

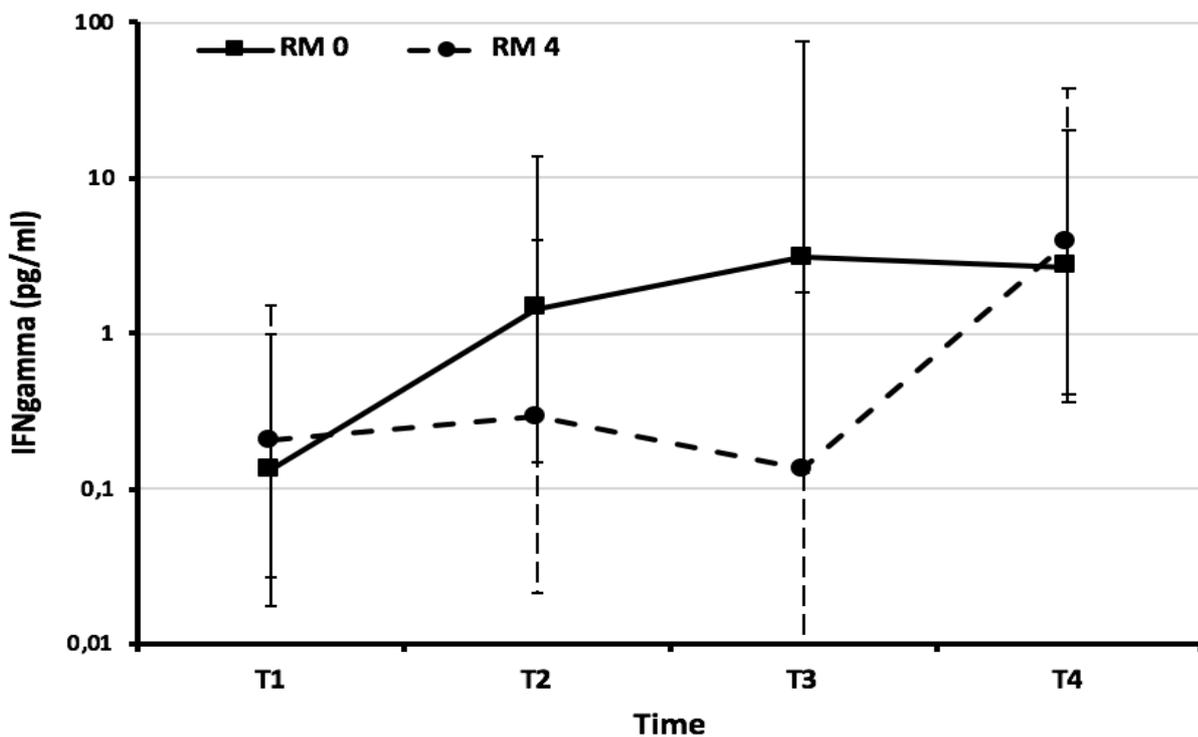
Supplemental file 1.

IFNgamma: Estimated mean values from a mixed linear regression model

Time	RM 0			RM 4			p value
	n	mean	95%CI	n	mean	95%CI	
T1	5	0,132	0,018 0,993	5	0,202	0,027 1,522	0,77
T2	4	1,430	0,150 13,659	3	0,290	0,021 3,931	0,37
T3	2	3,092	0,127 75,221	3	0,134	0,010 1,813	0,14
T4	5	2,686	0,357 20,220	4	3,909	0,409 37,338	0,81

p=0.48

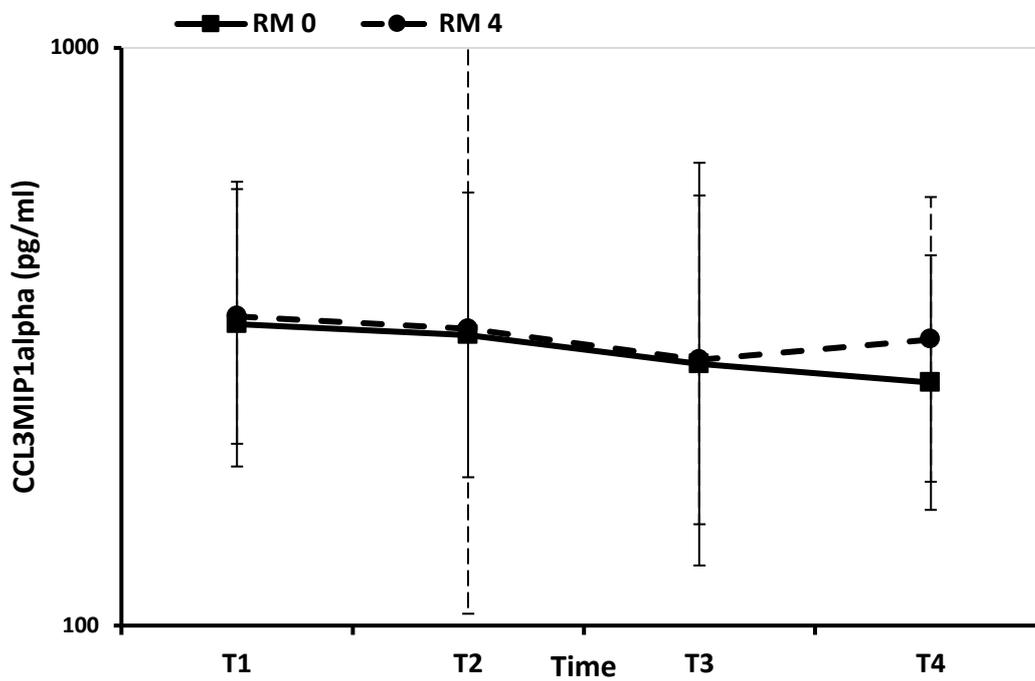
IFN gamma levels at time point T1 are similar in the two groups of patients. Then both grow, minus those of the group with normal MRI. The group of patients with pathological brain MRI, after a decrease at T3, at the cessation of therapeutic hypothermia reaches values similar to those of group 0 at T4.



Supplemental file 2. CCL3MIP1alpha: Estimated mean values from a mixed linear regression

Time	RM 0			RM 4			p value
	n	mean	95%CI	n	mean	95%CI	
T1	4	333	189 587	5	343	206 570	0,94
T2	4	319	181 562	1	326	105 1015	0,97
T3	2	284	127 633	3	288	150 555	0,97
T4	5	263	159 438	4	313	177 552	0,67

p=0.64



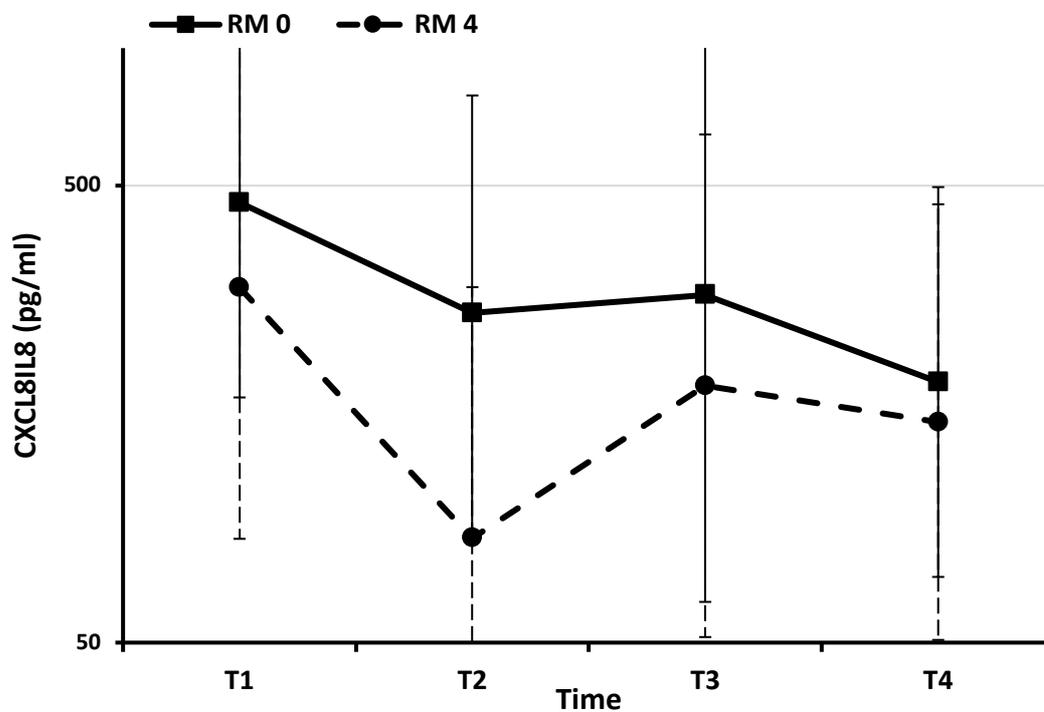
Concerning CCL3MIP1 alpha, we did find any difference between the two groups of neonates at any time.

Supplemental file 3

CXCL8IL8: Estimated mean values from a mixed linear regression model

Time	RM 0			RM 4			p value
	n	mean	95%CI	n	mean	95%CI	
T1	5	459	172 1226	3	299	84 1062	0,60
T2	4	263	88 788	3	85	24 300	0,18
T3	2	288	61 1355	3	182	51 647	0,65
T4	5	186	70 496	4	152	51 455	0,79

p=0.31



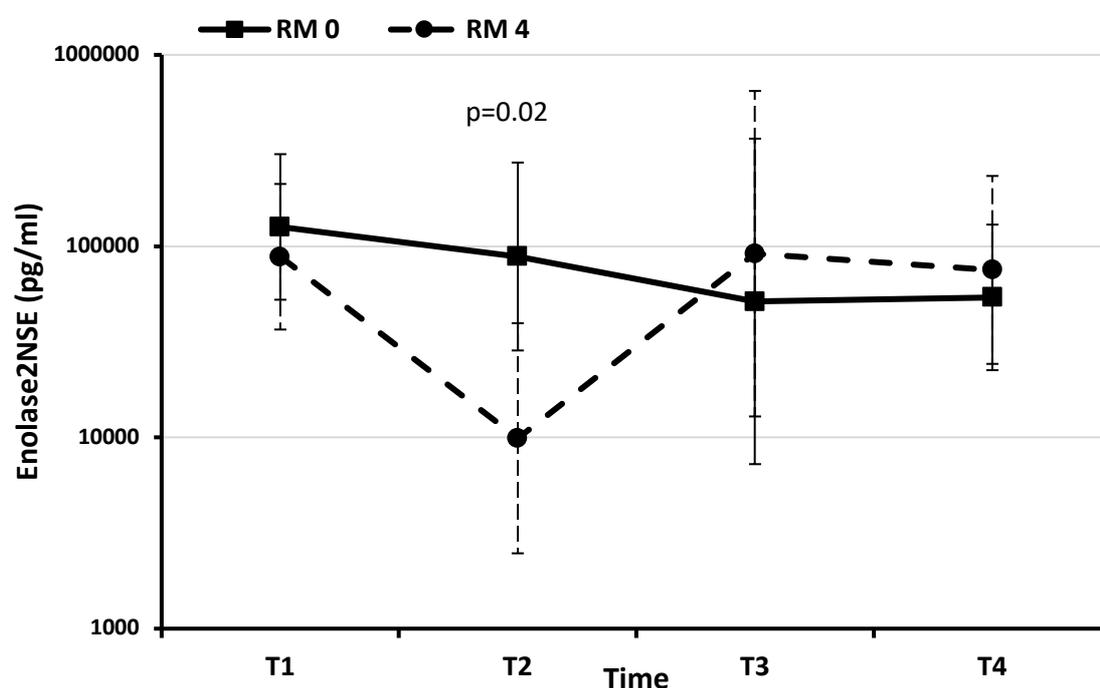
Concerning CCL8IL-8, Group 0 starts and maintains, through the observation period, higher despite not significant values (more marked at time T2) than group 4.

Supplemental file 4

Enolase2NSE: Estimated mean values from a mixed linear regression model

Time	RM 0			RM 4			p value
	n	mean	95%CI	n	mean	95%CI	
T1	5	125978	52454 302559	5	87997	36640 211339	0,57
T2	3	88252	28476 273504	2	9899	2477 39560	0,02
T3	1	51404	7247 364631	1	91278	12868 647465	0,68
T4	5	53957	22466 129589	3	75097	24232 232738	0,65

p=0.43



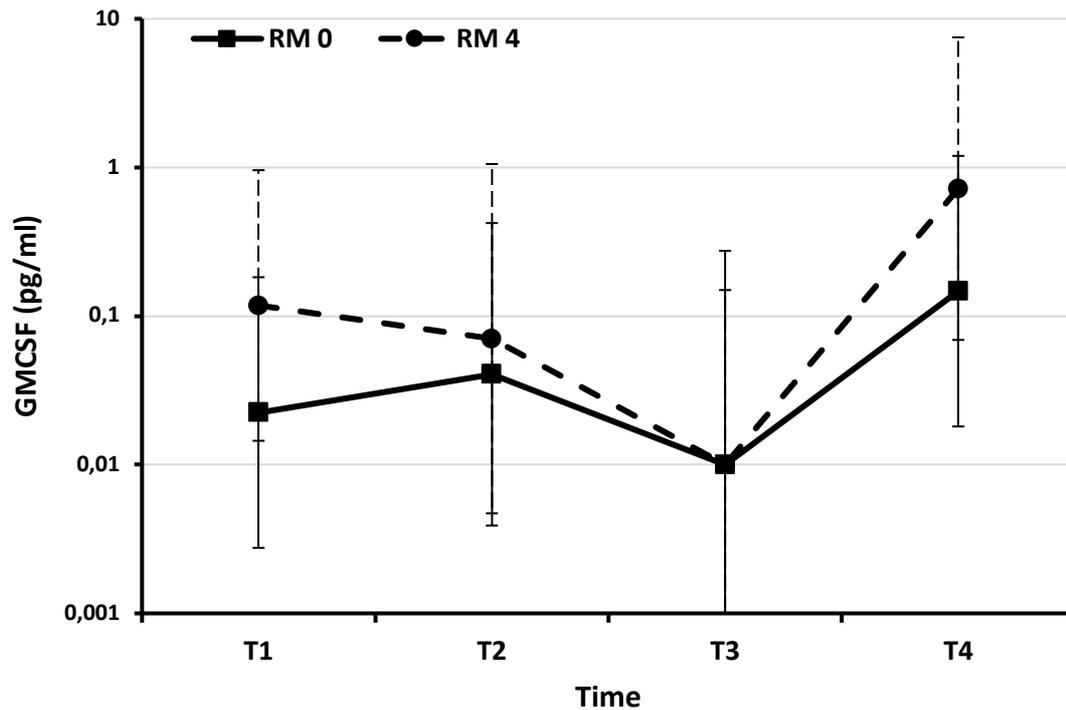
Concerning ENOLASE 2NSE, values are fairly superimposable even if at time T2, during TH the group 4 has a significantly lower value than group 0, that show an upward trend during and after rewarming.

Supplemental file 5

GMCSF: Estimated mean values from a mixed linear regression model

Time	RM 0			RM 4			p value
	n	mean	95%CI	n	mean	95%CI	
T1	5	0,022	0,003 0,183	5	0,118	0,014 0,959	0,27
T2	4	0,041	0,004 0,423	3	0,070	0,005 1,055	0,76
T3	2	0,010	0,000 0,275	3	0,010	0,001 0,150	1,00
T4	5	0,147	0,018 1,197	4	0,720	0,069 7,504	0,32

p=0.31



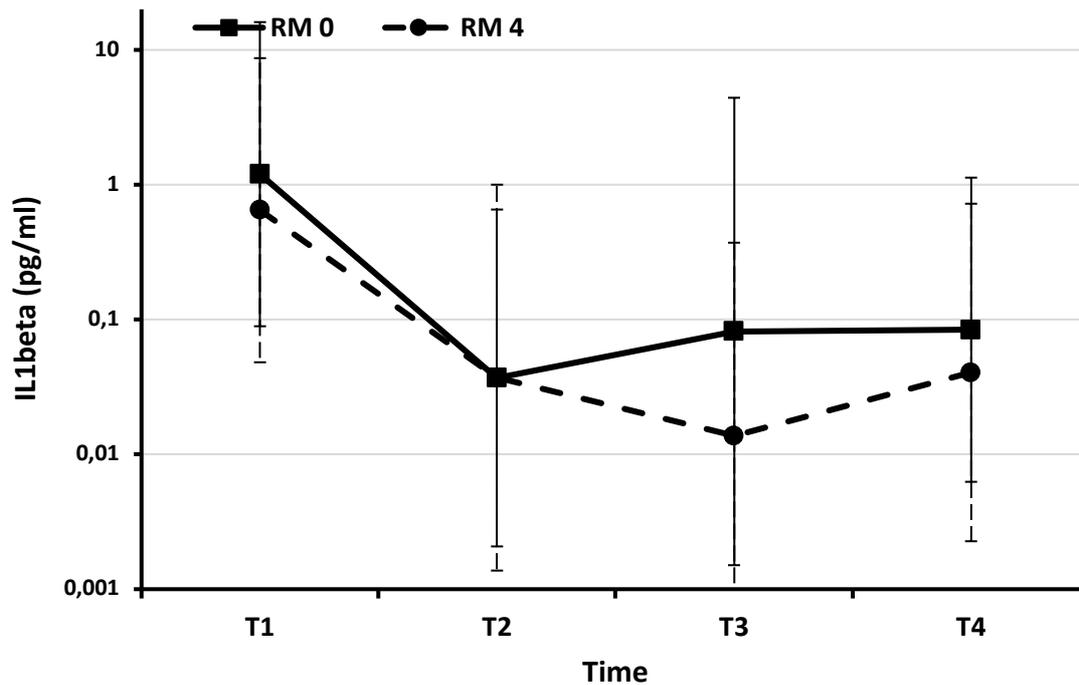
Concerning GMCSF we found no difference between the two groups at any time, although the values of group 4 appear to be slightly higher (at T1 and T4) than those of group 0.

Supplemental file 6

IL1beta: Estimated mean values from a mixed linear regression model

Time	RM 0				RM 4				p value
	n	mean	95%CI		n	mean	95%CI		
T1	5	1,198	0,089	16,080	5	0,647	0,048	8,689	0,74
T2	4	0,037	0,002	0,655	3	0,037	0,001	1,000	1,00
T3	2	0,082	0,002	4,419	3	0,014	0,001	0,372	0,50
T4	5	0,084	0,006	1,128	4	0,040	0,002	0,723	0,71

p=0.55



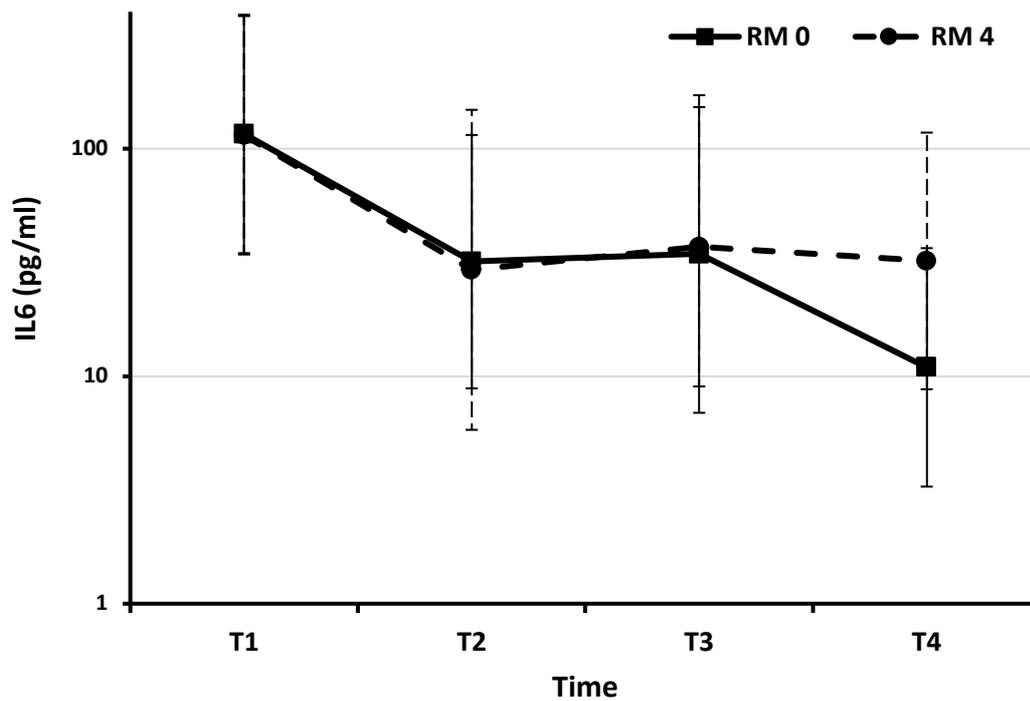
Concerning IL1-beta we found no difference between the two groups at any time, although the value of group 0 seems to be slightly higher at time T3.

Supplemental file 7

IL6: Estimated mean values from a mixed linear regression model

Time	RM 0			RM 4			p value
	n	mean	95%CI	n	mean	95%CI	
T1	5	116,14	34,75 388,19	5	114,55	34,27 382,89	0,99
T2	4	31,88	8,84 114,91	2	29,35	5,81 148,21	0,94
T3	2	34,44	6,90 171,83	3	37,06	9,01 152,36	0,95
T4	5	10,93	3,27 36,54	4	32,12	8,76 117,68	0,23

p=0.56



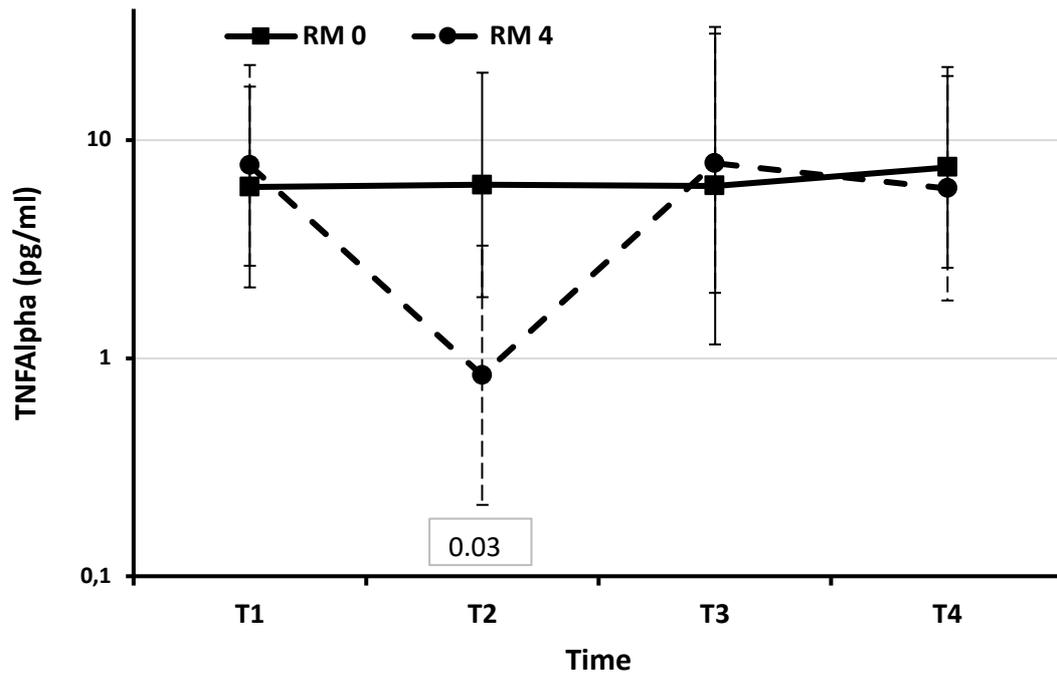
Concerning IL-6 we found no difference between the two groups at any time; at time T4 neonates with MRI4 has value lightly higher than the others.

Supplemental file 8

TNF-Alpha: Estimated mean values from a mixed linear regression model

Time	RM 0			RM 4			p value
	n	mean	95%CI	n	mean	95%CI	
T1	5	6,10	2,11 17,60	5	7,66	2,65 22,11	0,77
T2	4	6,23	1,90 20,40	3	0,84	0,21 3,28	0,03
T3	2	6,18	1,16 33,06	3	7,84	1,99 30,80	0,83
T4	5	7,50	2,60 21,65	4	6,02	1,84 19,69	0,79

p=0.46

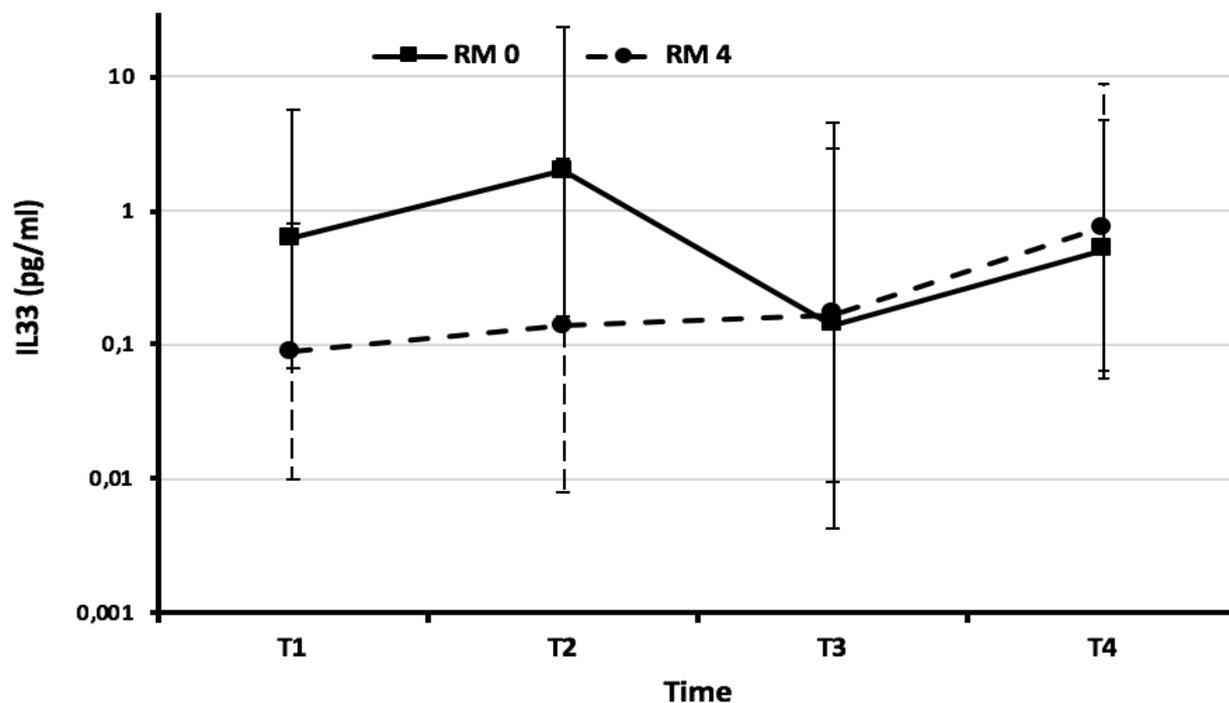


Concerning TNF Alpha, values remain almost constant in the group MRI 0 over the whole period whilst in the group MRI 4 we found a decrease at the time point T2. The values of the two groups are significantly different at time point T2, and then they return practically to overlap.

Supplemental file 9

IL33: Estimated mean values from a mixed linear regression model

Time	RM 0				RM 4				p value
	n	mean	95%CI		n	mean	95%CI		
T1	5	0,62	0,07	5,66	5	0,09	0,01	0,81	0,22
T2	4	1,96	0,17	23,17	3	0,14	0,01	2,39	0,17
T3	2	0,14	0,00	4,58	3	0,17	0,01	2,91	0,94
T4	5	0,51	0,06	4,65	4	0,74	0,06	8,75	0,83

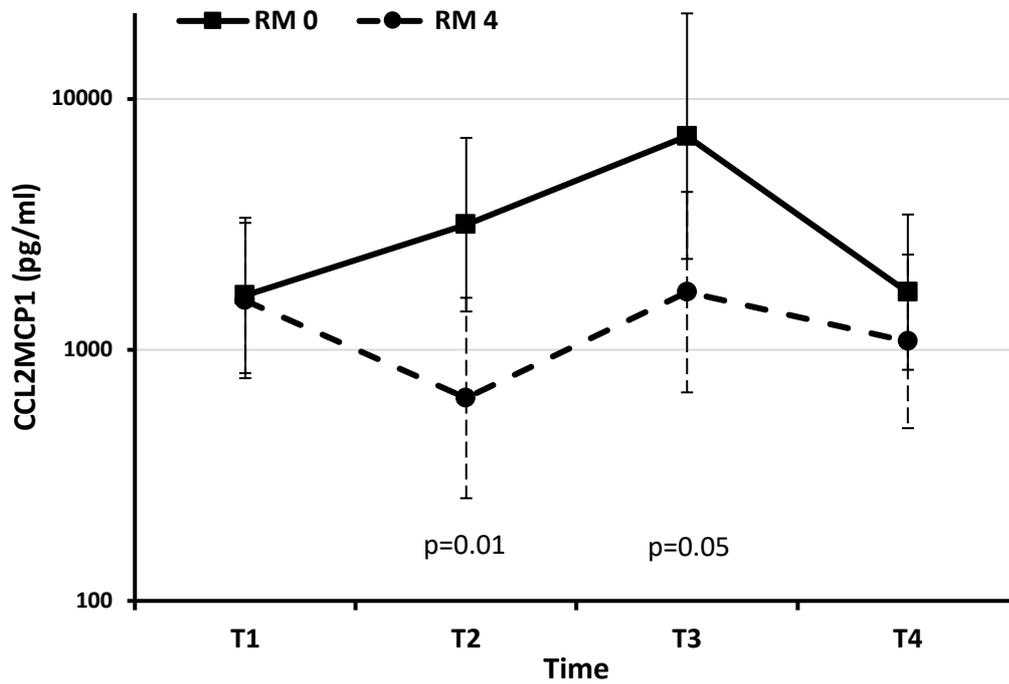


The values of IL-33 in the neonates with normal MRI (Barkovich group 0) are higher than those of the neonates with pathological MRI (Barkovich group 4) at T1 and T2, without statistical significance. Then, at T3 and T4 IL-33 plasma levels overlapped with those of group 4.

Supplemental file 10

CCL2/MCP1: Estimated mean values from a mixed linear regression model

Time	RM 0			RM 4			p value
	n	mean	95%CI	n	mean	95%CI	
T1	5	1650	809 3364	5	1574	772 3210	0,93
T2	4	3158	1424 7004	3	643	256 1614	0,01
T3	2	7113	2305 21943	3	1700	677 4264	0,05
T4	5	1700	834 3466	4	1082	488 2400	0,41



For CCL2MCP1, at time T1, the values are similar in the two group, subsequently group 0 has significantly higher values ($p=0.01$ and $P=0.05$, at T2 and T3, respectively) and then, at time T4, it returns to almost the same value as group 4.

Supplemental table 1

Molecule	Patients with normal MRI (N=5)	Patients with pathological MRI (N=5)	p
CCL2-MCP1	3297,7±2718,76	1510,64±697,75	0,19
CCL3-MIP1 alpha	319,66±167,94	276,56±51,17	0,59
CXCL8-IL8	289,57±94,04	215,82±69,38	0,19
ENOLASE 2	101991,48±55353,97	95240±39932,66	0,83
GFAP	1,04±2,32	6,82±6,41	0,09
GMCSF	0,4±0,5	1,07±0,7	0,12
IFN-gamma	2,75±1,43	2,19±1,47	0,56
IL-1	2,19±1,89	3,76±5,71	0,57
IL-6	85,11±106,33	104,85±121,41	0,8
IL-10	35,23±42,95	107,62±200,77	0,45
IL-12	0	0	0
IL-18	291,31±96,52	215,82±69,38	0,19
IL-33	1,25±0,69	1,28±1,44	0,97
TNF-alpha	7,96±3,14	6,84±1,3	0,48