(PS2242) CAN QUANTIFERON CMV® PREDICT THE NEED FOR EXTENDED LETERMOVIR PROPHYLAXIS?

Topic: 23. Stem cell transplantation - Clinical

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Background

QuantiFERON CMV®, an assay evaluating CMV-specific cell-mediated immunity, has been demonstrated to predict the risk of CMV infection following allogeneic stem cell transplantation in various clinical settings. Letermovir prophylaxis is routinely employed to prevent early post-transplant CMV infection and has recently received approval for extended use for up to 200 days after transplant in patients at high risk for CMV infection.

Aims

To assess the clinical utility of QuantiFERON CMV® in identifying patients at high risk for CMV infection who may benefit from extended letermovir prophylaxis.

Methods

We conducted a retrospective analysis of CMV IgG-positive patients undergoing allogeneic stem cell transplantation who received in vivo T-cell depletion with anti-T-lymphocyte globulin (ATLG) or post-transplant cyclophosphamide (PTCy), along with letermovir prophylaxis for 100 days, prior to the approval of extended prophylaxis. The diagnostic utility of QuantiFERON®-CMV, measured on day 90 post-transplant, was evaluated for predicting subsequent clinically significant CMV infections (csCMVi), defined as CMV reactivations detected by quantitative PCR requiring initiation of anti-CMV therapy. Sensitivity, specificity, positive predictive value and negative predictive value of the test were calculated.

Results

A total of 43 patients were eligible for the analysis, including three patients previously experiencing breakthrough CMV reactivations during letermovir prophylaxis. The majority of patients received ATLG compared to PTCy (37 and 6 patients, respectively), alongside graft-versus-host disease prophylaxis with cyclosporine A and antimetabolite (methotrexate with ATG or mycophenolate mofetil with PTCy). Most patients were transplanted for acute myeloid leukemia (20/43, 47%), were male (23/43, 53%), received myeloablative conditioning (29/43, 67%), had a matched-unrelated donor (24/43, 56%), and had a CMV seropositive donor (29/43, 67%). The mean patient and donor ages were 43 (range 18-61) and 36 (range 20-63), respectively. A total of 14 patients experienced csCMVi (33%), with only two having a prior positive QuantiFERON CMV® result. Therefore, the positive predictive value of QuantiFERON CMV® in protecting from subsequent CMV reactivation was 90% (95% CI 67-98%), while the negative predictive value was 50% (95% CI 29-70%). The assay demonstrated a specificity of 85% (95% CI 57%-98%) and a sensitivity of 58% (95% CI 39-76%). Among the two patients with positive test who developed CMV reactivation, both were receiving corticosteroids in addition to cyclosporine A, with one of them having a prior CMV infection during letermovir prophylaxis (when preemtive treatment was initiated and letermovir interrupted). Among twelve patients with a negative/indeterminate test and no subsequent CMV reactivation, eight had available CMV serological results prior to any transfusion. Of these, six were initially seronegative, highlighting the importance of serological testing at diagnosis for predicting future CMV reactivations.

Summary/Conclusion

QuantiFERON CMV® has a high positive predictive value for identifying patients with a protective immunity against CMV and can be used as an effective and useful tool in delineating high-risk patients in need of extended letermovir prophylaxis. Accurate determination of true CMV serostatus at diagnosis is essential to define patients at genuine risk of CMV reactivation.