

発癌抑制目的のインターフェロン 少量長期投与の これまでの報告について

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発癌抑制目的のインターフェロン少量長期投与のこれまでの報告について

1. Arase Y, Ikeda K, Suzuki F, Suzuki Y, Kobayashi M, Akuta N, Hosaka T, et al. Prolonged-interferon therapy reduces hepatocarcinogenesis in aged-patients with chronic hepatitis C. *J Med Virol* [2007](#);79:1095-1102.

2. Nomura H, Kashiwagi Y, Hirano R, Tanimoto H, Tsutsumi N, Higashi M, Ishibashi H. Efficacy of low dose long-term interferon monotherapy in aged patients with chronic hepatitis C genotype 1 and its relation to alpha-fetoprotein: A pilot study. *Hepatol Res* [2007](#);37:490-497.

3. Di Bisceglie AM, Shiffman ML, Everson GT, Lindsay KL, Everhart JE, Wright EC, Lee WM, et al. Prolonged therapy of advanced chronic hepatitis C with low-dose peginterferon. *N Engl J Med* [2008](#);359:2429-2441.

4. Lok AS, Everhart JE, Wright EC, Di Bisceglie AM, Kim HY, Sterling RK, Everson GT, et al. Maintenance peginterferon therapy and other factors associated with hepatocellular carcinoma in patients with advanced hepatitis C. *Gastroenterology* [2011](#);140:840-849; quiz e812.

5. Di Bisceglie AM, Stoddard AM, Dienstag JL, Shiffman ML, Seeff LB, Bonkovsky HL, Morishima C, et al. Excess mortality in patients with advanced chronic hepatitis C treated with long-term peginterferon. *Hepatology* [2011](#);53:1100-1108.

6. Bruix J, Poynard T, Colombo M, Schiff E, Burak K, Heathcote EJ, Berg T, et al. Maintenance therapy with peginterferon alfa-2b does not prevent hepatocellular carcinoma in cirrhotic patients with chronic hepatitis C. *Gastroenterology* [2011](#);140:1990-1999.

7. Izumi N, Asahina Y, Kurosaki M, Yamada G, Kawai T, Kajiwara E, Okamura Y, Takeuchi T, Yokosuka O, Kariyama K, Toyoda J, Inao M, Tanaka E, Moriwaki H, Adachi H, Katsushima S, Kudo M, Takaguchi K, Hiasa Y, Chayama K, Yatsushashi H, Oketani M, Kumada H. Inhibition of hepatocellular carcinoma by PegIFN α -2a in patients with chronic hepatitis C: a nationwide multicenter cooperative study. *J Gastroenterol*. [2012](#) Aug 9. [Epub ahead of print]

1. Arase Y, et.al. 2007

Prolonged-interferon therapy reduces hepatocarcinogenesis in aged-patients with chronic hepatitis C. J Med Virol.2007;79(8): 1095-102

Arase らは、60 歳以上のC 型慢性肝炎または肝硬変患者120 例に対して天然型IFN α -3MU 週3 回投与を平均2.47 年施行し、年齢と性別をマッチさせた240 例の非IFN 投与群と比較した。その結果10 年発癌率はIFN 治療群17.3%、非IFN 治療群32.8%で、発癌の相対危険度は0.3 であったと報告した。

2. Nomura H et.al. 2007

Efficacy of low dose long-term interferon monotherapy in aged patients with chronic hepatitis C genotype 1 and its relation to alpha-fetoprotein: A pilot study. Hepatol Res. 2007 ;37(7):490-7

Nomuraらは、60 歳以上のHCV ゲノタイプ1 型患者44 例を対象とし、天然型IFN 3MU 週3 回投与を3 年間行い、年齢、性別、肝組織所見をマッチさせた44 例の非IFN 治療例と比較した結果、累積発癌率は有意にIFN 治療群において低いことを報告した。

3.HALT-C 2008

N Engl J Med 2008;359:2429-41.

Prolonged Therapy of Advanced Chronic Hepatitis C with Low-Dose Peginterferon

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Gregory T. Everson, M.D., Karen L. Lindsay, M.D., James E. Everhart, M.D., M.P.H.,
Elizabeth C. Wright, Ph.D., M.P.H., William M. Lee, M.D., Anna S. Lok, M.D.,
Herbert L. Bonkovsky, M.D., Timothy R. Morgan, M.D., Marc G. Ghany, M.D.,
Chihiro Morishima, M.D., Kristin K. Snow, Sc.D., and Jules L. Dienstag, M.D.,
for the HALT-C Trial Investigators*

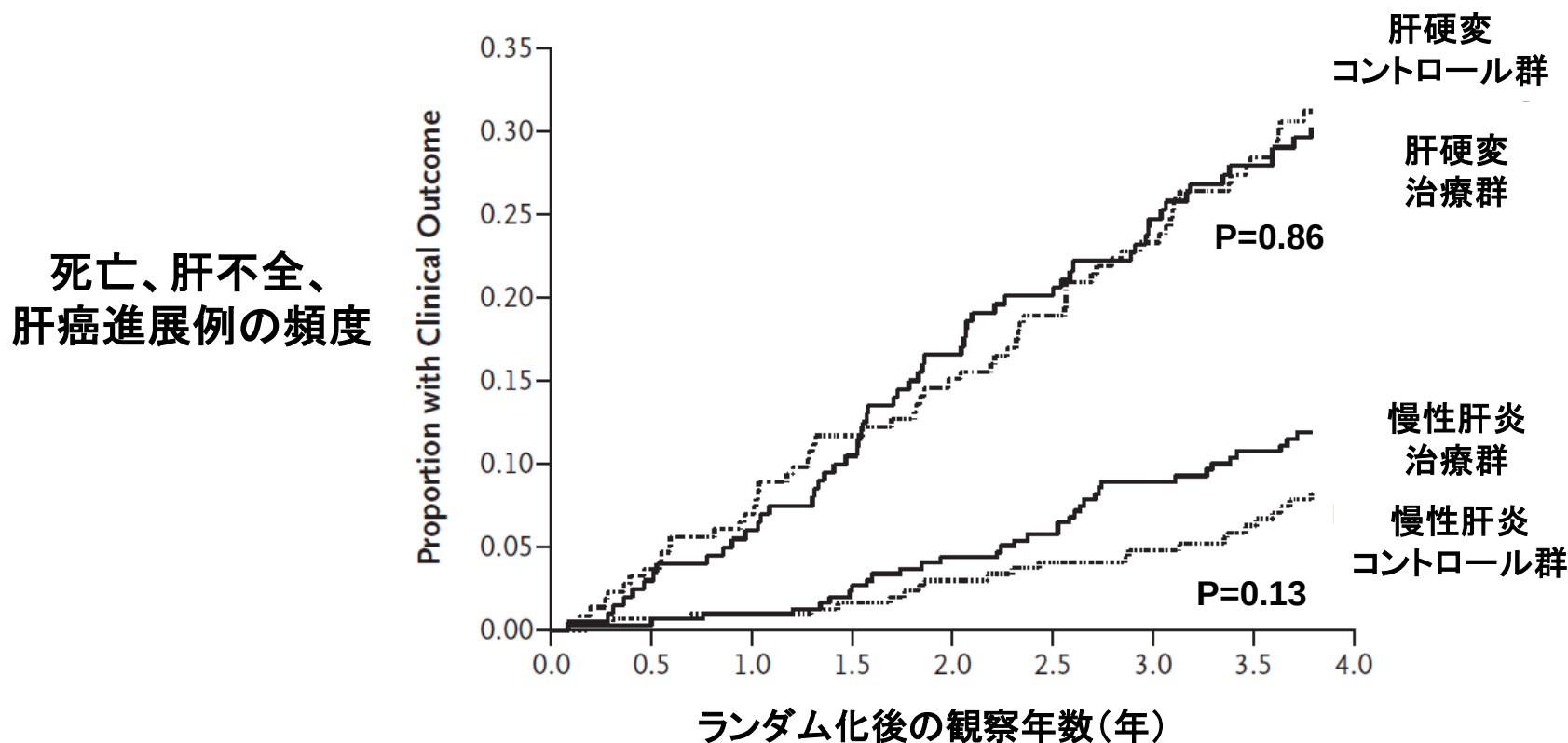
CONCLUSIONS

Long-term therapy with peginterferon did not reduce the rate of disease progression in patients with chronic hepatitis C and advanced fibrosis, with or without cirrhosis, who had not had a response to initial treatment with peginterferon and ribavirin. (ClinicalTrials.gov number, NCT00006164.)

ペグインターフェロンの長期投与(90 μ g 3.5年投与)は、
肝硬変例、慢性肝炎肝線維化進展例ともに、コントロール群
との比較では、肝病変の進展を抑制しなかった。

3.HALT-C 2008

Clinical Outcome (death, hepatic decompensation, or hepatocellular carcinoma)



No. at Risk

Cirrhosis treatment group	208	195	187	178	165	159	146	131	124
Cirrhosis control group	220	206	198	187	177	167	156	136	125
Noncirrhotic-fibrosis treatment group	309	300	295	287	281	270	259	243	234
Noncirrhotic-fibrosis control group	313	300	297	288	281	272	266	248	234

4.HALT-C 2011

Gastroenterol 2011 Mar;140(3):840-849.

Maintenance Peginterferon Therapy and Other Factors Associated with Hepatocellular Carcinoma in Patients with Advanced Hepatitis C

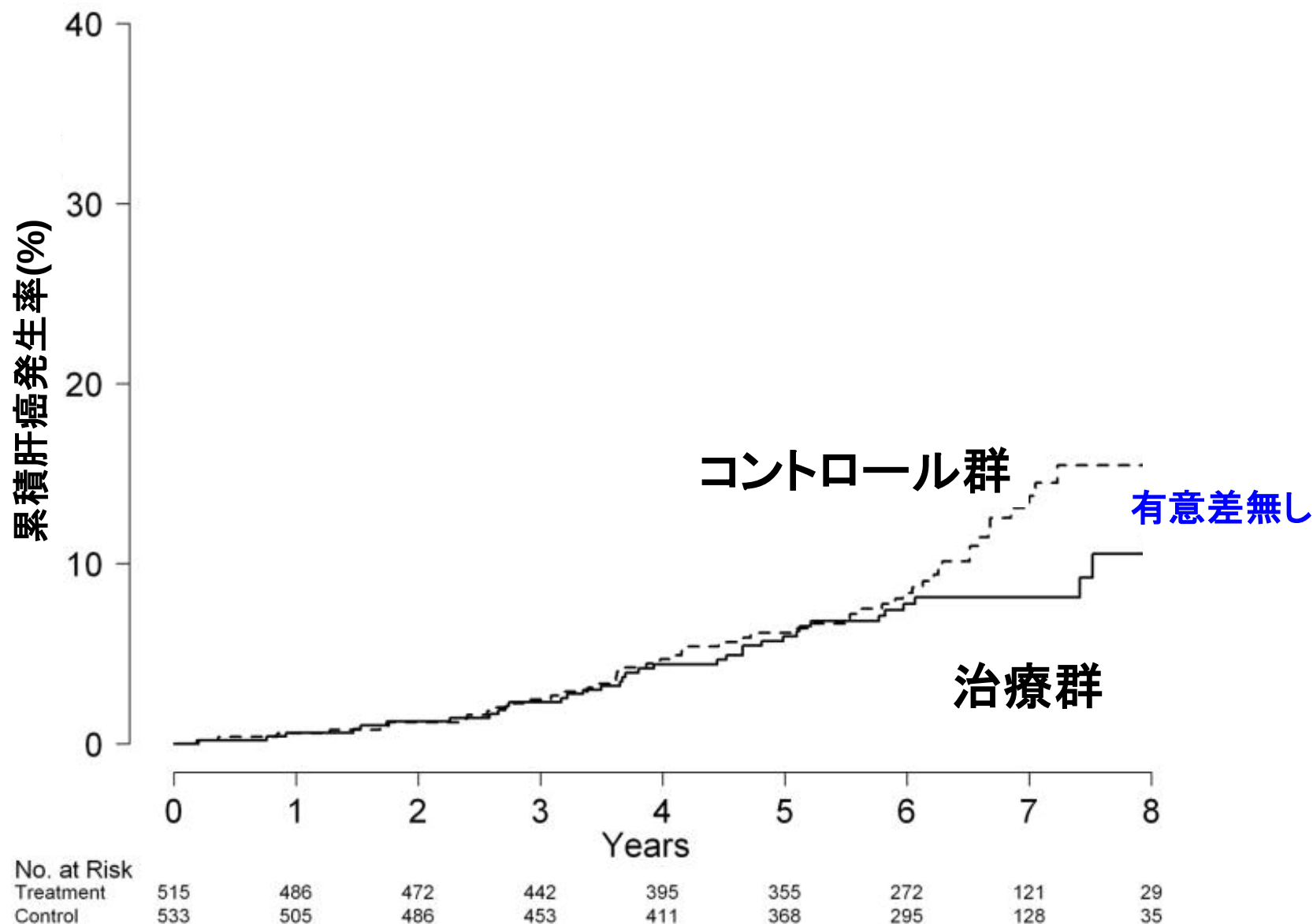
Lok AS, Everhart JE, Wright EC, Di Bisceglie AM, Kim HY, Sterling RK, Everson GT, Lindsay KL, Lee WM, Bonkovsky HL, Dienstag JL, Ghany MG, Morishima C, Morgan TR, HALT-C Trial Group.

Conclusions

Extended analysis of the HALT-C cohort showed that long-term peginterferon therapy does not reduce the incidence of HCC among patients with advanced hepatitis C who did not achieve SVRs. Patients with cirrhosis who received peginterferon treatment had a lower risk for HCC than controls.

HALT-Cの長期観察結果では、ペグインターフェロンの長期投与（90 μ g 3.5年投与）は、慢性肝炎例では、肝癌の発生頻度を抑制しなかった。肝硬変例では、コントロール群に比較して低い発癌リスクを示した。

4.HALT-C 2011

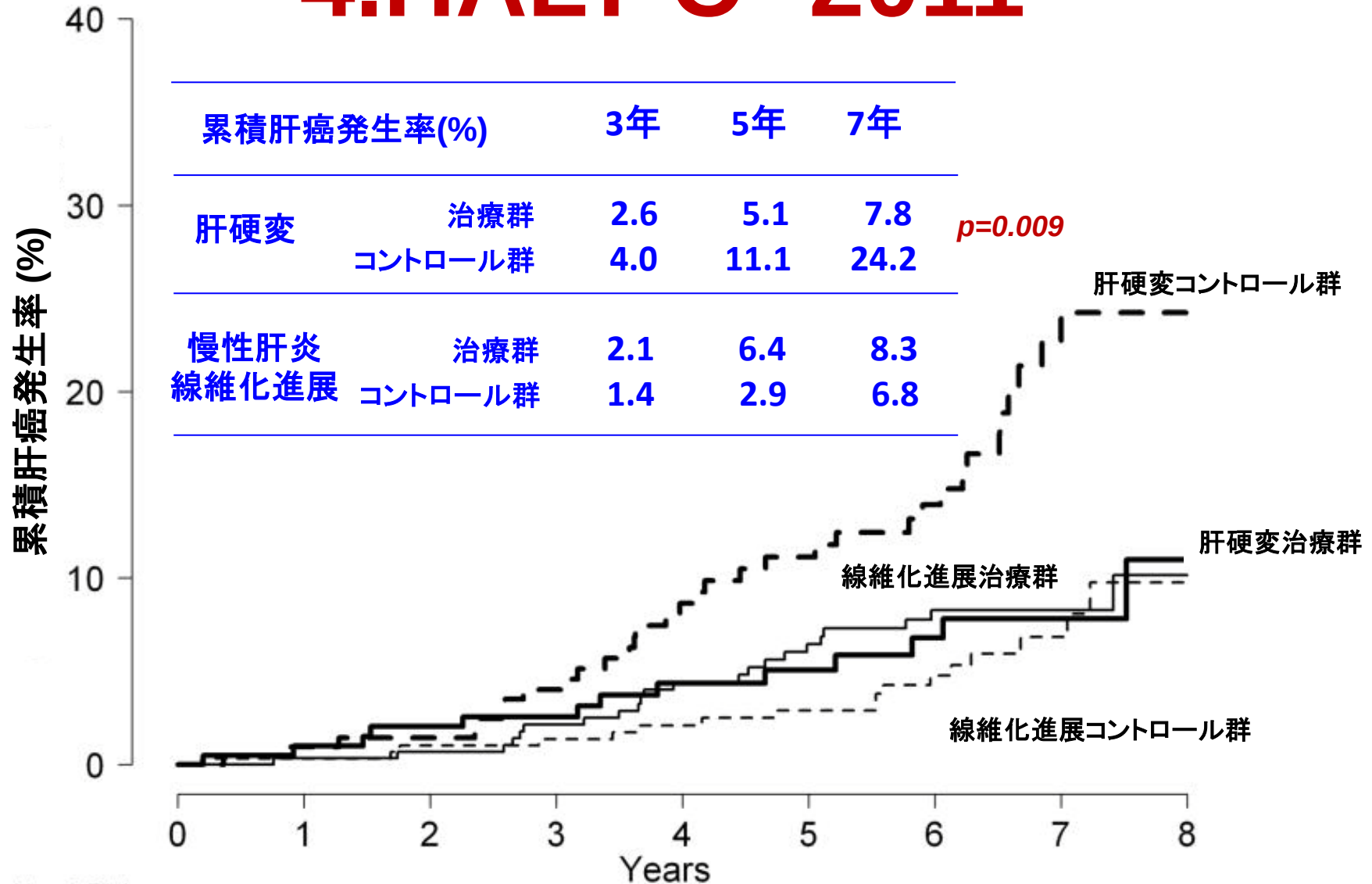


4.HALT-C 2011

	慢性肝炎群		肝硬変群		全患者		
	治療群	コントロール群	治療群	コントロール群	治療群	コントロール群	合計
患者数	308	313	207	220	515	533	1048
肝癌患者数 (%)	23 (7.5)	17 (5.4)	14 (6.8)	34 (15.5)	37 (7.2)	51 (9.6)	88 (8.4)

HR :0.45
95%CI 0.24-0.83
P=0.01

4.HALT-C 2011



No. at Risk

Fibrosis Trt	308	291	283	270	247	227	175	71	18
Fibrosis Cntl	313	296	287	276	259	232	187	81	23
Cirrhosis Trt	207	195	189	172	148	128	97	50	11
Cirrhosis Cntl	220	209	199	177	152	136	108	47	12

5.HALT-C 2011

HEPATOLOGY, Vol. 53, No. 4, 2011

Excess Mortality in Patients with Advanced Chronic Hepatitis C Treated with Long-Term Peginterferon

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Leonard B. Seeff,^{6,7} Herbert L. Bonkovsky,^{8,9} Chihiro Morishima,¹⁰ Elizabeth C. Wright,¹¹
Kristin K. Snow,² William M. Lee,¹² Robert J. Fontana,¹³ Timothy R. Morgan,^{14,15}
and Marc G. Ghany,⁷ for the HALT-C Trial Group

peginterferon. *Conclusion:* Long-term maintenance peginterferon in patients with advanced chronic hepatitis C is associated with an excess overall mortality, which was primarily due to non-liver-related causes among patients with bridging fibrosis. (HEPATOLOGY 2011;53:1100-1108)

慢性肝炎(肝線維化進展)例に対するペグインターフェロンの
長期投与と死亡率の上昇には関連が見られた。
その主な死因として、肝疾患以外の原因が関与していた。

5.HALT-C 2011

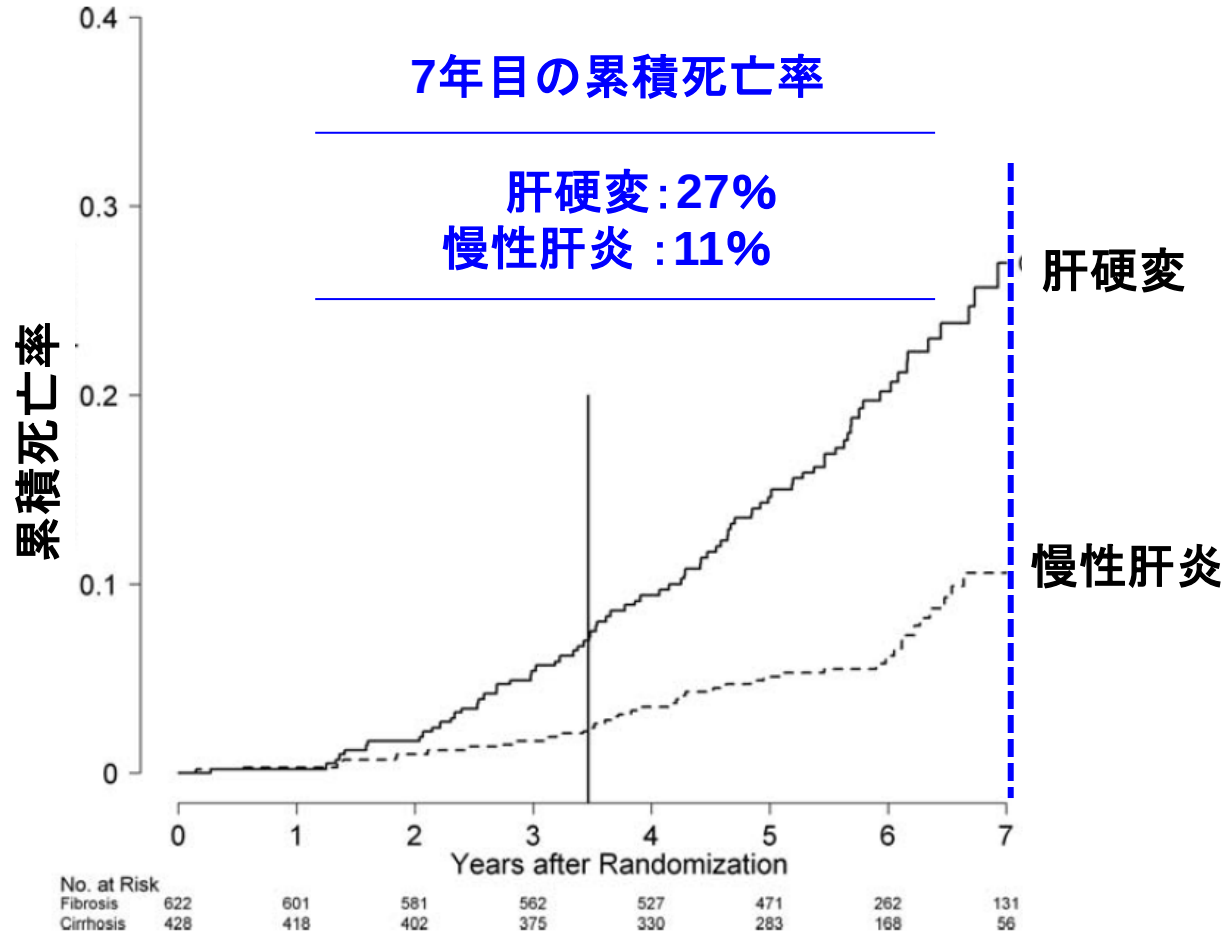


Fig. 2. Cumulative rates of death by fibrosis/cirrhosis stratum in the HALT-C Trial cohort: Kaplan-Meier analysis of 622 patients in the fibrosis stratum (fibrosis: dotted line) versus 428 patients in the cirrhosis stratum (cirrhosis: solid line). The vertical line at 3.5 years marks the end of the randomized trial phase. Test of equality of distributions, $P < 0.0001$.

5.HALT-C 2011

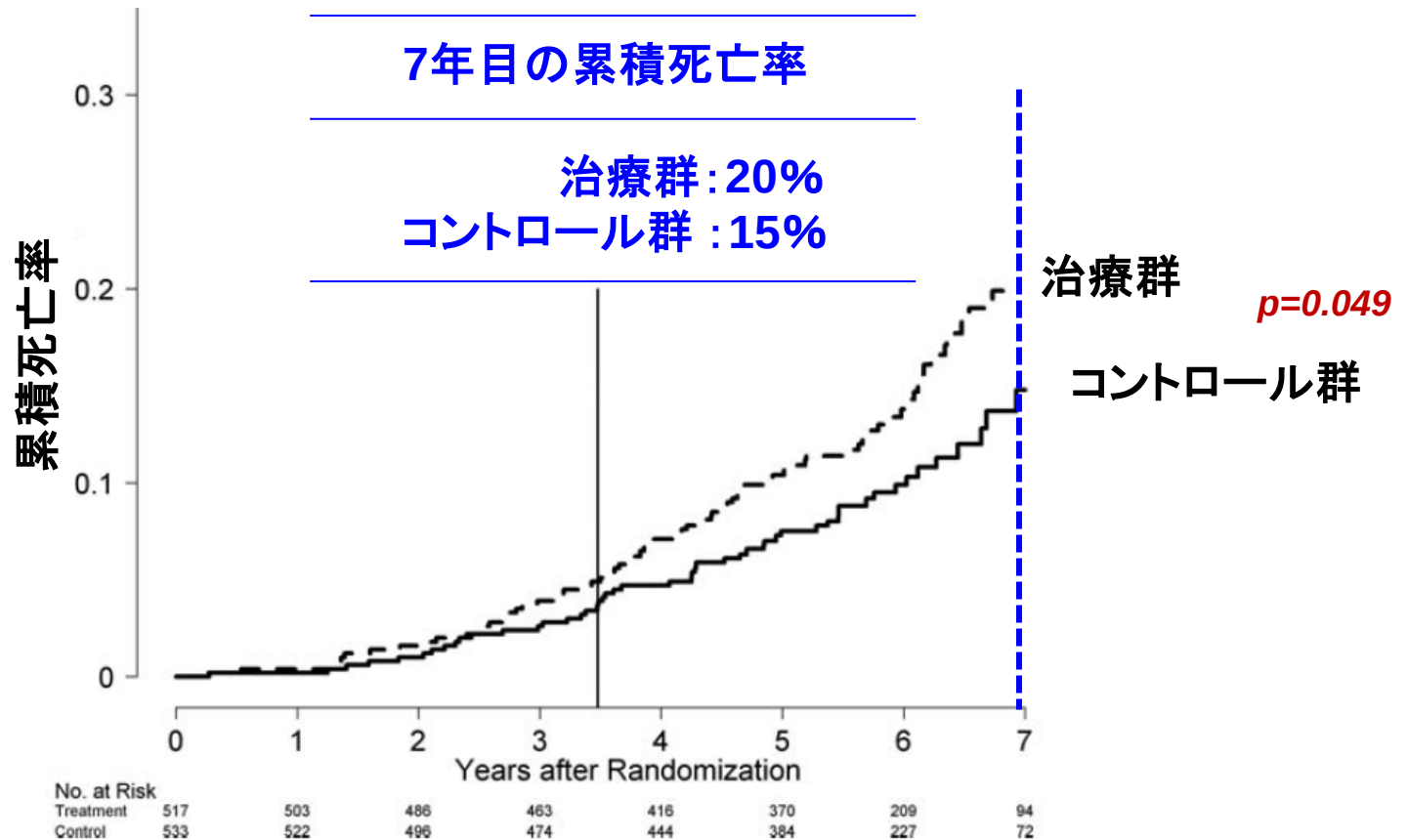
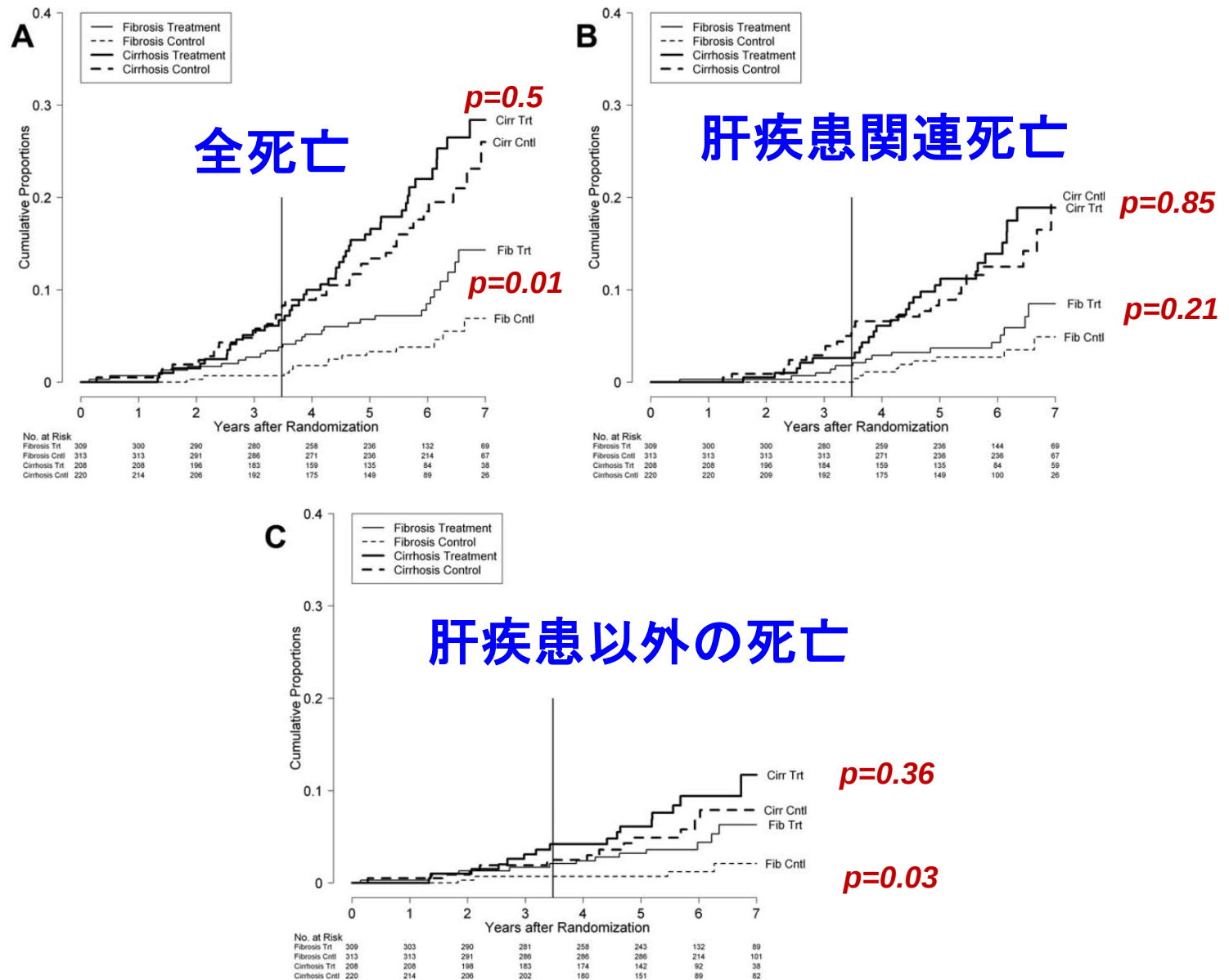


Fig. 3. Cumulative rates of death by randomization group in the HALT-C Trial cohort: Kaplan-Meier analysis of deaths in 517 patients randomized to the treatment group (Trt: dotted line) versus 533 patients randomized to the control group (Cntl: solid line). The vertical line at 3.5 years marks the end of the randomized trial phase. Test of equality of distributions: Fibrosis treatment versus control $P = 0.21$; Cirrhosis treatment versus control $P = 0.85$.

5.HALT-C 2011



5.HALT-C 2011

Table 2. Causes of Death by Fibrosis Stratum, Treatment Group, and Liver-Relatedness

Cause of Death	Fibrosis		Cirrhosis		Totals
	Treatment	Control	Treatment	Control	
	n = 309	n = 313	n = 208	n = 220	n = 1,050
Liver-related deaths					
Chronic liver disease	8	5	20	14	47
HCC	6	3	3	9	21
Malignant neoplasm (not HCC)*	0	1	0	1	2
Septicemia*	1	0	1	0	2
Accidental*	0	0	0	1	1
Influenza and pneumonia*	0	0	0	1	1
Unknown*	0	0	2	0	2
Totals	15	9	26	26	76
Nonliver-related deaths					
Malignant neoplasm (not HCC)	5	0	2	2	9
Other	1	0	5	3	9
Accidental	2	1	1	2	6
Heart disease	2	0	2	2	6
Septicemia	3	0	0	0	3
Cerebrovascular disease	0	0	2	0	2
Influenza and pneumonia	0	1	0	0	1
Unknown	1	2	4	3	10
Totals	14	4	16	12	46

*These eight deaths were attributed to liver disease even though other potentially fatal medical conditions were present.

Table 3. Malignant Neoplasms Other than HCC Causing Death in 11 Patients

Stratum	Randomization Group	Diagnosis
Liver-related*		
Fibrosis	Control	Colon cancer with liver metastases
Cirrhosis	Control	Lymphoma
Nonliver-related		
Fibrosis	Treatment	Nonsmall cell lung cancer
Fibrosis	Treatment	Nonsmall cell lung cancer
Fibrosis	Treatment	Squamous cell lung cancer
Fibrosis	Treatment	Prostate cancer
Fibrosis	Treatment	Colon cancer with liver metastases
Cirrhosis	Treatment	Gallbladder cancer
Cirrhosis	Treatment	Pancreatic cancer with lung metastases
Cirrhosis	Control	Lung cancer
Cirrhosis	Control	Gastric adenocarcinoma

*Death was considered to be liver-related in these patients because, even though they had otherwise potentially fatal nonliver diseases, the circumstances of their deaths were most consistent with advanced liver disease, which may have been exacerbated by treatment of the malignancies.

慢性肝炎治療群ではコントロール群に比較して死亡率が高い。その理由として肝疾患以外の死因が関与していた。

6.EPIC study 2011

GASTROENTEROLOGY 2011;140:1990–1999

Maintenance Therapy With Peginterferon Alfa-2b Does Not Prevent Hepatocellular Carcinoma in Cirrhotic Patients With Chronic Hepatitis C

JORDI BRUIX,^{*} THIERRY POYNARD,[‡] MASSIMO COLOMBO,[§] EUGENE SCHIFF,^{||} KELLY BURAK,[¶] ELIZABETH J. L. HEATHCOTE,[#] THOMAS BERG,^{**} JORGE-LUIS POO,^{††} CARLOS BRANDAO MELLO,^{§§} RAINER GUENTHER,^{|||} CLAUS NIEDERAU,^{¶¶} RUBEN TERG,^{##} PIERRE BEDOSSA,^{***} NAVDEEP BOPARAI,^{†††} LOUIS H. GRIFFEL,^{†††} MARGARET BURROUGHS,^{†††} CLIFFORD A. BRASS,^{†††} JANICE K. ALBRECHT,^{†††} for the EPIC³ Study Group

tions. **CONCLUSIONS:** Maintenance therapy with peginterferon alfa-2b is not warranted in all patients and does not prevent HCC. However, there is a potential clinical benefit of long-term suppressive therapy in patients with preexisting portal hypertension.

ペグインターフェロン α2b 単独長期投与療法は、発癌発生を抑止しないが、門脈圧亢進症状を有する患者では、臨床的有効性(腹水貯留、静脈瘤破裂の発生抑制など)をもたらす可能性がある。

7.Izumi N, et.al. 2012

J Gastroenterol. 2012 Aug 9. [Epub ahead of print]

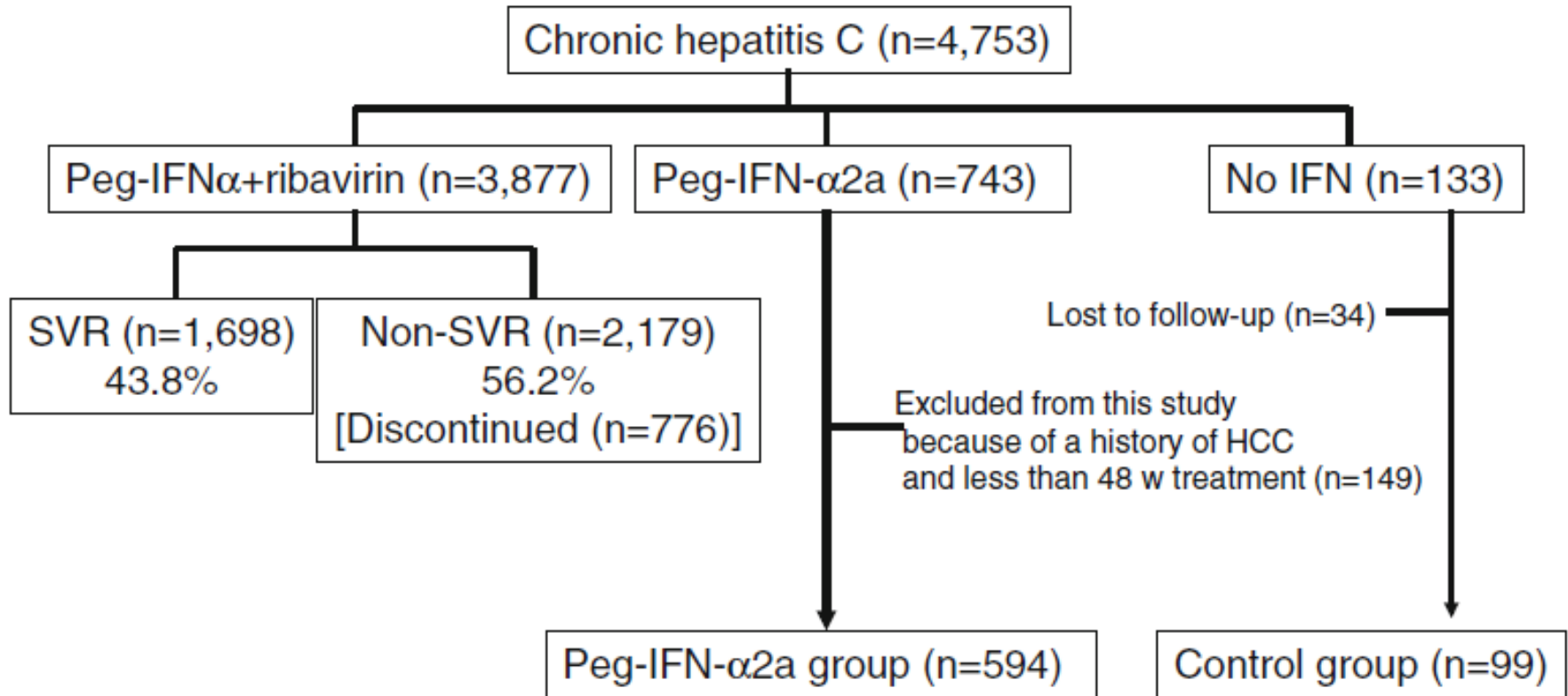
Inhibition of hepatocellular carcinoma by PegIFN α -2a in patients with chronic hepatitis C: a nationwide multicenter cooperative study

Namiki Izumi · Yasuhiro Asahina · Masayuki Kurosaki · Gotaro Yamada · Tsutomu Kawai · Eiji Kajiwarara · Yukishige Okamura · Takayuki Takeuchi · Osamu Yokosuka · Kazuya Kariyama · Joji Toyoda · Mie Inao · Eiji Tanaka · Hisataka Moriwaki · Hiroshi Adachi · Shinji Katsushima · Masatoshi Kudo · Kouichi Takaguchi · Yoichi Hiasa · Kazuaki Chayama · Hiroshi Yatsushashi · Makoto Oketani · Hiromitsu Kumada

Conclusions Low-dose and long-term maintenance administration of PegIFN α -2a decreased the incidence of HCC in patients with normalized ALT and AFP levels at 24 weeks compared with patients without normal ALT and AFP levels.

ペグインターフェロン α 2aの少量、長期投与法は、治療開始24週目でALT値、AFP値が正常化した例では肝癌発生率を低下させた。

7.Izumi N, et.al. 2012



国内21施設での多施設共同研究、Retrospective Study。
ペグインターフェロン α2a 90μgを、週1回もしくは2週に1回の投与方法で、1年間以上治療した594例を解析した。一方、治療をおこなわなかった99例をコントロール群とした。

7.Izumi N, et.al. 2012

Table 1 Background data of patients treated with PegIFN α -2a ($n = 594$)

	$n = 594$
Age (years)	61.7 ± 11.7
Sex (male/female)	258/336
BMI	23.2 ± 3.3
Genotype (1/2)	443/151
Diagnosis (ASC/CH/LC)	4/460/130
History of excess alcohol consumption (≥ 60 g/day; yes/no)	118/376
Fibrosis (F0, 1, 2/F3, 4)	443/151
Inflammatory activity (A0, 1/A2, 3)	469/125
Diabetes mellitus (no/yes)	499/95
LDL cholesterol (mg/dL)	94.2 ± 31.1
Fasting blood sugar (mg/dL)	106.3 ± 28.5
White blood cell count (/mm ³)	$4,360 \pm 1,470$
Red blood cell count ($\times 10^6/\mu\text{L}$)	423.8 ± 56.4
Hemoglobin (g/dL)	13.3 ± 1.8
Platelet count ($\times 10^3/\mu\text{L}$)	137 ± 56
Albumin (g/dL)	4.0 ± 0.5
Total bilirubin (mg/dL)	0.8 ± 0.6
AST (IU/L)	65.8 ± 47.8
ALT (IU/L)	72.1 ± 68.0
Gamma-GTP (IU/L)	55.2 ± 51.3
Esophageal varices (no/yes)	344/31
Alpha fetoprotein (ng/L)	$6.9 (4.2\text{--}13.8)$
Once weekly or biweekly PegIFN α -2a	512/82
Baseline HCV RNA (KIU/mL)	$1,024 (73\text{--}2,130)$
Development of HCC (no/yes)	545/49

PegIFN pegylated interferon, *BMI* body mass index, *ASC* asymptomatic carrier, *CH* chronic hepatitis, *LC* liver cirrhosis, *LDL* low-density lipoprotein, *AST* aspartate aminotransferase, *ALT* alanine aminotransferase, *GTP* guanosine triphosphate, *HCV* hepatitis C virus, *HCC* hepatocellular carcinoma

Values are means $\pm$ SD, with ranges in parentheses

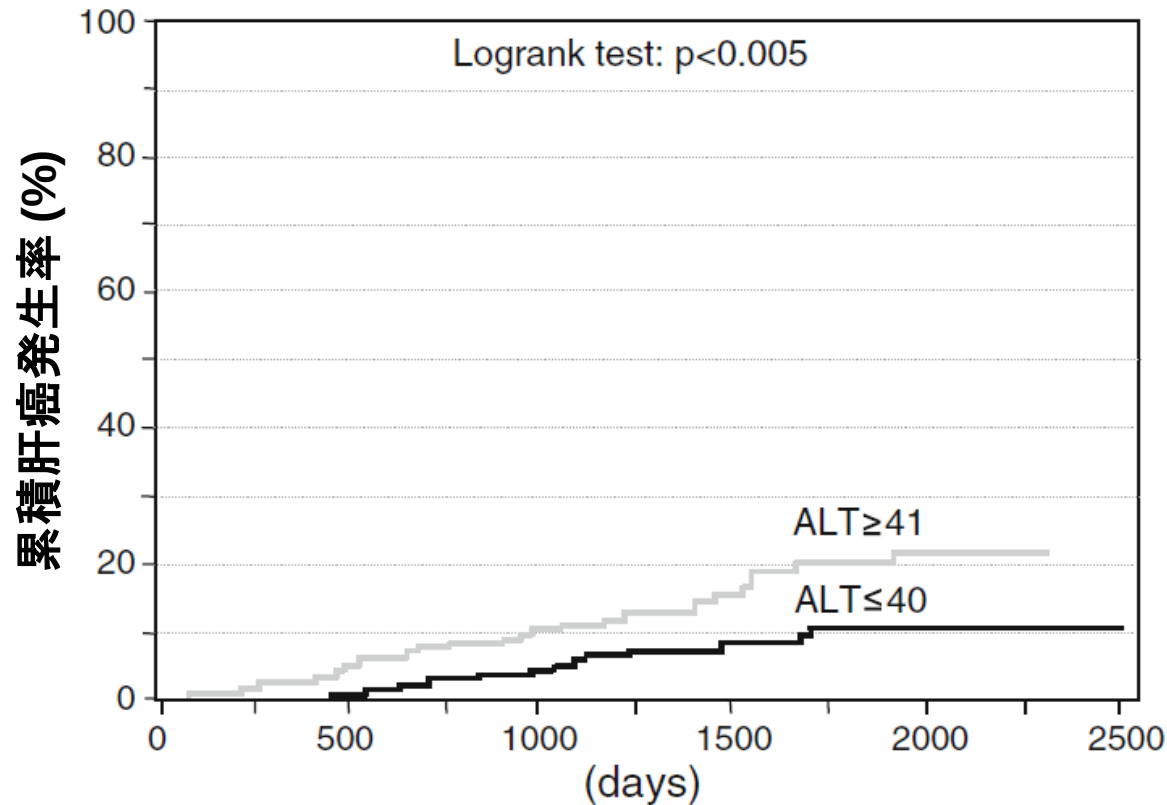
Table 2 Comparison of HCC and non-HCC patients with long-term PegIFN α -2a administration ($n = 594$)

	Patients with or without development of HCC		p value
	With HCC ($n = 49$)	Without HCC ($n = 545$)	
Pretreatment parameters			
Age (years)	63.8 ± 1.7	61.3 ± 0.5	<0.05
Sex (male/female)	32/17	226/319	<0.01
BMI	24.0 ± 0.5	23.1 ± 0.2	n.s.
Genotype (1/2)	47/6	397/148	n.s.
History of excess alcohol consumption (≥ 60 g/day; yes/no)	11/38	107/338	n.s.
Fibrosis (F0, 1, 2/F3, 4)	25/24	418/127	<0.001
Inflammatory activity (A0, 1/A2, 3)	7/42	462/83	<0.001
Diabetes mellitus (no/yes)	38/11	461/84	n.s.
LDL cholesterol (mg/dL)	88.2 ± 9.0	94.7 ± 2.6	n.s.
White blood cell count (/mm ³)	$4,355 \pm 210$	$4,360 \pm 64$	n.s.
Red blood cell count ($\times 10^6/\mu\text{L}$)	420.8 ± 8.1	424.1 ± 2.6	n.s.
Hemoglobin (g/dL)	13.6 ± 0.3	13.3 ± 0.1	n.s.
Platelet count ($\times 10^3/\mu\text{L}$)	106 ± 8	140 ± 2	<0.001
Albumin (g/dL)	3.8 ± 0.1	4.0 ± 0.1	<0.001
Total bilirubin (mg/dL)	1.2 ± 0.1	0.8 ± 0.1	<0.001
AST (IU/L)	78.1 ± 6.8	64.6 ± 2.1	n.s.
ALT (IU/L)	72.8 ± 9.7	72.0 ± 2.9	n.s.
Gamma-GTP (IU/L)	68.7 ± 7.5	53.9 ± 2.3	n.s.
Alpha fetoprotein (ng/L)	$17.1 (4.4\text{--}36.8)$	$16.7 (4.1\text{--}23.1)$	n.s.
Esophageal varices	29.0 % (9/31)	6.4 % (22/344)	<0.01
On-treatment parameters			
ALT (IU/L)	59.4 ± 5.7	44.6 ± 1.8	<0.05
Alpha fetoprotein (ng/L)	$9.8 (4.6\text{--}17.4)$	$5.5 (3.7\text{--}11.1)$	<0.01
HCV RNA level (KIU/mL)	$236 (<0.5\text{--}2,210)$	$21 (<0.5\text{--}1,780)$	<0.05

n.s. not significant

7.Izumi N, et.al. 2012

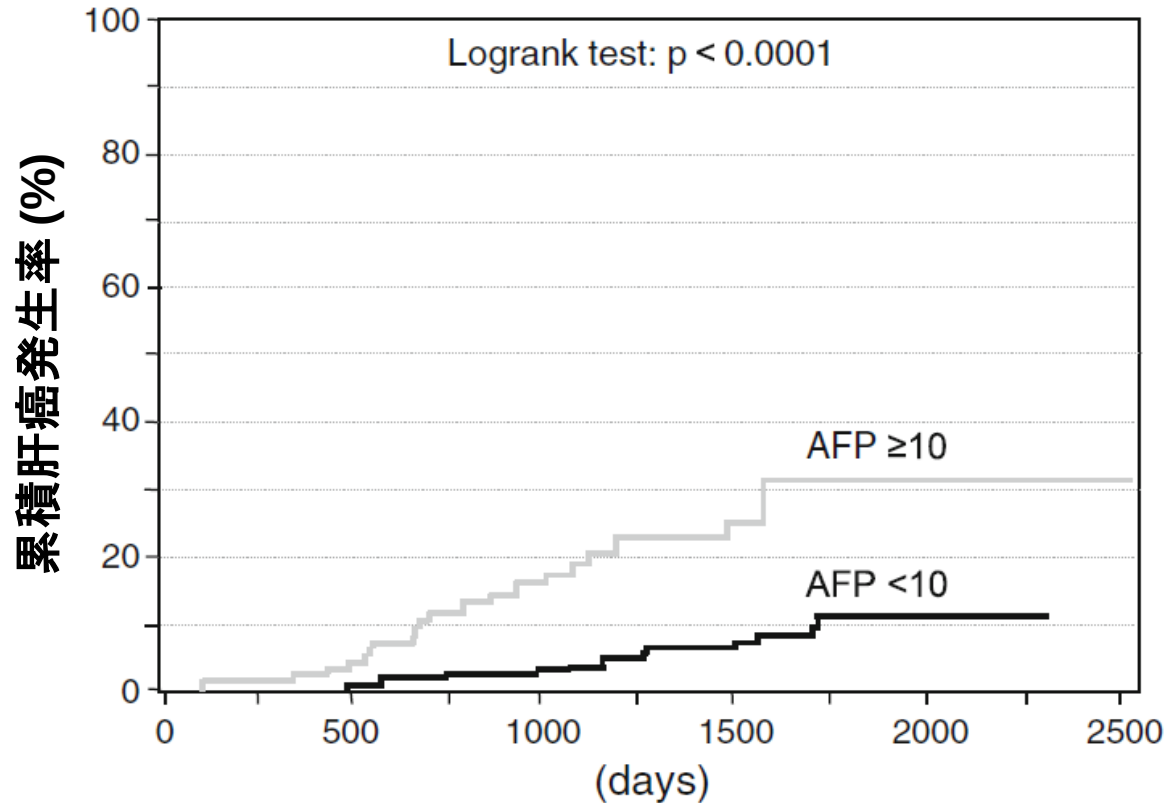
1.肝癌発生に関するリスク因子に関する検討



治療開始24週目のALT値が、40 IU/L以下の群では、41 IU/L以上の群に比較して肝癌発生率は低下していた。

7.Izumi N, et.al. 2012

1.肝癌発生に関するリスク因子に関する検討



治療開始24週目のAFP値が、10 ng/mL未満の群では、10 ng/mL以上の群に比較して肝癌発生率は低下していた。

7.Izumi N, et.al. 2012

1.肝癌発生に関するリスク因子に関する検討

肝癌発生に寄与する因子の解析(多変量解析)

		Multivariate analysis		
		Odds ratio	95 % Confidence interval (CI)	<i>p</i>
年齢	Age (years) (every 5 years)	2.24	1.76–9.33	<0.005
性	Sex (male/female)	3.16	1.56–10.7	<0.005
肝線維化	Fibrosis (F3, 4/F0, 1, 2)	1.69	1.18–5.2	<0.01
血小板数	Platelet count (<120 × 10 ³ /μL vs. ≥120 × 10 ³ /μL)	3.24	1.44–27.6	<0.01
ビリルビン値	Total bilirubin (mg/dL)	1.59	1.09–2.58	<0.05
24週目のALT値	ALT (at 24 weeks) (≥41 vs. <40 IU/L)	2.49	1.51–8.28	<0.05
24週目のAFP値	AFP (at 24 weeks) (≥10 vs. <10 ng/L)	3.78	1.92–11.8	<0.01

7.Izumi N, et.al. 2012

2.肝癌発生に関する治療群(N=59)と 無治療群(N=59)との比較 マッチ-コントロール研究

Table 4 Backgrounds of the patients in the propensity-matched control study (PegIFN α -2a group, $n = 59$; control group, $n = 59$)

	PegIFN α -2a group ($n = 59$)	Control group ($n = 59$)	p value
Age (years)	60.5 $\pm$ 13.0	63.3 $\pm$ 10.5	n.s.
Gender (male/female)	24/35	25/34	n.s.
BMI	22.9 $\pm$ 3.6	22.9 $\pm$ 3.4	n.s.
Genotype (1/2)	49/10	46/13	n.s.
History of excess alcohol consumption (60 g/day; yes/no)	10/49	4/55	n.s.
Fibrosis (F0, 1, 2/F3, 4)	37/22	43/16	<0.05
Development of HCC (F0–2/F3, 4)	1/1	1/7	n.s.
Inflammatory activity (A0,1/A2, 3)	19/40	30/29	<0.05
Diabetes mellitus (no/yes)	57/2	56/3	n.s.
LDL cholesterol (mg/dL)	95.3 $\pm$ 23.8	117.0 $\pm$ 4.2	n.s.
White blood cell count (/mm ³)	4,260 $\pm$ 1,239	5,193 $\pm$ 2,078	<0.05
Red blood cell count ($\times 10^{-4}$ / μ L)	430 $\pm$ 57.8	441 $\pm$ 44.9	n.s.
Hemoglobin (g/dL)	13.6 $\pm$ 1.5	13.6 $\pm$ 1.9	n.s.
Platelet count ($\times 10^{-3}$ / μ L)	14.5 $\pm$ 5.7	15.8 $\pm$ 5.7	n.s.
Albumin (g/dL)	4.1 $\pm$ 0.5	4.1 $\pm$ 0.4	n.s.
Total bilirubin (mg/dL)	0.7 $\pm$ 0.5	0.9 $\pm$ 0.7	n.s.
AST (IU/L)	58.3 $\pm$ 47.7	49.7 $\pm$ 26.6	n.s.
ALT (IU/L)	63.6 $\pm$ 68.7	58.0 $\pm$ 39.2	n.s.
Gamma-GTP (IU/L)	78.3 $\pm$ 81.3	55.3 $\pm$ 75.1	n.s.
Baseline alpha-fetoprotein (AFP) (ng/L)	7.2 (4.3–14.2)	7.7 (3.9–13.8)	n.s.
Baseline HCV RNA level (KIU/mL)	1,230 (24–3,870)	1,024 (38–3,110)	n.s.

7.Izumi N, et.al. 2012

2.肝癌発生に関する治療群(N=59)と無治療群(N=59)との比較 マッチ-コントロール研究

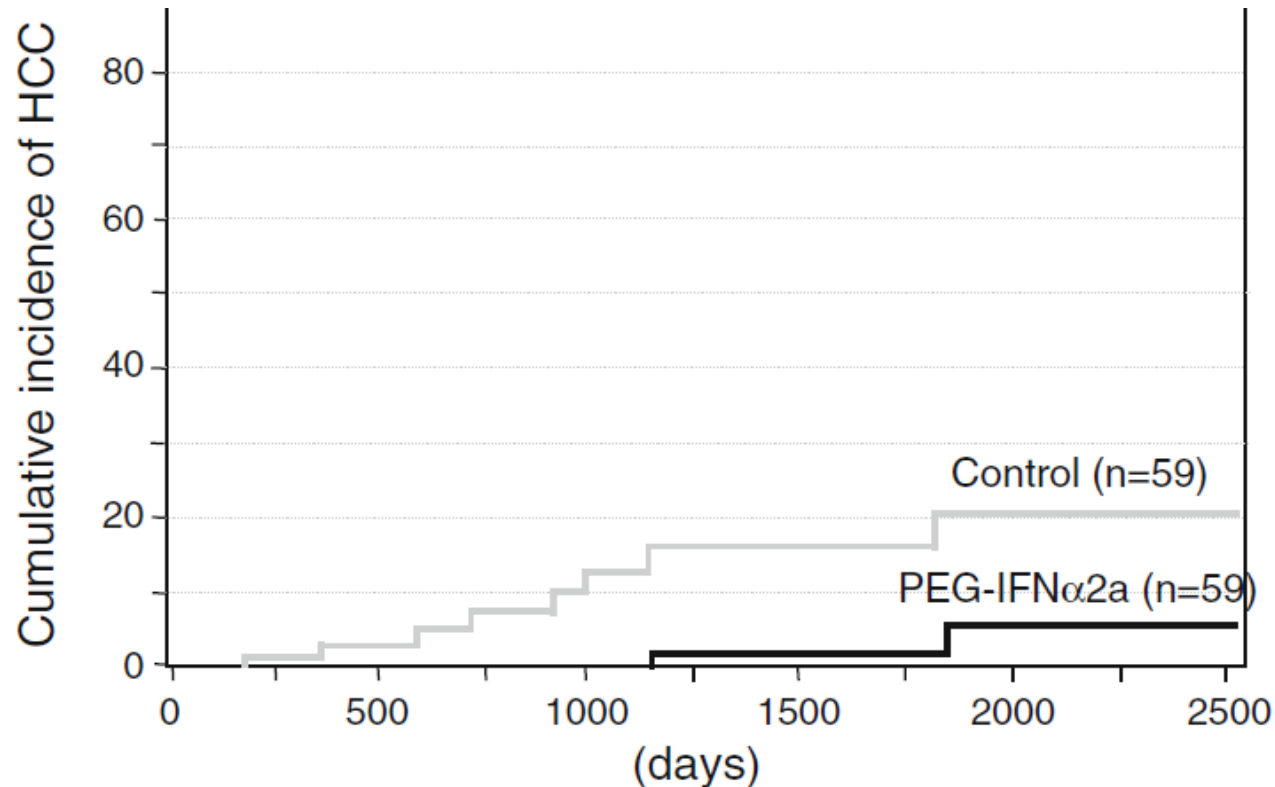


Fig. 4 Comparison of HCC rates between the long-term PegIFN α -2a administration group ($n = 59$) and non-administration group ($n = 59$) in the propensity-matched control study (Kaplan–Meier log-rank test, $p = 0.019$)

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マッチ-コントロール研究での肝癌発生に寄与する因子 の解析(多変量解析)

PegIFN 年齢	PegIFN versus control	0.17	0.03–0.75	<0.05
	Age (every 1 year)	1.12	1.02–1.25	<0.05
	Fibrosis (F3, 4 vs. F0, 1, 2)	1.70	0.75–4.16	n.s.
	Platelet count (every $10 \times 10^3/\mu\text{L}$)	0.89	0.73–1.09	n.s.
	Albumin (every 1.0 g/dL)	0.80	0.10–6.68	n.s.
	On-treatment AFP (<10 vs. ≥ 10 ng/L)	4.07	0.59–40.12	n.s.

発癌抑制目的のインターフェロン少量長期投与のこれまでの報告のまとめ

海外

2つの前向き、大規模無作為比較試験(HALT-C試験,EPIC試験)

全体像として、無治療群に比較してペグインターフェロン群で有意に肝癌発生を抑制したとは確認されず。

HALT-C試験の肝硬変群の長期観察(8年)において、無治療群に比較してペグインターフェロン群での肝癌発生率の低下が確認された。

HALT-C試験では、無治療群に比してペグインターフェロン群で死亡率が高い。その理由として慢性肝炎治療群での肝疾患以外の死因が関与。

EPIC試験では、門脈圧亢進症患者で、腹水貯留、静脈瘤破裂の発生抑制の可能性あり。

国内

3つの後ろ向き研究、(単独施設:2研究、多施設共同研究:1研究)

3つのマッチ-コントロール研究では、いずれもインターフェロン少量長期投与群(従来型インターフェロン300万単位週3回約3年投与、ペグインターフェロン90 μ g週1回か2週に1回投与1年間以上)では、無治療群に比して、有意に肝癌発生が低下していたと報告。
