PLASMABLAST RESPONSE AFTER PNEUMOCOCCAL REVACCINATION IN PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA

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Background and aim:

Between 2013-2016, 126 treatment naïve chronic lymphocytic leukemia (CLL) patients (median age, 69 years; range, 46–87 years) were vaccinated in a randomized trial with PCV13 (n=63) or PPSV23 (n=63) at eight hematological clinics in Sweden. Antibody response, measured with ELISA and OPA, was superior for PCV13. In the present study, we analyze the remaining immune response 4-6 years after primary vaccination in 77 CLL patients and 40 immunocompetent controls, and we analyze the response after revaccination with two different vaccination regimes (PCV13/PPSV23 or PCV13/PCV13). Immune cells, including plasmablasts, were analyzed before and after vaccination using flow cytometry. Analyzes of serotype specific antibodies (ELISA) and functionality (OPA) before and after eight weeks, 16 weeks and 12 months from the first revaccination is performed.

Methods:

Of 77 CLL patients included in the follow-up study 3-6 years after primary vaccination, 16 patients were included 2019-2020 in this study of plasmablast response after revaccination. If previously vaccinated with PCV13 revaccination was performed with PCV13 and after 8 weeks PPSV23. The group previously vaccinated with PPSV23 received two doses of PCV13. Immunophenotyping of peripheral plasmablasts (CD19+/CD38++/CD27++/CD138-/IgD-/IgM-) and plasma cells (CD19+/CD38++/ CD27++/ CD138+/ IgD-/IgM-) was performed before and seven days after revaccination using flow cytometry. Due to the Covid-19 pandemic, the ongoing recruitment of immunocompetent controls is delayed.

Patient, no	Gender, M/F	Age	Time since diagnose, months	Total IgG levels, g/L (ref 6,1-14,9)	IgG2 subclass levels, g/l (ref 1,69-7,86)	Lymphocyte count, 10*9/L ref(1,1-4,8)	Previous treatment, Y/N	Ongoing treatment, Y/N	Previous - vaccination	Time since first vaccination, months	Revaccination strategy	CD19+/CD38++/CD27++ /IgD-/IGM- (CD138+/CD138-) before first revaccination (%)	CD19+/CD38++/CD27++ /IgD-/IGM- (CD138+/CD138-) after first revaccination (%)	CD19+/CD38++/CD27++ /IgD-/IGM- (CD138+/CD138-) before second revaccination (%)	CD19+/CD38++/CD27++ /IgD-/IGM- (CD138+/CD138-) after second revaccination (%)
1	F	75	67	10,4	2,31	6,2	N	N	PCV13	68	PCV13/PPSV23	0 (0/0)	0,1 (40/60)	0,02 (44/56)	0,06 (47/53)
2	F	81	132	7,2	*1,53*	4,1	N	N	PCV13	67	PCV13/PPSV23	0 (0/0)	0,03 (76/24)	0 (0/0)	0,01 (52/48)
3	F	66	112	7,3	1,8	9,6	N	N	PCV13	67	PCV13/PPSV23	0 (0/0)	0,04 (63/37)	0 (0/0)	0,01 (59/41)
4	F	88	114	8,9	2,15	43,2	N	N	PCV13	67	PCV13/PPSV23	0 (0/0)	0 (0/0)	0,01 (18/82)	0 (0/0)
5	F	72	64	*5,9*	*1,47*	17,9	N	N	PCV13	62	PCV13/PPSV23	0 (0/0)	0 (0/0)	0 (0/0)	0 (0/0)
6	M	61	60	8,2	*1,25*	12,8	N	N	PCV13	54	PCV13/PPSV23	0 (0/0)	0 (0/0)	0 (0/0)	0 (0/0)
7	M	68	55	10	2,86	73,8	N	N	PPSV23	54	PCV13/PCV13	0 (0/0)	0,01 (90/10)	0 (0/0)	0,01 (84/16)
8	M	69	164	6,6	*1,63*	14	N	N	PPSV23	67	PCV13/PCV13	0 (0/0)	0 (0/0)	0 (0/0)	0,01 (87/13)
9	F	69	53	11,5	3,14	7,6	N	N	PPSV23	54	PCV13/PCV13	0 (0/0)	0 (0/0)	0,01 (64/36)	0,03 (54/46)
10	M	75	58	9	2,86	8,5	N	N	PPSV23	54	PCV13/PCV13	0 (0/0)	0 (0/0)	0,09 (28/72)	0,02 (52/48)
11	F	61	56	*6*	*1,08*	0,7	Y, FCR 2018	N	PPSV23	54	PCV13/PCV13	0 (0/0)	0 (0/0)	0,96 (16/84)	0,68 (27/73)
12	F	68	226	10,5	*0,99*	0,2	Y, BR 2019	N	PPSV23	67	PCV13/PCV13	0 (0/0)	0 (0/0)	0 (0/0)	0 (0/0)
13	M	79	131	*2,9*	*0,27*	18,8	Y, BR 2015	Y, Ibrutinib	PCV13	67	PCV13/PPSV23	0 (0/0)	0 (0/0)	0 (0/0)	0 (0/0)
14	M	75	136	*3,6*	*1,25*	15,3	Y, BR 2016	Y, Ibrutinib	PPSV23	67	PCV13/PCV13	0 (0/0)	0 (0/0)	0 (0/0)	0 (0/0)

FCR - Fludarabin/Cyklofosfamid/Rituximab
BR - Bendamustin/Rituximab

Results:

Of 16 included patients, 14 patients (88%) were sampled at all visits. Preliminary results show that none of the included patients had measurable plasmablasts at baseline. Plasmablasts were detectable in 4/14 patients seven days after first revaccination compared to baseline, previously vaccinated with PCV13 (n=3) and PPSV23 (n=1). After the second revaccination, additionally four patients had detectable plasmablasts, all of whom initially received PPSV23 and thus received double dose of PCV13. None of the patients with ongoing or earlier treatment had detectable plasmablast increase after vaccination. The interpretation of the results of patient 11 is difficult because of very low lymphocyte count (<8%) in the samples. Patients with total IgG or IgG2 levels below reference interval (n=9) only had detectable plasmablasts if previously vaccinated with PCV13 or given double dose of PCV13.

Conclusion:

Preliminary results indicate superior response after PCV13 revaccination in CLL patients if previously vaccinated with PCV13 compared to patients previously vaccinated with PPSV23. Repeated doses of PCV 13 seems to be beneficial. Further analyzes of antibody response with ELISA and OPA and comparison with an immunocompetent control group will be conducted.

Ref:
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