Lupus and Neutropenia in a large European collaborative database (LBBR)

SYSTEMIC LUPUS ERYTHEMATOSUS AND NEUTROPENIA: A HALLMARK OF HEMATOLOGICAL MANIFESTATIONS

SUPPLEMENTARY MATERIAL

Table S1: Characteristics of patients at enrolment in the study

A. General variables

Gender, *n* (%)	
Female	885/996 (88.9)
Male	111/996 (11.1)
Age, mean (SD), years	43.5 (16.8)
Ethnical group, *n* (%)	
Europe	831/998 (83.3)
North Africa	55/998 (5.5)
Africa	18/998 (1.8)
Turkey	15/998 (1.5)
Asia	23/998 (2.3)
Antilles	5/998 (0.5)
unknown	51/998 (5.1)
Age of disease onset, *n* (%)	
before 10 years	15/992 (1.5)
between 10 and 19 years	165/992 (16.6)
between 20 and 29 years	333/992 (33.6)
between 30 and 39 years	226/992 (22.8)
between 40 and 49 years	142/992 (14.3)
between 50 and 59 years	76/992 (7.6)
between 60 and 69 years	28/992 (2.8)
after 70 years	7/992 (0.7)
BMI, mean (SD)	25.0 (8.4)
Tabacco, *n* (%)	
non active smoker	127/980 (13.0)
active smoker	190/980 (19.4)
never smoke	663/980 (67.7)

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B. Clinical variables

Malar rash, *n* (%)	540/997 (54.2)
Discoid lupus, *n* (%)	223/988 (22.6)
Photosensitivity, *n* (%)	626/995 (62.9)
Oral ulcers, *n* (%)	261/990 (26.4)
Arthritis, *n* (%)	710/997 (71.2)
Serositis, *n* (%)	249/994 (25.1)
Renal disease, *n* (%)	343/995 (34.5)
Neurological disease, *n* (%)	115/997 (11.5)
SLEDAI, mean (SD)	4.1 (4.8)
Other autoimmune diseases, *n* (%)	241/761 (31.7)
Sjögren syndrome, *n* (%)	76/761 (10.0)
Susceptibility to infections, *n* (%)	63/759 (8.3)
Malignancies, *n* (%)	47/757 (6.2)
Familial cases of lupus, *n* (%)	66/837 (7.9)
Familial cases of other autoimmune diseases, *n* (%)	168/965 (17.4)

C. Biological variables

Coombs test +, *n* (%)	184/613 (30.0)
Lymphopenia, *n* (%)	533/990 (53.8)
Thrombopenia, *n* (%)	175/982 (17.8)
Neutropenia, *n* (%)	208/987 (21.1)
Anti-nuclear antibodies, *n* (%)	980/998 (98.2)
Lupus anticoagulant, *n* (%)	137/635 (21.6)
Anti-β2 GP1 antibodies, *n* (%)	75/550 (13.6)
Anti-cardiolipines antibodies, *n* (%)	208/707 (29.4)
Anti-native DNA antibodies, *n* (%)	769/995 (77.3)

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Anti-Sm antibodies, *n* (%)	140/905 (15.5)
Anti-SSA antibodies, *n* (%)	288/688 (41.9)
Anti-nucléosome antibodies, *n* (%)	168/481 (34.9)
Low complement, *n* (%)	375/801 (46.8)
Low CH50, *n* (%)	177/589 (30.1)
Low C3, *n* (%)	352/744 (47.3)
Low C4, *n* (%)	348/737 (47.2)
High C3d, *n* (%)	86/214 (40.2)

D. <u>Therapies</u>

Steroïds, *n* (%)	825/953 (86.6)
Hydroxychloroquine, *n* (%)	843/918 (91.8)
Azathioprine, *n* (%)	360/865 (41.6)
Mycophénolate, *n* (%)	308/854 (36.1)
Methotrexate, *n* (%)	201/774 (26.0)
Cyclophosphamide, *n* (%)	214/805 (26.6)
Belimumab, *n* (%)	68/797 (9.5)
Rituximab, *n* (%)	69/760 (9.1)
IV Ig, *n* (%)	36/759 (4.7)

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Table S2 Univariate analysis of variables associated with neutropenia

A. **General variables**

Variables	Neutropenia (*n* = 208)	Without neutropenia (*n* = 779)	OR (95 % CI)	Uni-variate *p**
Female gender, *n* (%)	182 (87.9)	694 (89.2)	0.88 (0.55-1.42)	0.60
Age at sampling, mean (SD), years	43.7 (23.8)	43.5 (14.5)		0.14
Ethnical group, *n* (%)				0.26
Europe	168 (81.0)	656 (84.2)		
North Africa	16 (7.7)	39 (5.0)		
Africa	6 (2.9)	11 (1.4)		
Turkey	3 (1.4)	12 (1.5)		
Asia	2 (1.0)	21 (2.7)		
Antilles	2 (1.0)	3 (0.4)		
unknown	11 (5.3)	37 (4.8)		
Age of disease onset, *n* (%)				0.29
before 10 years	5 (2.4)	10 (1.3)		
between 10 and 19 years	44 (21.5)	121 (15.6)		
between 20 and 29 years	68 (33.2)	263 (33.8)		
between 30 and 39 years	42 (20.5)	181 (23.3)		
between 40 and 49 years	28 (13.7)	111 (14.3)		
between 50 and 59 years	10 (4.9)	65 (8.4)		
between 60 and 69 years	7 (3.4)	21 (2.7)		
after 70 years	1 (0.5)	6 (0.8)		
BMI, mean (SD)	24.2 (5.6)	25.2 (9.0)		0.10
Tabacco, *n* (%)				0.38
non active smoker	22 (11.0)	103 (13.4)		
active	35 (17.4)	155 (20.1)		
no	144 (71.6)	512 (66.5)		

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B. Clinical variables

Variables	Neutropenia (*n* = 208)	Without neutropenia (*n* = 779)	OR (95 % CI)	Uni-variate *p**
Malar rash, *n* (%)	120 (58.0)	413 (53.0)	1.22 (0.90-1.67)	0.20
Discoid lupus, *n* (%)	40 (19.6)	179 (23.2)	0.81 (0,55-1.19)	0.28
Photosensitivity, *n* (%)	119 (57.8)	479 (63.8)	0.78 (0,57-1.06)	0.11
Oral ulcers, *n* (%)	51 (24,6)	207 (26.8)	0.89 (0.63-1.27)	0.53
Arthritis, *n* (%)	151 (72.6)	550 (70.7)	1.10 (0.78-1.55)	0.59
Serositis, *n* (%)	60 (29.0)	186 (24.0)	1.29 (0.92-1.82)	0.14
Renal disease, *n* (%)	70 (33.8)	269 (34.6)	0.96 (0.70-1.33)	0.83
Neurological disease, *n* (%)	18 (8.7)	95 (12.2)	0.68 (0.40-1.16)	0.15
SLEDAI, mean (SD)	4.2 (4.6)	4.9 (4.9)		0.65
Other autoimmune diseases, *n* (%)	61 (35.5)	180 (31.0)	1.22 (0.85-1.75)	0.27
Sjögren syndrome, *n* (%)	24 (39.3)	52 (29.6)	1.55 (0.84-2.84)	0.16
Susceptibility to infections, *n* (%)	13 (7.6)	49 (8.5)	0.89 (0.47-1.68)	0.72
Malignancies, *n* (%)	12 (7.0)	34 (5.9)	1.21 (0,61-2.38)	0.59
Familial cases of lupus, *n* (%)	13 (7.5)	53 (8.1)	0.93 (0.49-1.74)	0.82
Familial cases of other autoimmune diseases, *n* (%)	35 (17.3)	133 (17.6)	0.98 (0.65-1.47)	0.92

C. Biological variables

Variables	Neutropenia (*n* = 208)	Without neutropenia (*n* = 779)	OR (95 % CI)	Uni-variate *p**
Coombs test +, *n* (%)	67 (48.6)	116 (24.5)	2.91 (1.96-4.32)	**<0.0001**
Lymphopenia, *n* (%)	157 (75.5)	373 (47.9)	3.34 (2.37-4.72)	**<0.0001**
Thrombopenia, *n* (%)	73 (35,8)	102 (13.1)	3.68 (2.58-5.25)	**<0.0001**
Anti-nuclear antibodies, *n* (%)	207 (99.5)	764 (98.1)	4.06 (0.53-30.9)	0.14
Lupus anticoagulant, *n* (%)	30 (22.7)	106 (24.4)	0.91 (0.57-1.44)	0.69

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Anti-β2 GP1 antibodies, *n* (%)	13 (10.9)	60 (14.1)	0.75 (0.40-1.42)	0.37
Anti-cardiolipines antibodies, *n* (%)	51 (31.9)	154 (28.5)	1.18 (0.80-1.72)	0.40
Anti-native DNA antibodies, *n* (%)	169 (81.3)	591 (76.1)	1.36 (0.93-2.00)	0.11
Anti-Sm antibodies, *n* (%)	31 (16.2)	109 (15.4)	1.06 (0.69-1.65)	0.78
Anti-SSA antibodies, *n* (%)	75 (45.2)	209 (40.5)	1.21 (0.85-1.72)	0.29
Anti-nucléosome antibodies, *n* (%)	41 (41.8)	126 (33.2)	1.44 (0.92-2.28)	0.11
Low CH50, *n* (%)	46 (32.2)	131 (29.6)	1.13 (0.75-1.69)	0.56
Low C3, *n* (%)	101 (59.1)	250 (44.1)	1.83 (1.29-2.59)	**0.0006**
Low C4, *n* (%)	96 (56.5)	249 (44.5)	1.62 (1.15-2.29)	**0.0060**
High C3d, *n* (%)	18 (40.0)	67 (41.1)	0.96 (0.49-1.87)	0.89

D. Therapies

Variables	**Neutropenia (*n* = 208)**	**Without neutropenia (*n* = 779)**	**OR (95 % CI)**	**Uni-variate *p****
Steroïds, *n* (%)	169 (83.3)	647 (87.3)	0.72 (0.47-1.11)	0.13
Hydroxychloroquine, *n* (%)	179 (91.8)	657 (91.9)	0,99 (0,55-1,76)	0.97
Azathioprine, *n* (%)	76 (40)	280 (42.0)	0,92 (0,66-1,28)	0.63
Methotrexate, *n* (%)	43 (24.6)	155 (26.2)	0,92 (0.62-1.35)	0.66
Cyclophosphamide, *n* (%)	43 (24.2)	168 (27.2)	0.85 (0,58-1.26)	0.42
Mycophénolate, *n* (%)	67 (36.8)	237 (35.8)	1,05 (0.74-1.47)	0.79
Rituximab, *n* (%)	16 (9.2)	53 (9.2)	1.00 (0,56-1.80)	1.00
Belimumab, *n* (%)	15 (8.2)	53 (8.8)	0.94 (0,51-1.71)	0.83
IV Ig, *n* (%)	8 (4.6)	28 (4.9)	0.95 (0.43-2.13)	0.90