

Ishak Score Analysis of Drug Groups (Primary Endpoint)

Baseline – 52 weeks	FAS				PPS			
	Placebo A	180mg C	270mg D	360mg B	Placebo A	180mg C	270mg D	360mg B
N(Missing)	43(0)	42(0)	41(0)	41(0)	42(0)	36(0)	35(0)	34(0)
Ishak decline ≥ 1 , n(%)	11(25.58%)	17(40.48%)	23(56.10%)	18(43.90%)	11(26.19%)	17(47.22%)	23(65.71%)	18(52.94%)
Ishak decline < 1 , n(%)	32(74.42%)	25(59.52%)	18(43.90%)	23(56.10%)	31(73.81%)	19(52.78%)	12(34.29%)	16(47.06%)
Intergroup p value	0.0245*				0.0058*			
Decline of Place minus decline of drug groups	Rate diff.(A-C)% and 95%CI -14.89(-33.32,4.99)				-21.03(-40.20,0.26)			
	Rate diff.(A-D)% and 95%CI -30.52(-48.12,-9.50)*				-39.52(-56.83,-17.26)*			
	Rate diff.(A-B)% and 95%CI -18.32(-36.76,1.96)				-26.75(-45.78,-4.75)*			

*Statistically significant

FIG. 1

Analysis of Intra Group Ishak Score Change

Baseline – 52 weeks	FAS				PPS			
	Placebo A	180mg C	270mg D	360mg B	Placebo A	180mg C	270mg D	360mg B
N(Missing)	43(0)	42(0)	41(0)	41(0)	42(0)	36(0)	35(0)	34(0)
Mean(SD)	0.26(1.60)	0.43(1.25)	0.78(1.11)	0.56(1.25)	0.26(1.62)	0.50(1.34)	0.91(1.15)	0.68(1.34)
median	0	0	1	0	0	0	1	1
组内Signed rank	27	74.5	151	88.5	27	74.5	151	88.5
P值	0.3205	0.0259*	<0.0001*	0.0033*	0.3205*	0.0259*	<0.0001*	0.0033*

*Statistically significant

FIG. 2

Analysis of Patients of Significant Fibrosis (Baseline Ishak ≥ 3)

Baseline – 52 weeks		FAS				PPS			
		Placebo A	180mg C	270mg D	360mg B	Placebo A	180mg C	270mg D	360mg B
N(Missing)		25(0)	24(0)	28(0)	29(0)	25(0)	22(0)	25(0)	25(0)
Ishak decline ≥ 1 , n(%)		9(36.00)	13(54.17)	18(64.29)	17(58.62)	9(36.00)	13(59.09)	18(72.00)	17(68.00)
Ishak decline < 1 , n(%)		16(64.00)	11(45.83)	10(35.71)	12(41.38)	16(64.00)	9(40.91)	7(28.00)	8(32.00)
Intergroup p value		0.1990				0.0470*			
Decline of Place minus decline of drug groups	Rate diff.(A-C)% and 95%CI	-18.17(-42.04,9.11)				-23.09(-46.75,5.09)			
	Rate diff.(A-D)% and 95%CI	-28.29(-50.04,-1.45)*				-36.00(-56.89,-8.38)*			
	Rate diff.(A-B)% and 95%CI	-22.62(-44.98,3.82)				-32.00(-53.61,-4.37)*			

*Statistically significant

FIG. 3

Combination Analysis of 270 mg and 360 mg Groups

Baseline – 52 weeks		FAS		PPS	
		Placebo	270mg+360mg	Placebo	270m+360mg
Baseline Ishak $\geq$ 3 Significant Fibrosis	N(Missing)	25(0)	57(0)	25(0)	50(0)
	Ishak decline $\geq$ 1,n(%)	9(36.00)	35(61.40)	9(36.00)	35(70.00)
	Pvalue	0.0348		0.0051	
	(A-B)% and 95%CI [#]	-25.40(-44.93,-2.00)		-34.00(-53.15,-10.15)	
Baseline Ishak $\geq$ 4 Advanced Fibrosis	N(Missing)	22(0)	34(0)	22(0)	31(0)
	Ishak decline $\geq$ 1,n(%)	9(40.91)	22(64.71)	9(40.91)	22(70.97)
	Pvalue	0.083		0.0302	
	(A-B)% and 95%CI [#]	-23.80(-46.21,2.59)		-30.06(-51.94,-3.18)	
Baseline Ishak $\geq$ 5 Early Cirrhosis	N(Missing)	16(0)	26(0)	16(0)	24(0)
	Ishak decline $\geq$ 1,n(%)	8(50.00)	17(65.38)	8(50.00)	17(70.83)
	Pvalue	0.3298		0.188	
	(A-B)% and 95%CI [#]	-15.38(-42.13,13.79)		-20.83(-47.05,8.90)	
Baseline Ishak = 6 Cirrhosis	N(Missing)	4(0)	10(0)	4(0)	10(0)
	Ishak decline $\geq$ 1,n(%)	1(25.00)	9(90.00)	1(25.00)	9(90.00)
	Pvalue	0.0191		0.0191	
	(A-B)% and 95%CI [#]	-65.00(-87.03,-10.74)		-65.00(-87.03,-10.74)	

FIG. 4

Combination Analysis of All Drug Groups

	Baseline – 52 weeks	FAS		PPS	
		Placebo	270mg+360mg	Placebo	
Baseline Ishak ≥ 3 Significant Fibrosis	N(Missing)	25(0)	81(0)	25(0)	72(0)
	Ishak decline ≥ 1, n(%)	9(36.00)	48(59.26)	9(36.00)	48(66.67)
	P value	0.0424		0.0076	
	(A-B)% and 95%CI [#]	-23.26(-41.94,-0.94)		-30.67(-49.22,-8.05)	
Baseline Ishak ≥ 4 Advanced Fibrosis	N(Missing)	22(0)	49(0)	22(0)	44(0)
	Ishak decline ≥ 1, n(%)	9(40.91)	29(59.18)	9(40.91)	29(65.91)
	P value	0.1563		0.0545	
	(A-B)% and 95%CI [#]	-18.27(-39.96,6.40)		-25.00(-46.47,0.15)	
Baseline Ishak ≥ 5 Early Cirrhosis	N(Missing)	16(0)	38(0)	16(0)	34(0)
	Ishak decline ≥ 1, n(%)	8(50.00)	23(60.53)	8(50.00)	23(67.65)
	P value	0.4792		0.2352	
	(A-B)% and 95%CI [#]	-10.53(-36.54,16.56)		-17.65(-43.31,10.04)	
Baseline Ishak = 6 Cirrhosis	N(Missing)	4(0)	15(0)	4(0)	14(0)
	Ishak decline ≥ 1, n(%)	1(25.00)	12(80.00)	1(25.00)	12(85.71)
	P value	0.0407		0.0201	
	(A-B)% and 95%CI [#]	-55.00(-79.20,-3.49)		-60.71(-83.59,-8.97)	

FIG. 5

Ishak Score Changes of Baseline HBeAg (+) Patients after 52 Weeks

	FAS			PPS		
	Placebo	270mg +360mg	All Drug Groups	Placebo	270mg +360mg	All Drug Groups
Impairment,n(%)	3(9.68)	7(14.00)	12(16.90)	3(10.00)	7(16.28)	12(19.67)
Steady,n(%)	19(61.29)	20(40.00)	29(40.85)	18(60.00)	13(30.23)	19(31.15)
Improvement,n(%)	9(29.03)	23(46.00)	30(42.25)	9(30.00)	23(53.49)	30(49.18)
Fisher P value		0.2001	0.1646		0.042	0.0359

FIG. 6

Ishak Score Changes of Baseline HBeAg (-) Patients after 52 Weeks

	FAS			PPS		
	Placebo	270mg +360mg	All Drug Groups	Placebo	270mg +360mg	All Drug Groups
Impairment,n(%)	6(50.00)	2(6.25)	4(6.55)	6(50.00)	2(7.69)	4(9.09)
Steady,n(%)	4(33.33)	12(37.50)	21(39.62)	4(33.33)	6(23.08)	12(27.27)
Improvement,n(%)	2(16.67)	18(56.25)	28(52.83)	2(16.67)	18(69.23)	28(63.64)
Fisher P value		0.0036	0.0015		0.0018	0.0016

FIG. 7

Change of Liver Stiffness Measurement LSM (kPa) (FAS)

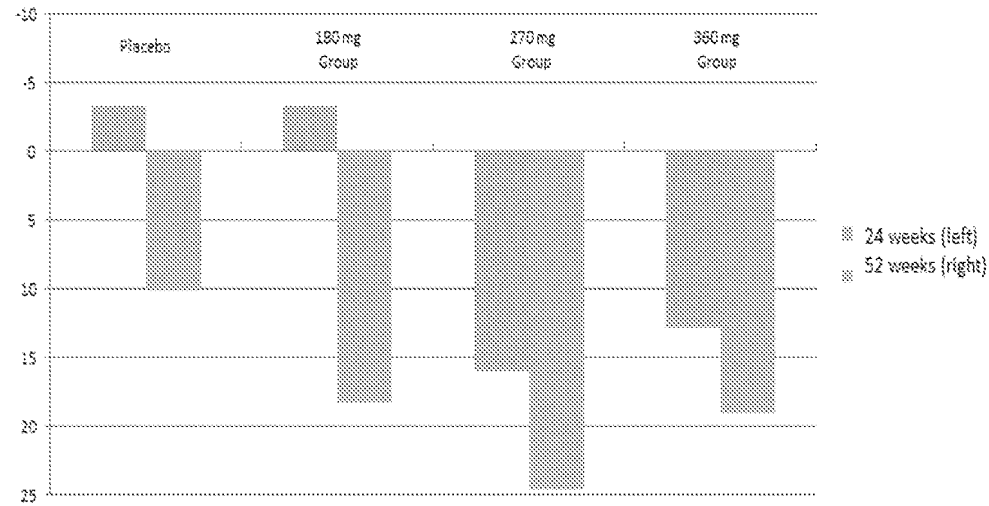


FIG. 8

Combination of Drug Groups for LSM Analysis (Ishak Score ≥ 3 , 4, 5 and 6)

FAS				PPS		
Baseline Ishak ≥ 3	Placebo	All Drug Groups	270mg +360mg	Placebo	All Drug Groups	270mg +360mg
Impairment.n(%)	6(24.00)	5(6.94)	4(8.16)	6(24.00)	5(7.14)	4(8.33)
Stable.n(%)	5(20.00)	21(29.17)	12(24.49)	5(20.00)	20(28.57)	12(25.00)
Improvement.n(%)	14(56.00)	46(63.89)	33(67.35)	14(56.00)	45(64.29)	32(66.67)
P value		0.0648	0.1733		0.0749	0.1853
Baseline Ishak ≥ 4	Placebo	All Drug Groups	270mg +360mg	Placebo	All Drug Groups	270mg +360mg
Impairment.n(%)	6(27.27)	1(2.27)	1(3.33)	6(27.27)	1(2.33)	1(3.33)
Stable.n(%)	3(13.64)	10(22.73)	5(16.67)	3(13.64)	9(20.93)	5(16.67)
Improvement.n(%)	13(59.09)	33(75.00)	24(80.00)	13(59.09)	33(76.74)	24(80.00)
P value		0.0132	0.0526		0.0132	0.0526
Baseline Ishak ≥ 5	Placebo	All Drug Groups	270mg +360mg	Placebo	All Drug Groups	270mg +360mg
Impairment.n(%)	5(31.25)	1(2.94)	1(4.35)	5(31.25)	1(3.03)	1(4.35)
Stable.n(%)	2(12.50)	7(20.59)	3(13.04)	2(12.50)	6(18.18)	3(13.04)
Improvement.n(%)	9(56.25)	26(76.47)	19(82.61)	9(56.25)	26(78.79)	19(82.61)
P value		0.0212	0.0833		0.024	0.0833
Baseline Ishak =6	Placebo	All Drug Groups	270mg +360mg	Placebo	All Drug Groups	270mg +360mg
Impairment.n(%)	1(25.00)	0(0.00)	0(0.00)	1(25.00)	0(0.00)	0(0.00)
Stable.n(%)	1(25.00)	2(14.29)	2(20.00)	1(25.00)	2(14.29)	2(20.00)
Improvement.n(%)	2(50.00)	12(85.71)	8(80.00)	2(50.00)	12(85.71)	8(80.00)
P value		0.1971	0.4306		0.1971	0.4306

FIG. 9

Analysis of HBV DNA+ Patients after 52 Weeks Entecavir Therapy

* Fibrotouch

Group	Drug #	Baseline HBV DNA	52 weeks HBV DNA	Baseline Ishak	52 weeks Ishak	Baseline LSM(kPa)	52 weeks LSM(kPa)	Baseline Inflammation score	52 weeks Inflammation score	Baseline ALT	52 weeks ALT
Placebo	20	8.72E+6	2.83E+4	5	5	20.5*	19.8*	3	3	85	39
Placebo	290	2.42E+8	6870	1	1	6.9	6.4	0	1	28	26.6
180mg	22	>1.0E+8	1760	1	1	4.2*	4.9*	1	2	19	20
180mg	256	8.41E+7	120	4	3	10.4	4.3	3	2	88.2	32.7
270mg	251	4.1E+7	110	4	2	10	6.3	3	1	165.3	22.9
360mg	55	≥5.00E+7	685	3	1	10	6.6	2	1	172	131
360mg组	209	5.91E+5	22.1	6	4	10.2	8.1	3	2	49	37

FIG. 10

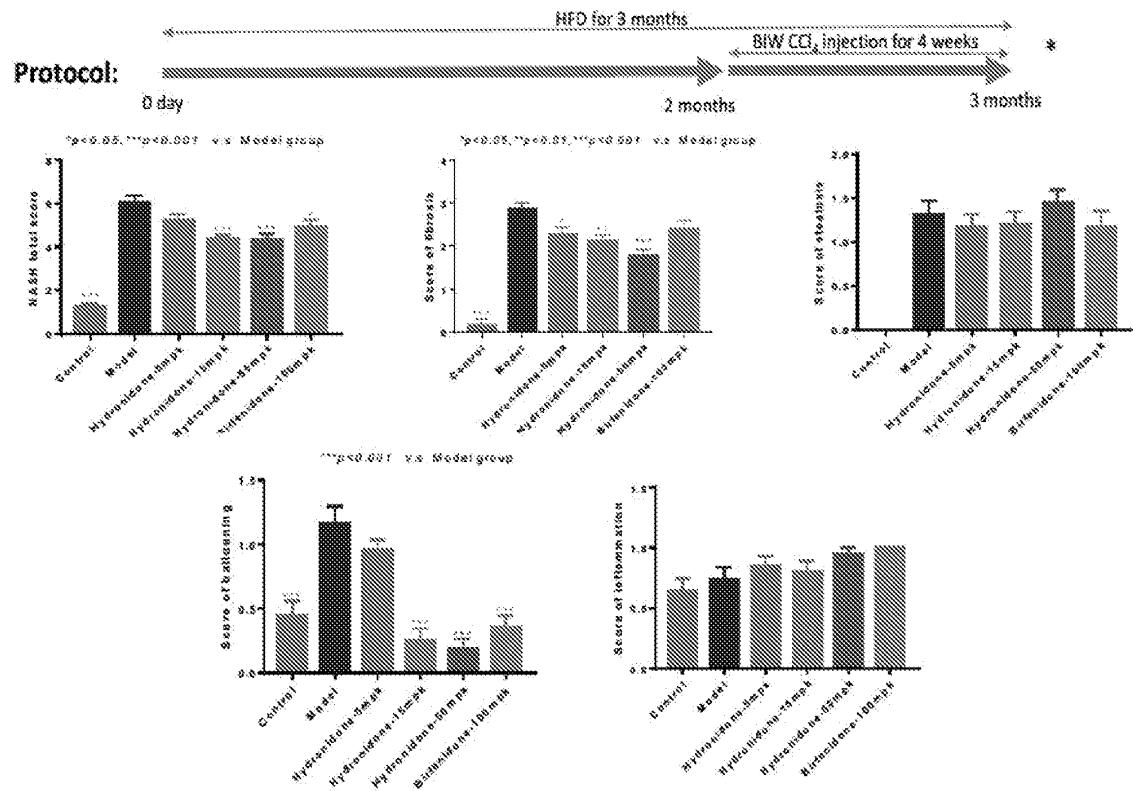


FIG. 11

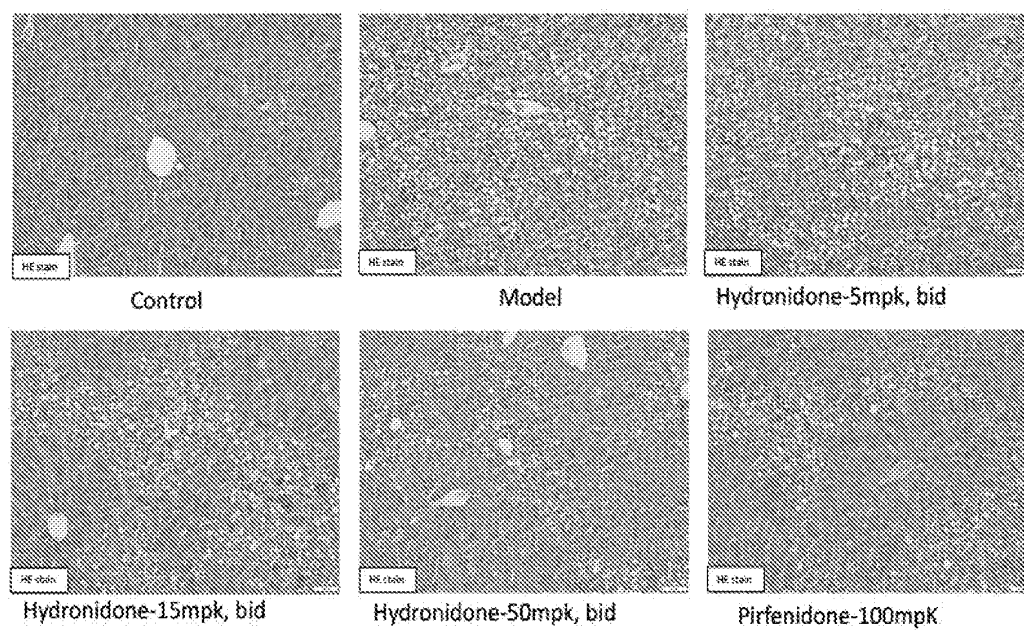


FIG. 12