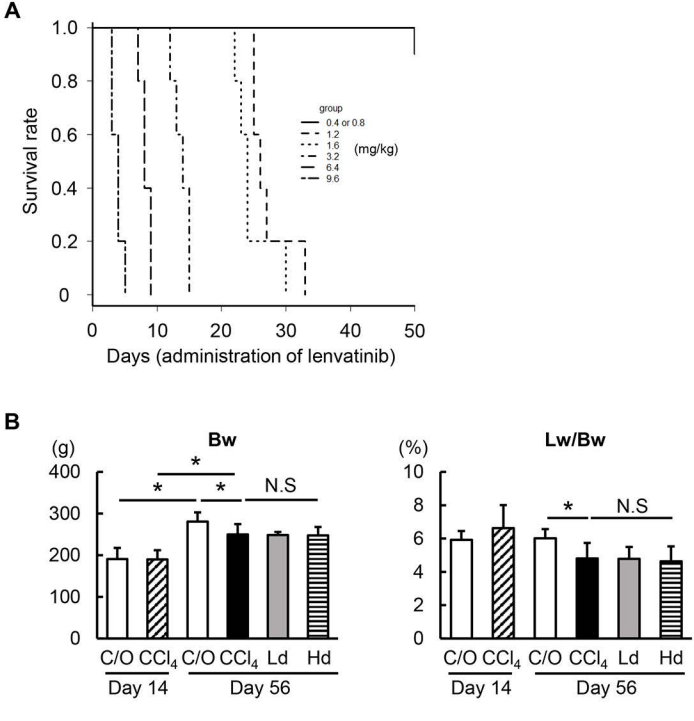
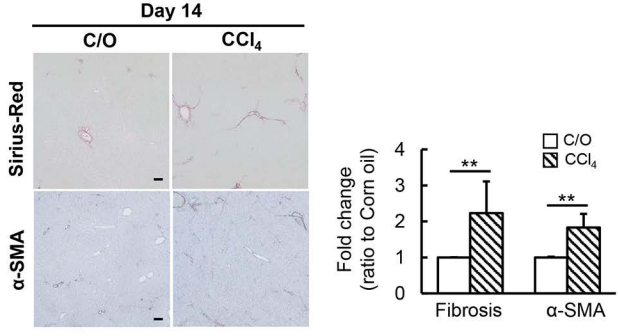

A
1.0
0.8
0.6
0.4
0.2
0
Survival rate
group
0.4 or 0.8
1.2
1.6
3.2
6.4
9.6
(mg/kg)
0
10
20
30
40
50
Days (administration of lenvatinib)
B
Bw
(g)
400
300
200
100
0
*
*
*
N.S
C/O
CCl4
C/O
CCl4
Ld
Hd
Day 14
Day 56
Lw/Bw
(%)
10
8
6
4
2
0
*
N.S
C/O
CCl4
C/O
CCl4
Ld
Hd
Day 14
Day 56


Day 14
C/O
CCl4
Sirius-Red
α-SMA
Fold change
(ratio to Corn oil)
4
3
2
1
0
**
**
C/O
CCl4
Fibrosis
α-SMA

Supplementary Materials

Lenvatinib prevents liver fibrosis progression and inhibits hepatic stellate cell activation and sinusoidal capillarization in experimental liver fibrosis

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1. Supplementary figure legend

2. Supplementary Table. 1

Supplementary figure legend

Supplementary Figure 1. In vivo dose optimization of lenvatinib and body and liver weight in CCl4-mediated rats.

(A) Kaplan-Meier curves show the overall survival of CCl4-treated rats receiving administration of the different doses (0.4, 0.8, 1.2, 1,6, 3.2, 6.4 and 9.6 mg/kg) of lenvatinib. (B) Body weight (Bw) and ratio of liver weight to body weight (Lw/Bw) in the experimental groups at the end of experiment. N.S; not significant. * $p < 0.05$ indicating a significant difference between groups.

Supplementary Figure 2. CCl4-induced liver fibrosis at the start of lenvatinib treatment.

(Left panel) Representative microphotographs of Sirius-Red and α-SMA at the start of lenvatinib treatment (Day 14) in Corn-oil (C/O)- or CCl4-mediated rats. Scale bar; 100 μm. (Right panel) Semi-quantitation of Sirius-Red-stained fibrotic area and α-SMA immuno-positive area in high-power field (HPF) by ImageJ software. ** $p < 0.01$ indicating a significant difference between groups. Data are mean ± SD (n=10). Histochemical quantitative analyses included five fields per section. Quantitative values are relatively indicated as fold changes to the values of C/O.

Supplementary Table 1. List of primers used in q-PCR

gene	Sense (5’-3’)	Antisense (5’-3’)
Rat		
Col1a1	TGCTGCCTTTTCTGTTCCTT	AAGGTGCTGGGTAGGGAAGT
Ctgf	AAATAAACTGCCTCCCAAACCA	GAAATGGCTTGCTCAGGGTAAC
Tgfb1	CGGCAGCTGTACATTGACTT	AGCGCACGATCATGTTGGAC
Cd31	CCAGAAAGACAAGGCGATCG	CGGCTGGAGGAGAGTTCTAG
Vegfa	TTCCTGTAGACACACCCACC	TCCTCCCAACTCAAGTCCAC
Vegfr1	TGCAGGAAACCATAGCAGGA	GTATAGTCCCCTGCGTCCTC
Vegfr2	CAACGTGGGGCTTGATTTCA	CGCTGTGCAGGTGTATTCTC
Pdgfb	ATCGAGCCAAGACACCTCAA	ATCACTCCAAGGACCCCATG
Pdgfrb	AACTCTTCTACCGCTGTGCT	ACAGCAACAATTGGCCTCTG
Fgf2	CATTCCTGGCCTCTGTCTCC	GCAACTTTCTCCCTTCCTGC
Fgfr2	CCAGCACCTGTGAGAGAGAA	TTGGAGTTCATGGACGAGCT
Gapdh	AGACAGCCGCATCTTCTTGT	CTTGCCGTGGGTAGAGTCAT
Human		
COL1A1	CCAAATCTGTCTCCCCAGAA	TCAAAAACGAAGGGGAGATG
ACTA2	TTCAATGTCCCAGCCATGTA	GAAGGAATAGCCACGCTCAG
TGFB1	GGGACTATCCACCTGCAAGA	CCTCCTTGGCGTAGTAGTCG
CCND1	CCGTCCATGCGGAAGATC	ATGGCCAGCGGGAAGAC
CDK4	CCCACACAAGCGAATCT¥CTG	ACCCTCCATAGCCTCAGAGA
CDK6	AGGCATTTTGGGAACTGTTG	TCCCATCCACTTCAAAGGAG
CDC25A	GAGATCGCCTGGGTAATGAA	TGCGGAATTCTTCAGGTCT
GAPDH	CCAAGGAGTAAGACCCCTGG	TGGTTGAGCACAGGGTACTT