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Rituximab therapy in childhood steroid-resistant nephrotic syndrome: an international, multi-centre study

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Objectives : To evaluate the efficacy and safety of rituximab in childhood steroid-resistant nephrotic syndrome (SRNS).
Methods : We conducted a retrospective cohort study at 28 paediatric nephrology centres from 19 countries in Asia, Europe, North America and Oceania. Children with SRNS treated with rituximab were analysed according to the duration of calcineurin inhibitors (CNIs) treatment before rituximab [≥6 months (CNI-resistant) and <6 months]. Primary outcome was complete/partial remission (CR/PR) as defined by IPNA/KDIGO guidelines. Secondary outcomes included kidney survival and adverse events.
Results : Two-hundred-forty-six children (age, 6.9±4.2 years; 136 boys; 57% focal segmental glomerulosclerosis, FSGS) were followed for 32.4 (IQR, 18.6-64.9) months after rituximab. All patients were in non-remission before rituximab. 146 and 100 children received CNIs for ≥ and <6 months before rituximab, respectively. Patients with CNI-resistant SRNS, compared to those treated with CNIs for <6 months, had lower rates of NS remission (CR/PR) at 6- (36% vs 52%) and 12-months (35% vs 55%) post-rituximab (ps<0.01). Among CNI-resistant patients, multivariable analysis demonstrated that subnephrotic-range proteinuria at rituximab (OR_{adj} 5.6, 95%CI 1.1-37.1, p=0.049) and late SR (OR_{adj} 2.6, 95%CI 1.1-6.2, p=0.03) were predictive of CR/PR at 12-months. Non-response to rituximab (HR_{adj} 7.0, 95%CI 2.2-21.8, p<0.001), pre-existing CKD (HR_{adj} 2.4, 95%CI 1.0-5.6, p=0.04), and FSGS (HR_{adj} 4.3, 95%CI 1.4-13.2, p=0.01) were predictors for kidney failure and/or death. Adverse events occurred in 30.5% and most were mild.
Conclusions : Rituximab enhances remission in a subset of children with SRNS. Late SR and subnephrotic-range proteinuria predict favourable response to rituximab in children with CNI-resistant SRNS.

Table 1.jpg

Table 1. Remission status following rituximab therapy in children who received A) ≥6 months (CNI-resistant) and B) <6 months of CNIs before rituximab administration

A) ≥6 months of CNIs (CNI-resistant	3 months			6 months			12 months			24 months		
	Total	Initial SR	Late SR	Total	Initial SR	Late SR	Total	Initial SR	Late SR	Total	Initial SR	Late SR
All patients, n	146	78	68	146	78	68	134	71	63	92	48	44
Complete or partial remission, n (%)	38 (26)	13 (16.6)	25 (36.8)	52 (35.6)	17 (21.8)	35 (51.5)	47 (35.1)	19 (26.8)	28 (44.4)	36 (39.1)	14 (29.2)	22 (50)
Complete remission, n (%)	24 (16.4)	9 (11.5)	15 (22.1)	26 (17.8)	9 (11.5)	17 (25)	22 (16.4)	9 (12.7)	13 (20.6)	22 (23.9)	7 (14.6)	15 (34.1)
Partial remission, n (%)	14 (9.6)	4 (5.1)	10 (14.7)	26 (17.8)	8 (10.2)	18 (26.5)	25 (18.7)	10 (14.1)	15 (23.8)	14 (15.2)	7 (14.6)	7 (15.9)
Nephrotic-range proteinuria, n	126	68	58	126	68	58	118	63	55	82	42	40
Complete or partial remission, n (%)	32 (25.4)	11 (16.2)	21 (36.2)	38 (30.1)	11 (16.2)	27 (46.6)	35 (29.7)	11 (17.5)	24 (43.6)	31 (37.8)	11 (26.2)	20 (50)
Complete remission, n (%)	19 (13)	8 (11.7)	11 (19)	20 (15.9)	8 (11.8)	12 (20.7)	19 (16.1)	7 (11.1)	12 (21.8)	21 (25.6)	7 (16.7)	14 (35)
Partial remission, n (%)	13 (10.3)	3 (4.4)	10 (17.2)	18 (14.3)	3 (4.4)	15 (25.9)	16 (13.6)	4 (16.7)	12 (21.8)	10 (12.2)	4 (9.5)	6 (15)
Subnephrotic-range proteinuria, n	20	10	10	20	10	10	16	8	8	10	6	4
Complete or partial remission, n (%)	6 (30)	2 (20)	4 (40)	14 (70)	6 (60)	8 (80)	9 (56.3)	5 (62.5)	4 (50)	5 (50)	3 (50)	2 (50)
Complete remission, n (%)	5 (25)	1 (10)	4 (40)	6 (30)	1 (10)	5 (50)	3 (18.8)	2 (25)	1 (12.5)	1 (10)	0 (0)	1 (25)
Partial remission, n (%)	1 (5)	1 (10)	0 (0)	8 (40)	5 (50)	3 (30)	6 (37.5)	3 (37.5)	3 (37.5)	4 (40)	3 (50)	1 (25)

Subjects who developed kidney failure, received kidney transplant or death are considered as non response

B) <6 months of CNIs	3 months			6 months			12 months			24 months		
	Total	Initial SR	Late SR	Total	Initial SR	Late SR	Total	Initial SR	Late SR	Total	Initial SR	Late SR
All patients, n	100	34	66	100	34	66	99	34	65	70	23	47
Complete or partial remission, n (%)	42 (42)	8 (23.5)	34 (51.5)	52 (52)	10 (29.4)	42 (63.6)	54 (54.5)	14 (41.2)	40 (61.5)	42 (60)	11 (47.8)	31 (66)
Complete remission, n (%)	25 (25)	4 (11.8)	21 (31.8)	31 (31)	5 (14.7)	26 (39.4)	34 (34.3)	10 (29.4)	24 (36.9)	31 (44.3)	8 (34.8)	23 (48.9)
Partial remission, n (%)	17 (17)	4 (11.8)	13 (19.7)	21 (21)	5 (14.7)	16 (24.2)	20 (20.2)	4 (11.8)	16 (20)	11 (15.7_	3 (13)	8 (17)
Nephrotic-range proteinuria, n	86	32	54	86	32	54	85	32	53	60	23	37
Complete or partial remission, n (%)	29 (33.7)	7 (21.9)	22 (40.7)	39 (45.3)	9 (28.1_	30 (55.6)	46 (54.1)	15 (46.9)	31 (60)	32 (53.3)	11 (47.8)	21 (56.8)
Complete remission, n (%)	15 (17.4)	3 (9.4)	12 (22.2)	21 (24.4)	5 (15.6)	16 (29.6)	26 (30.6)	9 (28.1)	17 (30)	23 (38.3)	8 (34.8)	15 (40.5)
Partial remission, n (%)	14 (16.3)	4 (12.5)	10 (18.5)	18 (20.9)	4 (12.5)	14 (25.9)	20 (23.5)	6 (18.8)	14 (30)	9 (15)	3 (13)	6 (16.2)
Subnephrotic-range proteinuria, n	14	2	12	14	2	12	14	2	12	10	0	10
Complete or partial remission, n (%)	13 (92.9)	1 (50)	12 (100)	13 (92.9)	1 (50)	12 (100)	11 (78.6)	2 (100)	9 (80)	10 (100)	0	10 (100)
Complete remission, n (%)	10 (71.4)	1 (50)	9 (75)	10 (71.4)	0	10 (83.3)	8 (57.1)	1 (50)	7 (60)	8 (80)	0	8 (80)
Partial remission, n (%)	3 (21.4)	0	3 (25)	3 (21.4)	1 (50)	2 (16.7)	3 (21.4)	1 (50)	2 (20)	2 (20)	0	2 (20)

Abbreviation: CNIs, calcineurin inhibitors; SR, steroid resistance; SRNS, steroid resistant nephrotic syndome)

Table 1.jpg