Challenging the dogma's: quantitative analysis of mRNA-1273 vaccine (Moderna) response in a wide spectrum of immunodeficient hematology patients

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Abstract

Background:

Patients with hematologic conditions have a high mortality rate when infected with COVID-19. Protection of this group from severe COVID-19 infections is therefore important. The prioritization of COVID-19 vaccination in high-risk patients in the Netherlands allowed us to prospectively investigate mRNA-1273 vaccine immunogenicity in these patients. Based on previous (non-COVID-19) vaccination studies among hematology patients, we hypothesized that a significant group of patients may acquire sufficient protection following vaccination, despite disease and therapy related immunodeficiencies.

Methods:

We prospectively included 723 hematology patients, distributed over 17 cohorts with each cohort representing severely immunocompromised patients due to their underlying condition and/or current or recent treatment. Serum IgG antibodies to spike subunit 1 (S1), receptor binding protein (RBD) and nucleocapsid (N) antigens were quantified using a bead-based multiplex immune assay (MIA) prior to the 1st vaccination, 4 weeks after the 1st and 4 weeks after the 2nd vaccination. Clinical parameters including medication schedules, immunoglobulin levels and absolute B-, T-, and NK-cell numbers were collected at each time point.

Results:

Despite their severely immunocompromised status, 55% of previously COVID-19 uninfected patients (349/634) obtained S1-specific antibody serum concentrations ≥ 300 BAU/ml after completion of the vaccination schedule. Antibody binding concentration correlated significantly with antibody neutralization. At least 90% of the following patient groups obtained S1 antibody titers ≥ 300 BAU/ml: patients with sickle cell disease (despite functional asplenia and use of hydroxyurea), patients with chronic myeloid leukemia (CML) treated with tyrosine kinase inhibitor therapy, and patients with acute myeloid leukemia (AML) or high-risk myelodysplastic syndrome (MDS) during and shortly after high-dose cytarabine-containing remission-induction or consolidation therapy. Around 70% of patients with chronic GvHD, with multiple myeloma on second- or third line (including daratumumab-containing) therapy, or with untreated chronic lymphocytic leukemia (CLL) obtained S1 antibody concentrations ≥ 300 BAU/ml. In contrast, fewer than 30% of B-non Hodgkin lymphoma (B-NHL) patients during or early after rituximab containing therapy, of CLL patients on ibrutinib, and of patients who received CAR T cell therapy obtained S1 antibodies ≥ 300 BAU/ml. The minimal time-interval to reach S1 antibody concentrations ≥ 300 BAU/ml was 2 months after autologous HCT for multiple myeloma, 4-6 months after allogeneic HCT, and 8 months after autologous HCT or rituximab-chemotherapy for B-NHL. The use of more than two immunosuppressants impeded an adequate antibody response.

Conclusion:

Our data demonstrate that more than half of severely immunocompromised hematology patients obtain adequate SARS-CoV-2 antibody titers. Even though full antibody-mediated protection cannot be guaranteed for all, hematology patients on chemotherapy, shortly after HCT, or with chronic GvHD should not be precluded from vaccination. The increase in antibody concentrations that we observed after each vaccination suggests that antibody responses can be further enhanced with one or more extra mRNA-1273 vaccinations.