

TITLE

The isoform GC1f of the vitamin D binding protein is associated to bronchiectasis severity**Authors**

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Table S1. Clinical characteristics of the study population presented as median (IQR) or n (%)

Demography	
Sex (Female)	78 (67.2%)
Age	62.0 (48.8, 72.0)
BMI	21.7 (19.0, 24.9)
Radiology	
Reiff score	4.0 (3.0, 6.0)
Disease severity	
BSI score	6.0 (4.0, 9.0)
BSI risk classes	40 (34.5%)
	38 (32.8%)
	38 (32.8%)
FACED score	2.0 (1.0, 4.0)
FACED risk classes	63 (54.3%)
	41 (35.3%)
	12 (10.3%)
Clinical status	
Exacerbation in the previous year	2.0 (1.0, 3.0)
Hospitalization (at least one previous year)	13 (11.3%)
Comorbidities	
Osteoporosis	8 (6.9%)
Depression	12 (10.3%)
Anxiety	5 (4.3%)
Asthma	20 (17.2%)
Lung function	
FEV1%	84.0 (69.2, 99.0)
FEV1%<50%	15 (13.2%)
FEV1%<35%	8 (7.0%)
Standard microbiology	
Chronic infection	50 (49.0%)
Chronic <i>P. aeruginosa</i>	30 (29.4%)
Chronic <i>H. influenzae</i>	6 (5.9%)
Chronic <i>MSSA</i>	8 (7.8%)
Chronic <i>A. xylosoxidans</i>	2 (2.0%)

Chronic Others	4 (3.9%)
Aetiology	
Idiopathic	63 (54.3%)
Primary Ciliary Dyskinesia	10 (8.6%)
Primary immunodeficiency	13 (11.2%)
Post Infective	6 (5.2%)
Secondary Immunodeficiency	6 (5.2%)
Others*	
QoL-B questionnaire	
Physical section	60.0 (40.9, 80.0)
Role section	66.7 (53.3, 86.7)
Vitality section	55.6 (33.3, 69.5)
Emotion section	75.0 (58.3, 91.7)
Social section	66.7 (41.7, 83.3)
Treatment Burden section	66.7 (55.6, 77.8)
Health section	41.7 (22.2, 58.3)
Respiration section	74.1 (59.3, 81.5)
Vitamin D	
Vitamin D (ng/mL)	20.4 (13.0, 28.4)

* Other includes COPD, Connective Tissue Diseases, Alpha1-antitrypsin deficiency, ABPA, Asthma, CFTR-RD, Aspiration

Table S2: SNPs in GC gene in bronchiectasis patients

SNPs	Genotype	Bronchiectasis n (%)
rs7041	A A	21(18.1)%
	A C	58(50.0)%
	C C	37(31.9)%
rs4588	G G	61(52.6)%
	G T	47(40.5)%
	T T	8(6.9)%
SNPs	Allele	Bronchiectasis n (%)

rs7041	A	100 (43.1%)
	C	132(56.9%)
rs4588	G	169(72.8%)
	T	63(27.2%)

Table S3. Comparison of clinical characteristics of patients with GC2 isoform vs other isoforms

Demography				
		GC2 (N=55)	Other isoforms (N=61)	p-value
Sex (Female)		33 (60.0%)	45 (73.8%)	0.115
Age		62.0 (46.0, 71.0)	62.0 (54.0, 72.0)	0.453
BMI		22.0 (19.0, 25.8)	21.3 (19.0, 24.0)	0.328
Radiology				
Reiff score		4.0 (2.0, 5.0)	4.0 (3.0, 6.0)	0.77
Disease severity				
BSI score		5.0 (3.0, 9.0)	8.0 (4.0, 10.0)	0.081
BSI risk classes	mild	23 (41.8%)	17 (27.9%)	0.288
	moderate	16 (29.1%)	22 (36.1%)	
	severe	16 (29.1%)	22 (36.1%)	
BSI Moderate-severe		32 (58.2%)	44 (72.1%)	0.114
BSI Severe		16 (29.1%)	22 (36.1%)	0.424
FACED score		2.0 (1.0, 4.0)	2.0 (1.0, 4.0)	0.574
FACED risk classes	mild	31 (56.4%)	32 (52.5%)	0.854
	moderate	18 (32.7%)	23 (37.7%)	
	severe	6 (10.9%)	6 (9.8%)	
FACED Moderate-severe		24 (43.6%)	29 (47.5%)	0.673
FACED Severe		6 (10.9%)	6 (9.8%)	0.85
Clinical status				
Exacerbation in the previous year		2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	0.397
Hospitalization (at least one previous year)		2 (3.6%)	11 (18.0%)	0.015
Comorbidities				
BACI		0.0 (0.0, 3.0)	0.0 (0.0, 2.0)	0.317
Osteoporosis		1 (1.8%)	7 (11.5%)	0.040
Depression		4 (7.3%)	8 (13.1%)	0.302
Anxiety		1 (1.8%)	4 (6.6%)	0.209
Asthma		12 (21.8%)	8 (13.1%)	0.215
Lung function				
FEV1%		84.5 (70.0, 99.0)	81.5 (68.8, 101.0)	0.901
FEV1%<50%		7 (13.0%)	8 (13.3%)	0.953
FEV1%<35%		4 (7.4%)	4 (6.7%)	0.877
Standard microbiology				
Chronic infection		22 (50.0%)	28 (48.3%)	0.863
Chronic <i>P. aeruginosa</i>		15 (34.1%)	15 (25.9%)	0.366
Chronic <i>H. influenzae</i>		3 (6.8%)	3 (5.2%)	0.726
Chronic MSSA		2 (4.5%)	6 (10.3%)	0.281

Chronic <i>A. xylosoxidans</i>	2 (4.5%)	0 (0.0%)	0.101
Chronic Others	1 (2.3%)	3 (5.2%)	0.455
Aetiology			
Idiopathic	37 (67.3%)	26 (42.6%)	0.292
Primary Ciliary Dyskinesia	4 (7.3%)	6 (9.8%)	
Primary immunodeficiency	6 (10.9%)	7 (11.5%)	
Post Infective	2 (3.6%)	4 (6.6%)	
Secondary Immunodeficiency	2 (3.6%)	4 (6.6%)	
Others*	4 (7.3%)	14 (23.2%)	
QoL-B questionnaire			
Physical section	60.0 (46.7, 83.3)	63.4 (40.0, 80.0)	0.894
Role section	80.0 (53.3, 86.7)	66.7 (53.3, 86.7)	0.333
Vitality section	55.6 (33.3, 66.7)	55.6 (33.3, 72.2)	0.872
Emotion section	75.0 (50.0, 91.7)	79.2 (58.3, 91.7)	0.482
Social section	75.0 (41.7, 83.3)	57.0 (41.7, 83.3)	0.362
Treatment Burden section	66.7 (55.6, 77.8)	66.7 (55.6, 77.8)	0.913
Health section	41.7 (25.0, 66.7)	33.3 (20.8, 58.3)	0.627
Respiration section	74.1 (62.5, 81.5)	72.2 (58.3, 85.2)	0.919
Vitamin D			
Vitamin D (ng/mL)	19.5 (13.0, 26.8)	20.5 (13.2, 29.7)	0.536

* Other includes COPD, Connective Tissue Diseases, Alpha1-antitrypsin deficiency, ABPA, Asthma, CFTR-RD, Aspiration

Table S4. Comparison of clinical characteristics of patients among isoform phenotypes

Demography						
	GC1s-GC1f (N=24)	GC1s-GC1s (N=37)	GC2-GC1f (N=13)	GC2-GC1s (N=34)	GC2-GC2 (N=8)	p-value
Sex (Female)	17 (70.8%)	28 (75.7%)	9 (69.2%)	19 (55.9%)	5 (62.5%)	0.488
Age	61.0 (51.8, 72.2)	63.0 (54.0, 72.0)	62.0 (53.0, 69.0)	60.0 (44.5, 70.2)	66.0 (46.8, 72.8)	0.737
BMI	21.5 (19.7, 25.0)	21.3 (19.0, 24.0)	22.0 (19.0, 25.0)	21.9 (18.9, 25.4)	22.9 (21.0, 26.5)	0.739
Radiology						
Reiff score	4.0 (2.0, 6.0)	4.0 (3.0, 6.0)	4.0 (3.0, 6.0)	4.0 (2.0, 4.0)	3.0 (2.0, 4.2)	0.757
Disease severity						
BSI score	7.5 (3.8, 10.0)	8.0 (5.0, 9.0)	6.0 (5.0, 11.0)	5.0 (3.0, 8.8)	4.0 (3.8, 8.5)	0.196
BSI risk classes	mild	9 (37.5%)	8 (21.6%)	2 (15.4%)	16 (47.1%)	5 (62.5%)
	moderate	6 (25.0%)	16 (43.2%)	6 (46.2%)	9 (26.5%)	1 (12.5%)
	severe	9 (37.5%)	13 (35.1%)	5 (38.5%)	9 (26.5%)	2 (25.0%)
FACED score	2.0 (1.0, 3.2)	3.0 (1.0, 4.0)	3.0 (2.0, 4.0)	2.0 (1.0, 3.0)	2.5 (1.8, 4.0)	0.556
FACED risk classes	mild	15 (62.5%)	17 (45.9%)	6 (46.2%)	21 (61.8%)	4 (50.0%)
	moderate	5 (20.8%)	18 (48.6%)	4 (30.8%)	10 (29.4%)	4 (50.0%)
	severe	4 (16.7%)	2 (5.4%)	3 (23.1%)	3 (8.8%)	0 (0.0%)
Clinical status						
Exacerbation in the previous year	3.0 (2.0, 3.0)	2.0 (1.0, 4.0)	1.0 (1.0, 3.2)	2.5 (1.0, 3.0)	2.0 (1.8, 3.0)	0.878
Hospitalization (at least one previous year)	7 (29.2%)	4 (10.8%)	0 (0.0%)	0 (0.0%)	2 (25.0%)	0.005 (1)
Comorbidities						
BACI	0.0 (0.0, 2.2)	0.0 (0.0, 0.0)	0.0 (0.0, 3.0)	0.0 (0.0, 2.2)	3.0 (0.0, 4.2)	0.223

Osteoporosis	2 (8.3%)	5 (13.5%)	0 (0.0%)	1 (2.9%)	0 (0.0%)	0.289
Depression	2 (8.3%)	6 (16.2%)	0 (0.0%)	4 (11.8%)	0 (0.0%)	0.409
Anxiety	1 (4.2%)	3 (8.1%)	0 (0.0%)	1 (2.9%)	0 (0.0%)	0.663
Asthma	1 (4.2%)	7 (18.9%)	1 (7.7%)	7 (20.6%)	4 (50.0%)	0.039 (2)
Lung function						
FEV1%	81.0 (72.5, 102.5)	82.0 (68.0, 97.0)	73.0 (54.0, 99.0)	88.0 (72.0, 101.0)	84.0 (74.8, 86.5)	0.7
FEV1%<50%	3 (13.0%)	5 (13.5%)	3 (23.1%)	3 (9.1%)	1 (12.5%)	0.808
FEV1%<35%	1 (4.3%)	3 (8.1%)	2 (15.4%)	1 (3.0%)	1 (12.5%)	0.577
Standard microbiology						
Chronic infection	12 (57.1%)	16 (43.2%)	9 (75.0%)	13 (48.1%)	0 (0.0%)	0.059
Chronic <i>P. aeruginosa</i>	6 (28.6%)	9 (24.3%)	6 (50.0%)	9 (33.3%)	0 (0.0%)	0.267
Chronic <i>H. influenzae</i>	2 (9.5%)	1 (2.7%)	0 (0.0%)	3 (11.1%)	0 (0.0%)	0.467
Chronic MSSA	4 (19.0%)	2 (5.4%)	0 (0.0%)	2 (7.4%)	0 (0.0%)	0.248
Chronic <i>A. xylosoxidans</i>	0 (0.0%)	0 (0.0%)	1 (8.3%)	1 (3.7%)	0 (0.0%)	0.377
Chronic Others	1 (4.8%)	2 (5.4%)	1 (8.3%)	0 (0.0%)	0 (0.0%)	0.702
Aetiology						
Idiopathic	8 (33.3%)	18 (48.6%)	9 (69.2%)	21 (61.8%)	7 (87.5%)	0.631
Primary Ciliary Dyskinesia	5 (20.8%)	1 (2.7%)	0 (0.0%)	4 (11.8%)	0 (0.0%)	
Primary immunodeficiency	1 (4.2%)	6 (16.2%)	3 (23.1%)	2 (5.9%)	1 (12.5%)	
Post Infective	3 (12.5%)	1 (2.7%)	0 (0.0%)	2 (5.9%)	0 (0.0%)	
Secondary Immunodeficiency	3 (12.5%)	1 (2.7%)	1 (7.7%)	1 (2.9%)	0 (0.0%)	
Others*	4 (16.7%)	10 (27.1%)	0 (0%)	4 (11.7%)	0 (0%)	
QoL-B questionnaire						
Physical section	66.7 (43.4, 96.7)	60.0 (40.0, 74.2)	61.2 (46.6, 68.4)	63.4 (46.7, 85.9)	53.3 (30.0, 73.3)	0.72
Role section	73.3 (53.3, 93.3)	60.0 (48.4, 81.7)	70.0 (58.3, 88.4)	80.0 (55.0, 86.7)	80.0 (60.0, 86.7)	0.652
Vitality section	66.7 (47.2, 77.8)	55.6 (33.3, 66.7)	55.6 (44.4, 77.8)	55.6 (33.3, 66.7)	55.6 (38.9, 72.2)	0.803
Emotion section	83.3 (75.0, 95.8)	75.0 (54.1, 91.7)	91.7 (72.9, 100.0)	75.0 (50.0, 83.3)	58.3 (41.6, 66.7)	0.143
Social section	70.8 (33.3, 85.4)	55.6 (41.7, 72.9)	79.2 (60.5, 91.7)	66.7 (41.7, 83.3)	83.3 (70.8, 83.3)	0.654
Treatment Burden section	77.8 (63.9, 80.6)	55.6 (55.6, 77.8)	72.2 (58.4, 77.8)	66.7 (55.6, 77.8)	55.6 (50.0, 77.8)	0.535
Health section	44.4 (33.3, 66.7)	33.3 (16.7, 58.3)	38.8 (18.7, 68.8)	41.7 (27.1, 64.6)	50.0 (37.5, 50.0)	0.509
Respiration section	77.8 (66.7, 87.5)	66.7 (55.6, 82.4)	74.1 (65.8, 75.9)	75.9 (63.5, 81.5)	66.7 (63.0, 74.1)	0.643
Vitamin D						
Vitamin D (ng/mL)	20.5 (11.7, 27.9)	20.5 (14.8, 29.9)	13.4 (6.6, 24.6)	20.4 (15.9, 28.6)	17.8 (13.7, 21.0)	0.313

1) GC1s-GC2 vs GC2-GC2, p=0.003; GC1s-GC1f vs GC1s-GC2, p=0.001

(2) GC1s-GC1f vs GC2-GC2, p=0.002