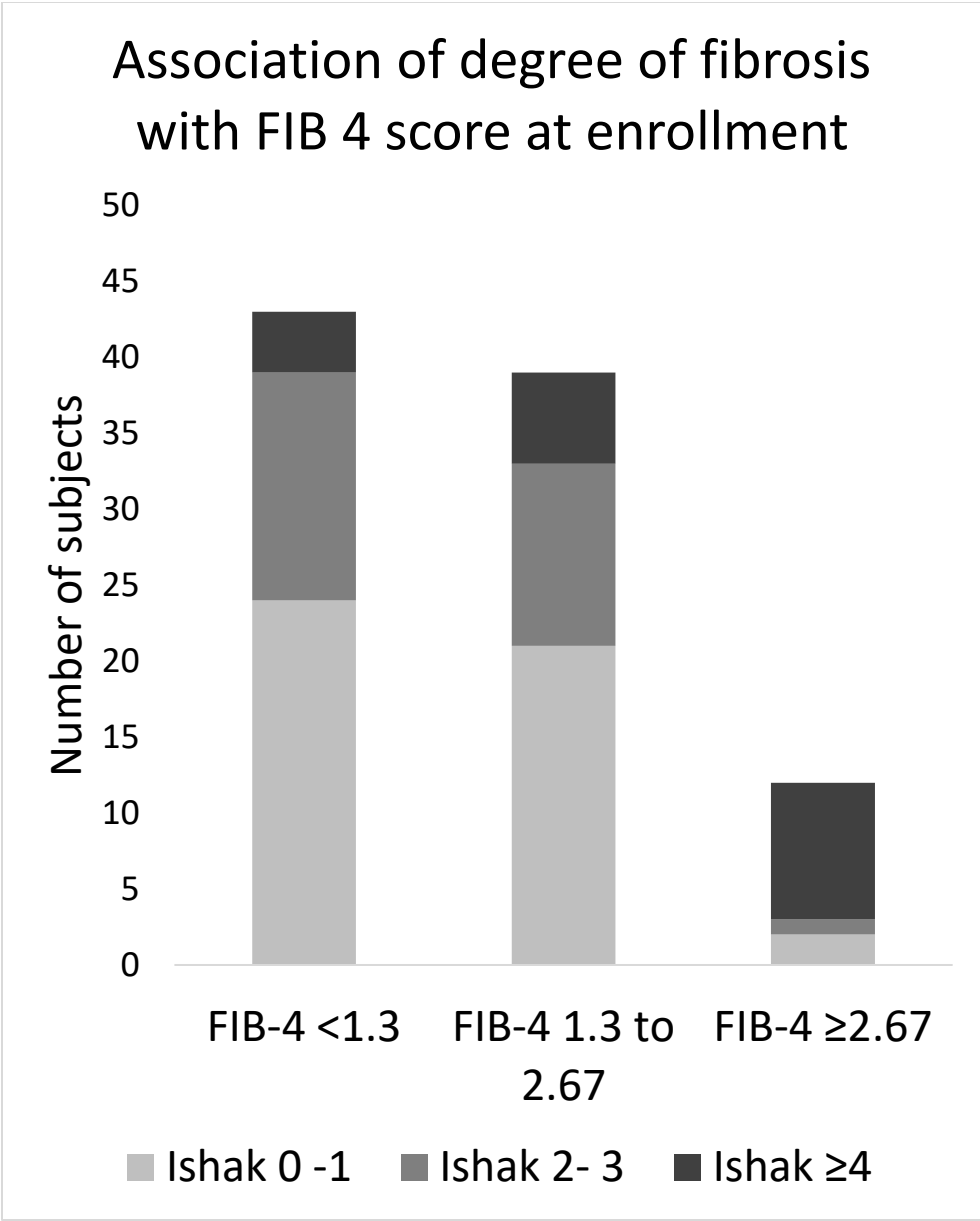


Supplementary table 1: Lung function and augmentation therapy parameters of the cohort

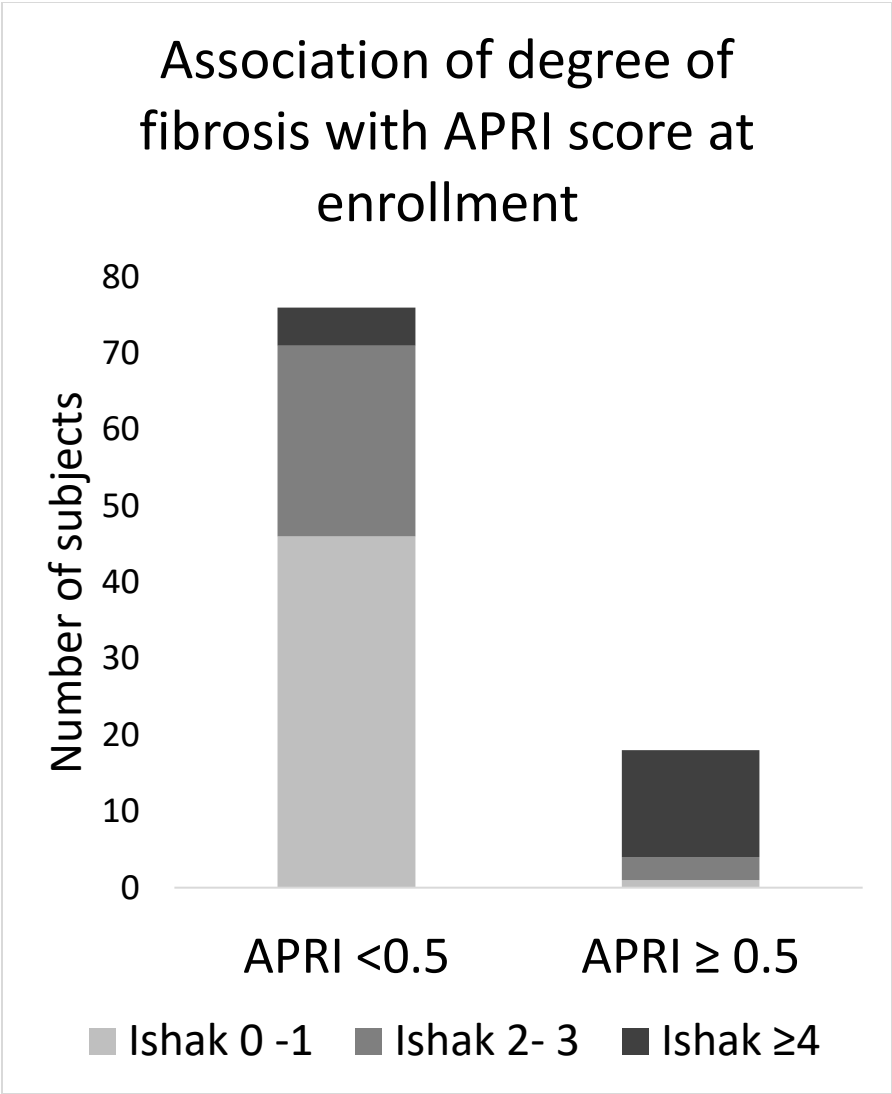
Lung Function (Mean (SD))	Overall (N=52)	Non-smoker (N=38)	Past smoker (N=14)	p value
	Mean (SD)	Mean (SD)	Mean (SD)	P value
ppFVC	95.6 (15.5)	96.8 (15.8)	92.3 (14.8)	0.3523
ppFEV1	82.0 (22.6)	86.3 (21.0)	70.2 (23.1)	0.0212
ppFEV1/FVC	86.0 (21.7)	89.6 (20.1)	76.4 (23.6)	0.0501
Lung Function	Overall (N=52)	≤ 20 pack-year (N=38)	> 20 pack-year (N=13)	
	Mean (SD)	Mean (SD)	Mean (SD)	P value
ppFVC	95.6 (15.5)	96.8 (15.8)	92.2 (15.4)	0.3566
ppFEV1	82.0 (22.6)	86.3 (21.0)	67.5 (21.6)	0.0079
ppFEV1/FVC	86.0 (21.7)	89.6 (20.1)	73.7 (22.2)	0.0205
	ppFEV1 Estimate (SE)	P value	ppFEV1/FVC Estimate (SE)	P value
Age at enrollment, year	-0.559 (0.198)	0.0071	-0.545 (0.184)	0.0048
Sex: Female vs Male	5.099 (5.662)	0.3724	10.683 (5.255)	0.0477
Smoking: ≤ 20 vs >	16.194 (6.356)	0.0142	12.506 (5.899)	0.0393
	Overall (N = 96)	No Augmentation (N = 60)	Having Augmentation (N = 35)	p value
	Mean (SD)	Mean (SD)	Mean (SD)	p value
Age at enrollment, years	54.7 (14.0)	52.2 (15.4)	58.9 (10.2)	0.0119
Fibrosis (including Known Severe	1.8 (1.4)	2.0 (1.5)	1.5 (1.3)	0.1375
ppFEV1	82.0 (22.6)	95.0 (15.0)	65.5 (19.7)	<.0001
	%	%	%	p value
ppFEV1 at Year 1				<.0001
<80%	38.5	10.3	73.9	
≥80%	61.5	89.7	26.1	
Sex				0.5247
Female	50.0	52.5	45.7	
Male	50.0	47.5	54.3	
Smoking status at Year 1				0.0935
Non-Smoker	67.7	73.8	57.1	

Past Smoker	32.3	26.2	42.9	
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Supplementary Figure 1a: Association of FIB4 score and fibrosis



Supplementary Figure 1b: Association of APRI score and fibrosis



Supplementary Table 2: Association between inflammatory features and fibrosis on biopsy

	Overall	Minimal Fibrosis or Ishak 0-1	Fibrosis Ishak 2 - 3	Significant Fibrosis or Ishak >3	
	N = 82	N = 47	N = 29	N = 6	
Periportal inflammation	%	%	%	%	p value
Absent	53.7	76.6	27.6	0.0	<.0001
Mild (focal, few portal areas)	25.6	17.0	41.4	16.7	
Mild/ moderate (focal, most portal areas)	14.6	6.4	31.0	0.0	
Moderate (continuous around < 50% of tracts or septa)	2.4	0.0	0.0	33.3	
Severe (continuous around > 50% of tracts or septa)	3.7	0.0	0.0	50.0	
Lobar Inflammation	%	%	%	%	p value
Absent	39.0	51.1	20.7	33.3	0.0280
1 focus or less per x 10 objective	51.2	44.7	58.6	66.7	
2-4 foci per x 10 objective	9.8	4.3	20.7	0.0	
Portal Inflammation	%	%	%	%	p value
Absent	29.3	40.4	17.2	0.0	<.0001
Mild, some or all portal areas	54.9	55.3	62.1	16.7	
Moderate, some or all portal areas	13.4	4.3	20.7	50.0	
Moderate/ marked, all portal areas	2.4	0.0	0.0	33.3	
Lobular Necrosis	%	%	%	%	p value
no acidophil bodies	91.4	93.6	85.7	100.0	0.4395
a few acidophil bodies	7.4	4.3	14.3	0.0	
frequent acidophil bodies	1.2	2.1	0.0	0.0	

Necroinflammatory activity score	%	%	%	%	p value
1 to 2	58.5	80.9	31.0	16.7	<.0001
3	12.2	8.5	20.7	0.0	
>3	29.3	10.6	48.3	83.3	
Macrovesicular Steatosis	%	%	%	%	p value
Grade 0 (< 5% of hepatocytes affected)	64.6	70.2	55.2	66.7	0.5332
Grade 1 (5-33% of hepatocytes affected)	29.3	25.5	34.5	33.3	
Grade 2 (34 to 66% of hepatocytes affected)	3.7	4.3	3.5	0.0	
Grade 3 (>66% of hepatocytes affected)	2.4	0.0	6.9	0.0	
Hepatocellular Ballooning	%	%	%	%	p value
Grade 0 (None)	96.3	100.0	93.1	83.3	0.063
Grade 1 (Few)	3.7	0.0	6.9	16.7	
Microvesicular Steatosis	%	%	%	%	p value
Absent	96.3	100.0	89.7	100.0	0.0581
Present	3.7	0.0	10.3	0.0	

Supplementary Table 3: Z polymer levels and clinically significant elevation of liver enzymes

and their association with inflammation

	Overall (N = 96)	Necro-inflammatory Activity Score $\leq$ 2 (N = 48)	Necro- inflammatory Activity Score >2 (N = 34)	
	%	%	%	p value
ALT >35 U/L	22.3	6.4	20.6	0.0857
AST > 35U/L	27.4	8.3	38.2	0.0010
GGT >40 U/L	22.5	11.4	27.3	0.0733
	Overall (N = 55)	Necro-inflammatory Activity Score $\leq$ 2 (N = 31)	Necro- inflammatory Activity Score >2 (N = 14)	
Z polymer ug/ml Mean (SD)	11.9 (7.1)	9.7 (6.4)	14.9 (5.9)	0.013
AAT% as Z polymer Mean (SD)	4.3 (2.7)	3.5 (1.8)	4.3 (2.2)	0.2157
	Overall (N = 96)	Periportal Inflammation: Absent (N = 44)	Periportal Inflammation: Present (N = 38)	
	%	%	%	p value
ALT >35 U/L	22.3	7.0	18.4	0.1771
AST > 35U/L	27.4	9.1	34.2	0.0051
GGT >40 U/L	22.5	9.8	27.8	0.0408

ug/ml	Overall (N = 55)	Periportal Inflammation: Absent (N = 30)	Periportal Inflammation: Present (N = 15)	
Z polymer Mean (SD)	11.9 (7.1)	8.7 (3.0)	16.6 (8.6)	0.0034
AAT% as Z polymer Mean (SD)	4.3 (2.7)	3.2 (1.2)	4.7 (2.7)	0.064
	Overall (N = 96)	Portal Inflammation: Absent/Mild (N = 69)	Portal Inflammation: Moderate/Marked (N = 13)	
	%	%	%	p value
ALT >35 U/L	22.3	8.8	30.8	0.0496
AST > 35U/L	27.4	17.4	38.5	0.1302
GGT >40 U/L	22.5	15.4	33.3	0.2145
	Overall (N = 55)	Portal Inflammation: Absent/Mild (N = 38)	Portal Inflammation: Moderate/Marked (N = 7)	
Z polymer Mean (SD)	11.9 (7.1)	10.4 (6.3)	16.3 (6.4)	0.0284
AAT% as Z polymer Mean (SD)	4.3 (2.7)	3.4 (1.8)	5.4 (2.2)	0.0125

	Overall (N = 96)	Lobar Inflammation: Absent (N = 32)	Lobar Inflammation: Present (N = 50)	
	%	%	%	p value
ALT >35 U/L	22.3	3.2	18.0	0.08
AST > 35U/L	27.4	6.3	30.0	0.0114
GGT >40 U/L	22.5	3.6	26.5	0.012
	Overall (N = 55)	Lobar Inflammation: Absent (N = 20)	Lobar Inflammation: Present (N = 25)	
Z polymer Mean (SD)	11.9 (7.1)	10.6 (7.5)	11.9 (6.0)	0.5146
AAT% as Z polymer Mean (SD)	4.3 (2.7)	3.7 (1.9)	3.8 (2.0)	0.8833
	Overall (N = 96)	Lobular Necrosis: No acidophil bodies (N = 74)	Lobular Necrosis: Present of acidophil bodies (N = 7)	
	%	%	%	p value
ALT >35 U/L	22.3	13.7	0.0	0.5873
AST > 35U/L	27.4	21.6	14.3	1
GGT >40 U/L	22.5	17.4	28.6	0.6063

	Overall (N = 55)	Lobular Necrosis: No acidophil bodies (N = 43)	Lobular Necrosis: Present of acidophil bodies (N = 2)	
ug/ml				
Z polymer Mean (SD)	11.9 (7.1)	11.3 (6.8)	11.4 (2.2)	0.9899
AAT% as Z polymer Mean (SD)	4.3 (2.7)	3.8 (1.9)	2.6 (2.5)	0.4087
	Overall (N = 96)	Macrovesicular Steatosis <5% (N = 53)	Macrovesicular Steatosis ≥5% (N = 29)	
	%	%	%	
ALT > 35	22.3	7.7	20.7	0.1554
AST > 35	27.4	5.7	48.3	<.0001
GGT > 40	22.5	12.2	28.6	0.074
	Overall (N = 55)	Macrovesicular Steatosis <5% (N = 29)	Macrovesicular Steatosis ≥5% (N = 16)	
Z polymer Mean (SD)	11.9 (7.1)	10.9 (4.5)	12.0 (9.5)	0.6761
AAT% as Z polymer Mean (SD)	4.3 (2.7)	3.7 (1.6)	3.8 (2.5)	0.9353

Supplementary Table 4: Relationship between Z polymer levels and biochemical markers of liver injury and lung function

Effect of Z polymer	N	Beta	p value
AST	53	0.1510	0.0292
ALT	55	0.0024	0.9566
GGT	50	0.0252	0.4383
ppFVC	37	-0.0685	0.4395
ppFEV1	37	-0.1910	0.0679
ppFEV1/FVC	37	-0.1173	0.3606
Effect of Percent AAT as Z polymer	N	Beta	p value
AST	52	0.0733	0.0077
ALT	54	-0.0046	0.7876
GGTP	49	0.0139	0.2597
ppFVC	36	-0.0694	0.0683
ppFEV1	36	-0.0765	0.0991
ppFEV1/FVC	36	0.0256	0.6531

Supplementary Table 5: Biochemical markers and association with fibrosis

Blood markers of chronic liver disease (Mean (SD))	Overall	Baseline Fibrosis Score 0 - 1	Baseline Fibrosis score 2 - 3	Baseline Fibrosis score >3 or Known Severe	p value
	N = 96	N = 47	N = 29	N = 20	
Albumin	4.3 (0.6)	4.5 (0.3)	4.4 (0.3)	3.6 (0.9)	<.0001
Total bilirubin	0.8 (0.9)	0.6 (0.3)	0.6 (0.3)	1.7 (1.7)	<.0001
Direct bilirubin	0.3 (0.5)	0.2 (0.1)	0.2 (0.1)	0.7 (0.9)	<.0001
Alkaline phosphatase	83.1 (34.5)	75.7 (20.6)	75.4 (20.3)	113.1 (57.4)	<.0001
Platelet (1,000 per mm ³)	218.8 (63.7)	236.9 (52.1)	230.1 (46.3)	157.0 (76.5)	0.0011
INR (second)	1.1 (0.2)	1.0 (0.1)	1.0 (0.1)	1.2 (0.3)	<.0001