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REMISSION INDUCTION IN MEMBRANOUS GLOMERULONEPHRITIS

A comparative case series of a new rescue therapy with plasmapheresis and rituximab in high risk patients compared to standard regimens

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Background

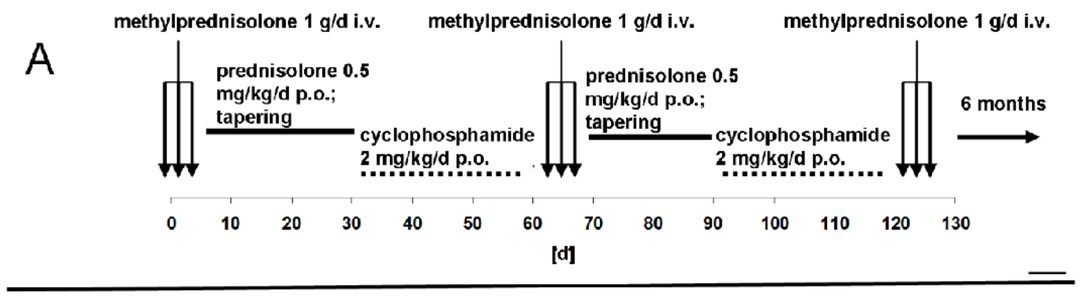
Even though current treatment guidelines for idiopathic membranous glomerulonephritis (iMGN) exist, many questions regarding an optimal therapy remain unanswered. Complete remission cannot be achieved in all patients; relapses occur and side-effects from the immunosuppressive therapy are common. Therapeutic options in high-risk patients not responding to standard immunosuppressive therapies are limited. Recent research reveals that the human M-type phospholipase A2 receptor (PLA2R) is a causative factor in iMGN that parallels clinical disease activity. Moreover anti-PLA2R-antibody levels at the end of the specific therapy seem to predict long-term outcome. However, in some patients this correlation is not evident and additional undetermined factors seem to play a role in the pathogenesis of iMGN.

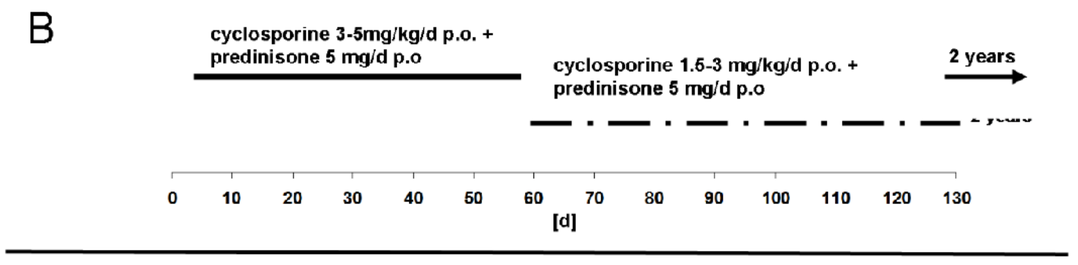
Study design

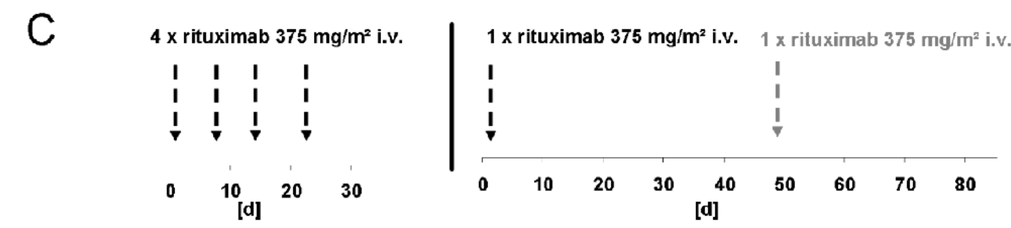
We evaluated a new rescue protocol including plasma-pheresis, i.v. immunoglobulins and rituximab (D) iMGN that was therapy-resistant to all conventional regimens and caused a UPC-ratio > 10,000 mg/g Crea.

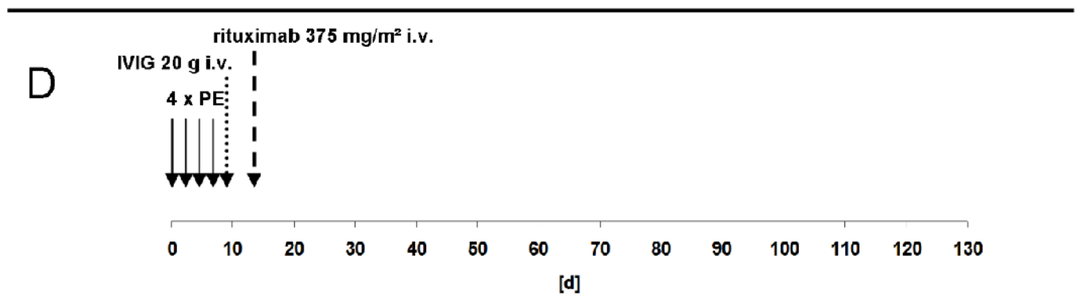
This protocol was compared to standard regimens including monthly alternating prednisolone plus cyclophosphamide (A), cyclosporine plus prednisolone (B) and rituximab alone (C) in a retrospective design.

Therapy	"Modified Ponticelli"	"Modified Cattran"	"Rituximab only"	"Rescue regimen"
Patients [n]	18	23	8	10
Male [n]	12	16	6	10
Female [n]	6	7	2	0
Age [years]	60 ± 14	59 ± 16	45 ± 8	51 ± 13
Stage of MGN	II	II	III	III
Previous therapy [n]				
• „modified Ponticelli"		15	8	10
• „modified Cattran"	4		8	10
• "Rituximab only"	0	0		0
UPC ratio at the beginning of regimen [mg/g Crea]	7,600 ± 4,631	7,925 ± 2,557	7,075 ± 3,933	17,430 ± 7,355
Serum creatinine [µmol/l] at the beginning of regimen	138 ± 70	117 ± 17	202 ± 97	187 ± 79
Anti-PLA_2R-antibody level	1:10 - 1:100	1:10 -1:100	1:100 -1:1.000	neg. -1:1,000
Patients in partial remission [%]	62	58	87.5	90
Mean time to partial remission ± SEM [months]	7.4 [± 1.4, range 1-20]	6.4 [± 1.2, range 1-20]	4.25 [± 1.2, range 1-10]	2.1 [± 0.5, range 0.6-8]
UPC ratio at the end of regimen [mg/g Crea]	4,970 ± 2,900 [all] 2,100 ± 673 [PR]	5,100 ± 2,760 [all] 2,458 ± 516 [PR]	3,800 ± 2,173 [all] 1,872 ± 516 [PR]	4,329 ± 2,490 [all] 1,158 ± 876 [PR]

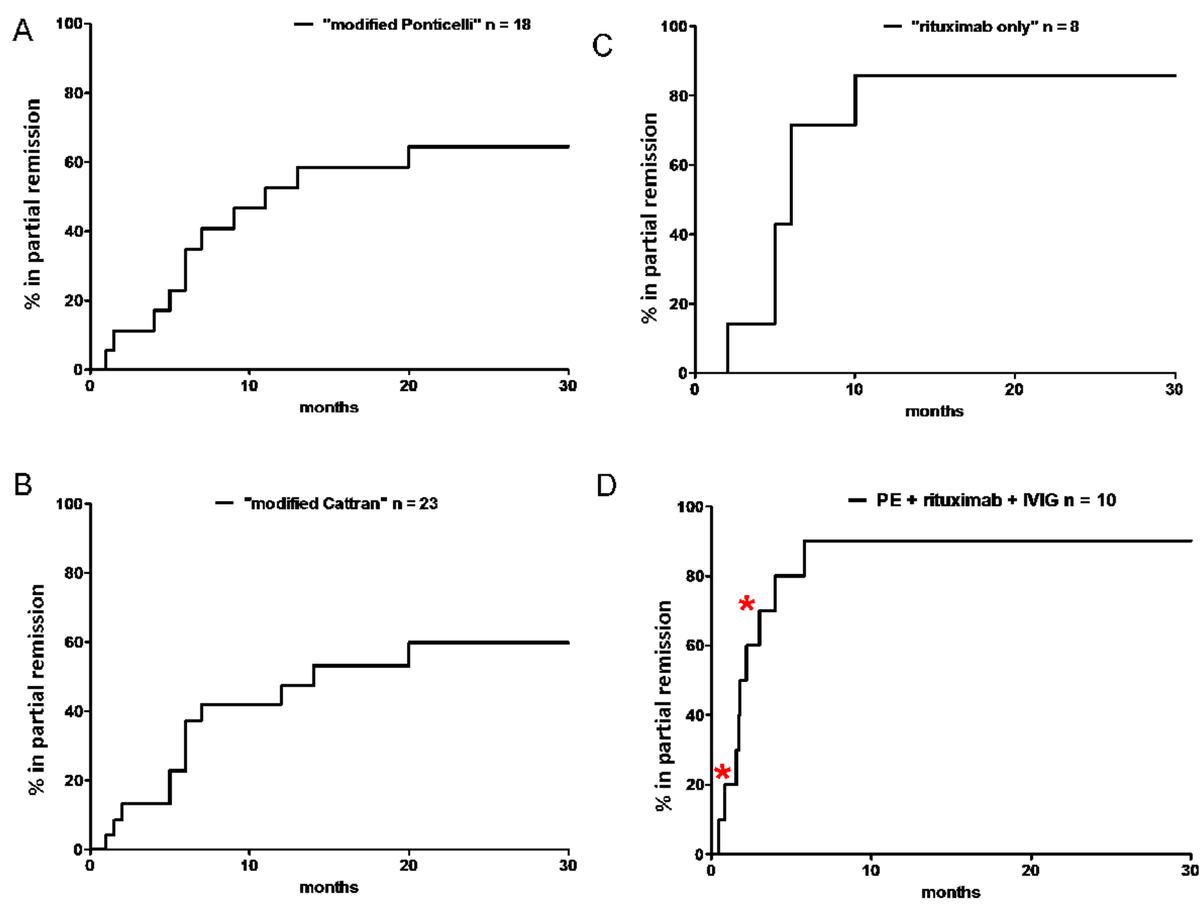






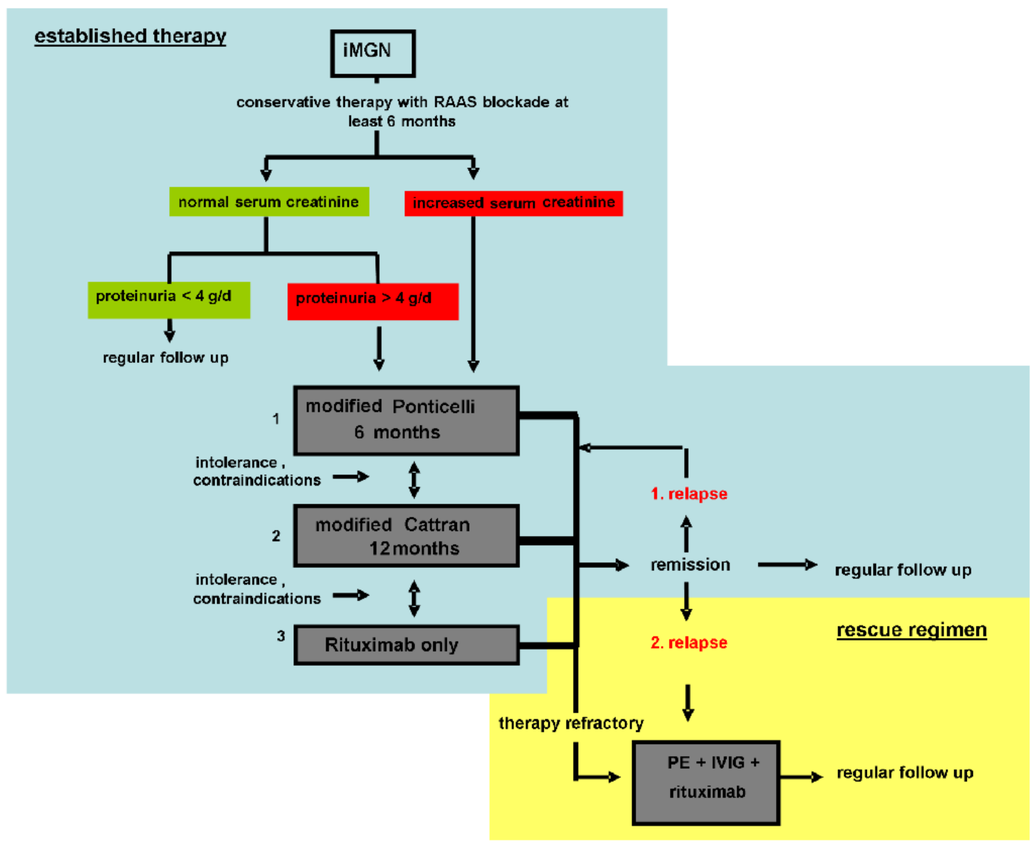


Results



Conclusion

Our rescue regimen achieved partial remission in 90% of high risk patients with iMGN. Mean time to partial remission was 2.1 months. Furthermore two anti-PLA2R-negative patients (red stars in D) also reached partial remission after one month and four months with this protocol. Therefore we suggest the following treatment strategy for iMGN:



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