

Supplemental Table S1. Clinical characteristics of CANOMAD/CANDA patients with or without an overt associated hematologic malignancy (HM).

Characteristics	With HM	Without HM	P
Total	16 (36)	29 (64)	-
Male	14 (88)	21 (72)	NS
Age at CANOMAD/CANDA onset of symptoms			
Median (range), years	62 (37-75)	58 (38-81)	NS
Type of onset			NS
Acute	1 (6)	7 (24)	-
Subacute	4 (25)	3 (10)	-
Chronic	11 (69)	19 (66)	-
Neurological symptoms			
Sensory ataxia	10 (63)	24 (83)	0.13
Paresthesia	11 (69)	24 (83)	NS
Hypoesthesia	15 (94)	27 (93)	NS
Ophthalmoplegia	5 (31)	15 (52)	0.18
Bulbar	4 (25)	2 (7)	0.08
Motor weakness	11 (69)	7 (24)	0.003
Areflexia	15 (94)	27 (93)	NS
Facial nerve paralysis	1 (6)	2 (7)	NS
Dysautonomic signs	5 (31)	2 (7)	0.03
Acute respiratory distress	1 (6)	2 (7)	NS
Modified Rankin score	/15	/27	NS
0 (asymptomatic)	0 (0)	0 (0)	-
1 (symptomatic but no significant disability)	5 (33)	10 (37)	-
2 (slight disability)	3 (20)	5 (19)	-
3 (moderate disability)	3 (20)	4 (15)	-
4 (moderately severe disability)	3 (20)	7 (26)	-
5 (severe disability)	1 (7)	1 (4)	-
Electrophysiological findings, pattern			0.01
Demyelinating	14 (87.5)	13 (50)	-
Axonal	1 (6)	11 (42)	-
Type of evolution			NS
Relapsing-remitting	5 (31)	9 (31)	-
Chronic progressive	11 (69)	19 (66)	-
Isolated symptomatic flare-up	0 (0)	1 (3)	-

Abbreviations: HM, hematologic malignancy; NS, non significant.

Supplemental Table S1bis. Clinical characteristics of CANOMAD/CANDA patients with or without an overt associated hematologic malignancy (HM) and for whom a bone marrow evaluation has been performed (n=31).

Characteristics	With HM	Without HM	P
Total	13 (36)	18 (64)	-
Male	10 (77)	13 (78)	NS
Age at CANOMAD/CANDA onset of symptoms			
Median (range), years	66 (52-75)	62 (38-81)	NS
Neurological symptoms			
Ophthalmoplegia	5 (38)	10 (55)	0.34
Bulbar	2 (23)	1 (6)	0.12
Modified Rankin score			
/13	/18		NS
0 (asymptomatic)	0 (0)	0 (0)	-
1 (symptomatic but no significant disability)	5 (38)	7 (38)	-
2 (slight disability)	2 (15)	3 (17)	-
3 (moderate disability)	3 (24)	3 (17)	-
4 (moderately severe disability)	2 (15)	4 (22)	-
5 (severe disability)	1 (8)	1 (6)	-

Abbreviations: HM, hematologic malignancy; NS, non significant.

Supplemental Table S1ter. Clinical characteristics of CANOMAD/CANDA patients according to the level of IgM peak value.

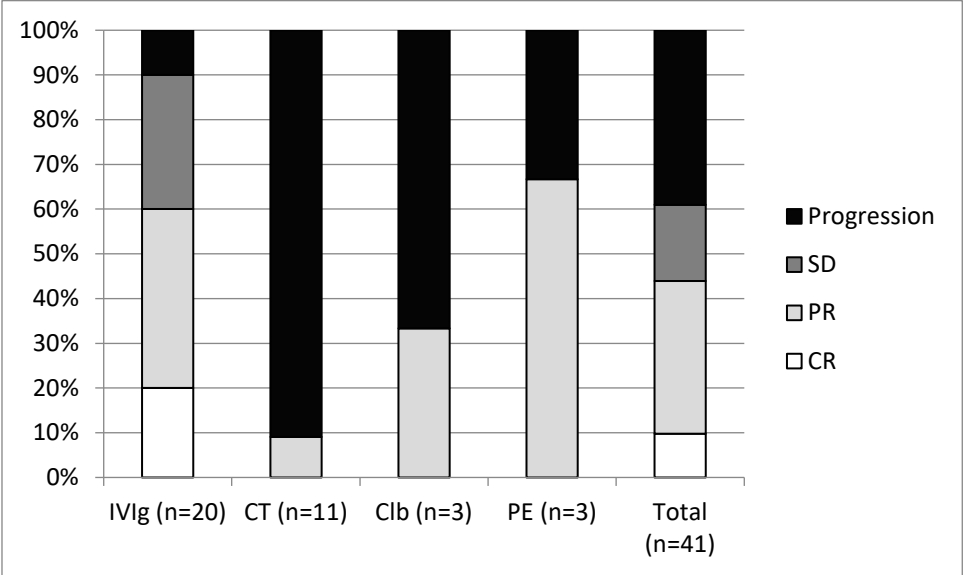
Characteristics	IgM peak value > median	IgM peak value < median	P
Total	22 (50)	23 (50)	-
Male	16 (73)	17 (74)	NS
Age at CANOMAD/CANDA onset of symptoms			
Median (range), years	62 (37-75)	60 (38-81)	NS
Neurological symptoms			
Ophthalmoplegia	8 (36)	12 (52)	0.15
Bulbar	3 (14)	3 (14)	0.95
Modified Rankin score			
/20	/22		NS
0 (asymptomatic)	0 (0)	0 (0)	-
1 (symptomatic but no significant disability)	7 (35)	8 (36)	-
2 (slight disability)	4 (20)	4 (18)	-
3 (moderate disability)	4 (20)	3 (14)	-
4 (moderately severe disability)	4 (20)	6 (27)	-
5 (severe disability)	1 (5)	1 (5)	-

Abbreviations: NS, non significant.

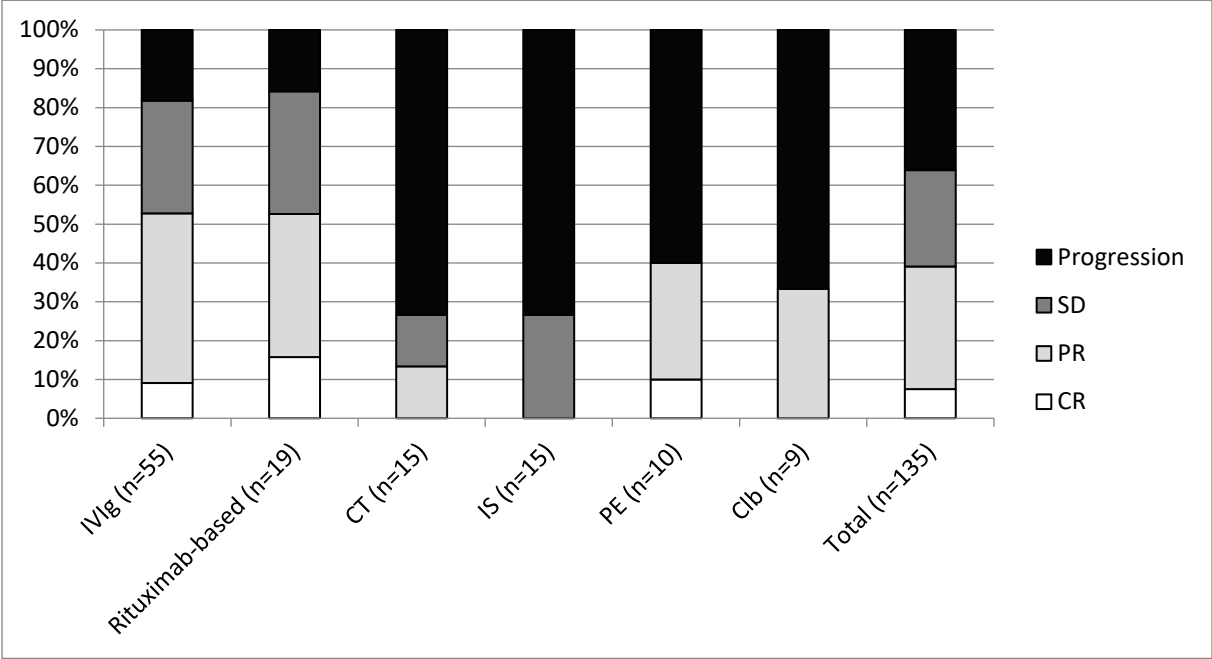
Supplemental Table S2. Evaluation of clinical responses according to biological responses for patients that received rituximab-based regimens. CR, complete response; PR, partial response; SD, stable disease; NA, not available; NI, not interpretable because of pre-treatment IgM peak below 0.5 g/L. NA and NI cases are represented in italic.

Patient	Line of treatment	Type of treatment	Response	
			Clinical	Biological
1	1	rituximab	PR	PR
2	2	rituximab-cyclophosphamide-dexamethasone	Progression	SD
3	2	rituximab	Progression	Progression
4	2	rituximab	PR	CR
5	2	rituximab	SD	SD
6	2	rituximab-fludarabine	CR	CR
7	3	rituximab	SD	SD
8	3	rituximab	SD	SD
9	3	rituximab-cyclophosphamide-dexamethasone	PR	PR
10	4	rituximab	PR	PR
11	4	rituximab	CR	PR
12	4	rituximab	PR	PR
13	5	rituximab	PR	PR
14	6	rituximab	SD	SD
15	2	<i>rituximab</i>	<i>PR</i>	<i>NA</i>
16	7	<i>rituximab</i>	<i>Progression</i>	<i>NI</i>
17	4	<i>rituximab-fludarabine</i>	<i>SD</i>	<i>NI</i>
18	3	<i>rituximab-corticosteroids</i>	<i>CR</i>	<i>NI</i>
19	5	<i>rituximab-ibrutinib</i>	<i>SD</i>	<i>NA</i>

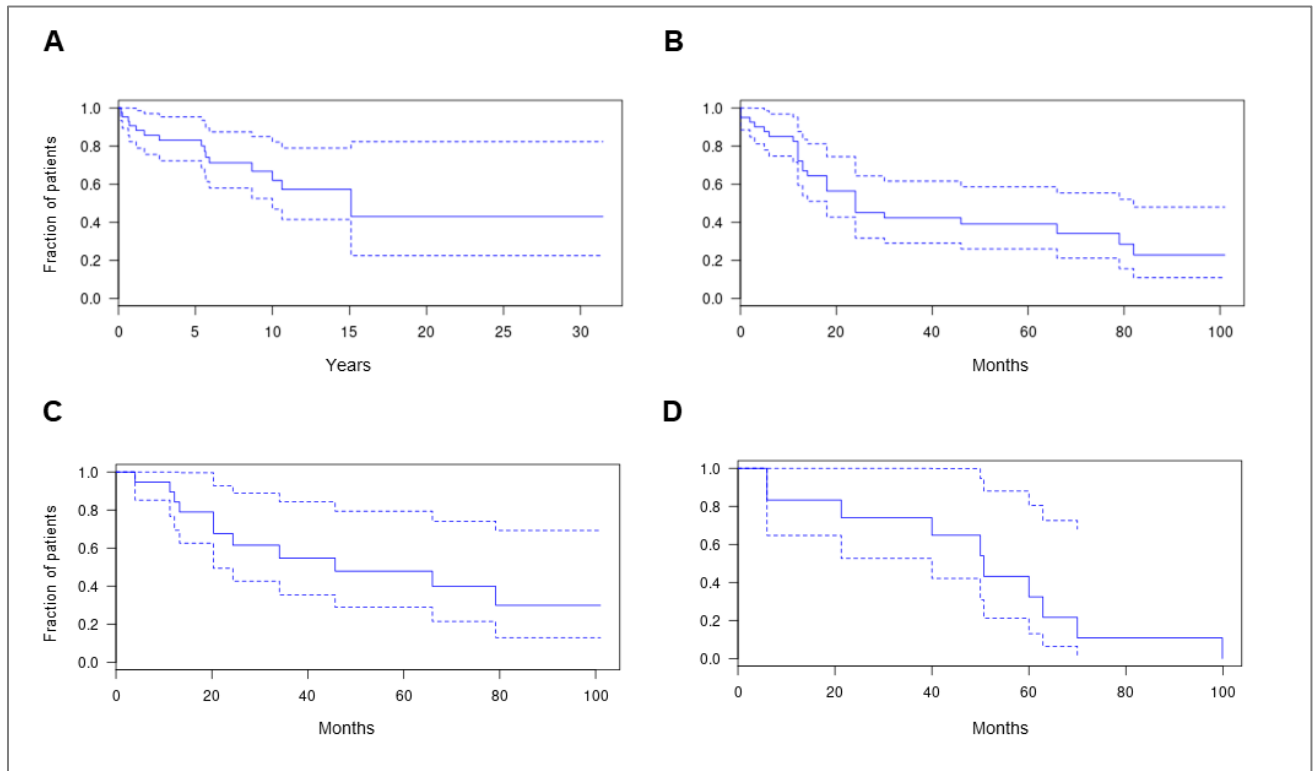
Supplemental Figure S1. Representation of different first-line therapies and their respective clinical responses. The proportion of different types of responses (complete response [CR], white; partial response [PR], light grey; stable disease [SD], dark grey; progression, black) are represented in percent for each respective type of first-line therapies (indicated above the x axis). The number of patients that received each respective treatment is indicated in brackets. IVIg, intravenous immunoglobulins; CT, corticosteroids; Clb, chlorambucil; PE, plasma exchange; SD, stable disease; PR, partial response; CR, complete response.



Supplemental Figure S2. Representation of all lines of treatment and respective clinical responses to each type of treatment. The proportion of different types of responses (complete response [CR], white; partial response [PR], light grey; stable disease [SD], dark grey; progression, black) are represented in percent of all lines of treatment (indicated in brackets) for each respective type of therapies (indicated above the x axis). IVIg, intravenous immunoglobulins; CT, corticosteroids; Clb, chlorambucil; IS, immunosuppressive therapy; PE, plasma exchange.



Supplemental Figure S3. Overall survival (A) of the whole cohort (n=45), time to next-treatment (TNT) (B, C, D) of first-line therapies (whole cohort (B) (n=41) and IVIg (C) (n=20)) and of first-use rituximab-based regimens (D) (n=14).



Supplemental Data

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