1154

# Impaired long-term antibody persistence after primary immunization with pneumococcal vaccines in patients with chronic lymphocytic leukemia compared to immunocompetent controls

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## Introduction

- Patients with Chronic Lymphocytic Leukemia (CLL) have increased risk for invasive pneumococcal disease (IPD).
- Impaired immune response to pneumococcal vaccination in CLL patients calls for improved vaccination strategies.
- A previous randomized study of treatment-naïve CLL patients (n=126) showed superior immune response after vaccination with T-cell dependent conjugated pneumococcal vaccine (PCV13) compared to non-T cell dependent polysaccharide vaccine (PPSV23).
- Cut-off levels commonly used for defining serological protection rates is serotype-specific IgG levels ≥0.35 µg/mL.
- More stringent cut-offs are sometimes used for evaluation of immune respons, in this study set to ≥1.0 µg/mL.
- Follow-up studies of long-term pneumococcal antibody persistence and revaccination strategies in CLL patients after PCV13 and PPSV23 are lacking.

## Objective

To assess the long-term antibody persistence, 3-6 years after primary immunization with PCV13 or PPSV23 in CLL patients and healthy controls.

## Methods

- CLL patients (n=74), primary immunized in our previous randomized study with PCV13 (group A) and PPSV23 (group B), were included in a revaccination study and assessed for long term antibody persistence.
- Immunocompetent controls (n=31) immunized with PCV13 (group C) or PPSV23 (group D) were recruited.
- A bead-based multiplex immunoassay was used for quantitation of IgG (µg/mL) against PCV13-related serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F).
- Rates of serotype-specific IgG levels ≥0.35 µg/mL for >50% (7-13/13) of the serotypes were calculated and used to evaluate persistent antibody levels.
- In an additional, more stringent cut-off analysis, rates ≥1.0 µg/mL for >50% (7-13/13) of the serotypes were evaluated.

| | CLL patients (group A+B) (n=74) | | Controls (group C+D) (n=31) | |
|---|---|---|---|---|
| **Primary immunization, n (%)** | **PCV13** 38 (51) | **PPSV23** 36 (49) | **PCV13** 9 (29) | **PPSV23** 22 (71) |
| **Age, median (range)** | 73 (54-90) | 77 (51-93) | 69 (54-81) | 76 (70-84) |
| **Female gender, n (%)** | 21 (55) | 17 (45) | 5 (56) | 16 (73) |
| **Time since immunization, median months (range)** | 65.5 (54-75) | 65 (52-74) | 61 (37-105) | 60.5 (46-87) |
| **Time from CLL diagnoses, median months (range)** | 90.5 (56-261) | 85 (53-305) | NA | NA |
| **ALC, median x 109/L (range)** | 13.1 (0.3-205) | 12.8 (0.5-189) | 1.6 (1.1-2.9) | 1.6 (1.1-2.4) |
| **Total IgG, median g/L (range)** | 8.5 (2.9-21.1) | 8.4 (3.6-8.2) | 11.5 (4.4-17.2) | 11 (8.5-18.6) |
| **Hypogammaglobulinema, n (%)** | 9 (24) | 7 (19) | 0 (0) | 0 (0) |
| **IgG levels ≥0.35 µg/mL, n (%)** | 16 (44) | 13 (34) | 8 (89) | 18 (82) |
| **IgG levels ≥1.0 µg/mL, n (%)** | 7 (19) | 3 (8) | 4 (44) | 6 (27) |

## Results

- After a median time of 5 years since primary immunization, the rate of persistent antibody levels in CLL patients were lower compared to controls (group A+B vs C+D) at ≥0.35 µg/mL (29/74, 39% vs 26/31, 84%; p<0.001).
- A significant difference was also present between group B and D at ≥0.35 µg/mL, 13/36, 34% vs 18/22, 82%; p<0.01).
- No significant difference was seen between CLL patients and controls using cut-off ≥1.0 µg/mL (10/74,14% vs 10/31, 32%; ns).
- Rates of patients with persistent antibody levels after primary immunization with PCV13 or PPSV23 did not differ significantly within the groups.
- Hypogammaglobulinemia was seen in 19/74 (26%) of CLL patients.
- Fifty-eight patients (78%) were still treatment-naïve, 9 (12%) were off treatment in remission and 6 (8%) had ongoing treatment with BTK inhibitors or anti-CD20 antibodies.

## Conclusions

- CLL patients have impaired long-term antibody persistence 5 years after primary immunization with pneumococcal vaccines compared to immunocompetent controls.
- Whether CLL patients will benefit from pneumococcal revaccinations is currently being analyzed.

**Reference:**

Svensson T, Kattstrom M, et.al Pneumococcal conjugate vaccine triggers a better immune response than pneumococcal polysaccharide vaccine in patients with chronic lymphocytic leukemia A randomized study by the Swedish CLL group. Vaccine. 2018;36(25):3701-7.

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