Tables

Table 1: Characteristics of the patients with cystic fibrosis (CF) at the time of their inclusion in the French CF Modifier Gene Study

Total (n)	3,328
Males: % (n)	52% (1731)
Current age (yrs), mean ± SD	15.9 ± 7.7
Year of Birth: 1986-1995	36% (1,183)
1996-2005	40% (1,333)
>2005	24% (812)
Age at enrollment : Birth	35% (1,172)
1-10	36% (1,195)
11-18	29% (961)
European origin: % (n)	89% (2,957)
CF Diagnosis < 1-year-old: % (n)	74% (2,461)
CFTR F508del homozygotes: % (n)	49% (1,645)
Meconium ileus: % (n)	13% (445)

Abbreviations: CF: cystic fibrosis; CFTR: cystic fibrosis transmembrane conductance regulator

Table 2: Cumulative incidence of cystic fibrosis related liver disease (CFLD) and severe CFLD

Age	CFLD				Severe CFLD			
(Years)	Number at risk	Cumulative number of events	Average annual risk* (%[95%CI])	Cumulative incidence of CFLD (%[95%CI])	Number at risk	Cumulative number of events	Average annual risk* (%[95%CI])	Cumulative incidence of severe CFLD (%[95%CI])
0-5	3328	94	0.8 [0.6, 0.9]	3.7 [3.0, 4.5]	3328	13	0.10 [0.06, 0.16]	0.5 [0.3, 0.8]
5-10	2978	252	1.3 [1.1, 1.6]	9.9 [8.4, 10.9]	3053	60	0.39 [0.26, 0.48]	2.4 [1.8, 3.1]
10-15	2286	405	1.5 [1.3, 1.8]	16.5 [14.8, 17.8]	2421	126	0.58 [0.46, 0.77]	5.2 [4.4, 6.3]
15-20	1584	519	1.6 [1.3, 2.0]	22.9 [20.9, 24.7]	1715	153	0.32 [0.23, 0.53]	6.7 [6.0, 8.3]
20-25	923	599	2.1 [1.6, 2.6]	30.6 [28.4, 33.0]	1037	173	0.54 [0.28, 0.71]	9.2 [7.8, 11.0]
25-30	395	605	0.5 [0.1, 0.9]	32.2 [29.7, 35.2]	471	175	0.22 [0.00, 0.67]	10.2 [8.5, 12.9]

Abbreviations: CFLD: cystic fibrosis related liver disease

CFLD was diagnosed when at least two of the following criteria were present: 1) clinical: abnormal physical examination with hepatomegaly and/or splenomegaly; 2) biochemical: abnormal liver function tests; 3) ultrasonographic: evidence of liver involvement, portal hypertension, or biliary abnormalities. Severe CFLD was diagnosed when at least one of the following criteria was present: portal hypertension, esophageal varices, or cirrhosis.

Table 3: Risk factors for cystic fibrosis related liver disease (CFLD) and severe CFLD

Patients' Characteristics	Univariable analysis	Multivariable analysis[*]
	HR [95%CI]	HR [95%CI]
CFLD		
Male sex	1.15 [0.99, 1.36]	1.15 [0.99, 1.37]
Meconium ileus	1.66 [1.36, 2.01]	1.64 [1.34, 2.01]
CFTR F508del homozygous	1.17 [1.00, 1.37]	1.14 [0.97, 1.33]
Severe CFLD		
Male sex	1.48 [1.10, 2.09]	1.48 [1.1, 2.08]
Meconium ileus	1.28 [0.78, 1.72]	1.28 [0.77, 1.70]
CFTR F508del homozygous	1.10 [0.82, 1.48]	1.09 [0.80, 1.48]

[*] In the multivariable analysis, each variable was adjusted for the remaining variables reported in the table.

Abbreviations: CF: cystic fibrosis; CFLD: cystic fibrosis related liver disease; CFTR: cystic fibrosis transmembrane conductance regulator; HR: hazard ratio

Table 4. Body mass index and forced expiratory volume in 1 second according to cystic fibrosis related liver (CFLD) disease status

	No CFLD	CFLD	Severe CFLD	P-value
n	(N=2723)	(N=431)	(N=174)	
Age (yrs), mean ± SD	15.7 ± 6.5	16.9 ± 6.2	18.9 ± 5.3	<0.001
Male Sex (%)	51%	52%	61%	0.036
FEV$_1$ percent predicted[*] (mean ± SD)	75.1 ± 23.6	71.0 ± 23.9	62.5 ± 22.7	<0.001
BMI Z-score[**] (mean ± SD)	-0.48 ± 0.97	-0.57 ± 1.00	-0.92 ± 0.95	<0.001
CF-specific FEV$_1$ percentile[***] (mean ± SD)	53 ± 26	51 ± 20	47 ± 26	0.004
CF-specific BMI percentile (mean ± SD)	48 ± 26	47 ± 27	39 ± 24	0.01

[*]GLI equations (14); [**]WHO2007 reference; [***]FEV$_1$ and BMI Z-scores were averaged over measurements of the last 3 and 2 years respectively.

Abbreviations: CF: cystic fibrosis; CFLD: cystic fibrosis related liver disease; BMI: body mass index; FEV$_1$: forced expiratory volume in 1 second