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Background. Impaired cytomegalovirus (CMV)-specific cell-mediated immunity (CMV-CMI) is a major cause of uncontrolled CMV reactivation and associated complications in both solid-organ transplantation (SOT) and hematopoietic stem cell transplantation (HSCT). Reliably assessing CMV-CMI is desirable to individually adjust antiviral and immunosuppressive therapy. We demonstrate here the suitability of a novel IFN-γ ELISpot assay (T-Track® CMV), based on the stimulation of PBMC with pp65 and IE-1 CMV proteins, to monitor CMV-CMI in SOT and HSCT patients.

Methods. Two independent prospective, longitudinal, observational, multicenter studies were conducted: in 86 intermediate-risk (D−/R+, D+/R+) renal transplant recipients (completed), and in 175 intermediate- or high-risk (D+/R+, D+/R−, D−/R+) HSCT recipients (ongoing). In both studies, patients underwent pre-emptive antiviral therapy. CMV-CMI, CMV load and clinical complications were monitored over ~6 months post-transplantation.

Results. In the kidney transplantation setting, 95% and 88–92% of IFN-γ ELISpot test results were positive pre- and post-transplantation, respectively. CMV-specific response was reduced following immunosuppressive therapy and increased in patients with graft rejection, indicating the ability of the assay to monitor the patients' immunosuppressive state. Interestingly, median pp65-specific response was 9-fold higher in patients with self-clearing viral load compared with antivirally-treated patients prior to first detection of CMV (MWU; $P < 0.001$), suggesting that reactivity to pp65 is a potential immunocompetence marker. In HSCT patients, interim data analysis indicates that pp65-specific CMI measured after resolution of a primary CMV reactivation (requiring antiviral treatment) is a fair predictor of occurrence of recurrent CMV reactivation. Out of 71 patients (25 D+/R+, 3 D+/R−, 43 D−/R+) who experienced a primary CMV reactivation, 27 encountered a recurrent CMV reactivation. Interestingly, 39/44 (89%) patients free of recurrent reactivation had a positive pp65-specific test result following primary CMV reactivation.

Conclusion. Altogether, this novel IFN-γ ELISpot assay is a highly sensitive immune-monitoring tool with a potential use for the risk assessment of CMV-related clinical complications after SOT and HSCT.

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1576. Risk of Clinical Tuberculosis (TB) Among Patients with Latent TB Infection (LTBI) Who Undergo Allogeneic Hematopoietic-Cell Transplantation (HCT)

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Background. *Mycobacterium tuberculosis* is a leading cause of morbidity and mortality worldwide. The risk of developing active TB in persons with hematological malignancies is higher than the general population. However, the magnitude and timing of this risk has not been determined in non-endemic settings after HCT. The purpose of this study was to evaluate treatment practices and active TB rates in a cohort of HCT recipients.

Methods. A retrospective cohort study was performed of all adult patients who underwent HCT at Dana-Farber Cancer Institute between January 2010 and January 2015. Baseline characteristics and laboratory parameters were collected. LTBI diagnostic tests included purified protein derivative (PPD) and interferon-gamma release assays (IGRA). Baseline chest radiography, history of BCG vaccination, and previous LTBI therapy were documented. Institutional guidance recommends that LTBI treatment begins upon discharge or by Day +28 after HCT, whichever is first. Patients were followed until April 2018 for development of active TB.

Results. In a cohort of 1,288 HCT recipients, 44 (3.4%) had evidence of LTBI, with 43 positive PPD tests and one positive IGRA. Median age was 55 years (range 19–72); 24/44 (54.5%) were male and 28/44 (63.6%) were non-US-born. Nine (20%) patients were treated for LTBI before HCT. Of the remaining 35 patients, 11 (25%) were treated within 3 months of HCT, three (6.8%) initiated treatment later than 3 months post HCT, and 21 (47.7%) did not receive treatment for reasons including death ($n = 14$, median survival 1.5 years from HCT) and treatment refusal ($n = 4$). Three patients were lost to follow-up. Among patients who initiated treatment, isoniazid ($n = 10$) and levofloxacin ($n = 4$) were used for a median of 145 days (range 7–326). There were no cases of active TB in the whole HCT cohort during the study period, which included a combined 139 person-years of follow-up in 44 patients with LTBI, of which 68 person-years were contributed by untreated individuals.

Conclusion. These data suggest that TB reactivation does not usually occur very early after HCT. LTBI therapy could be deferred in the immediate post-transplant setting and initiated once patients are clinically stable with a lower risk of synergistic hepatotoxicity.

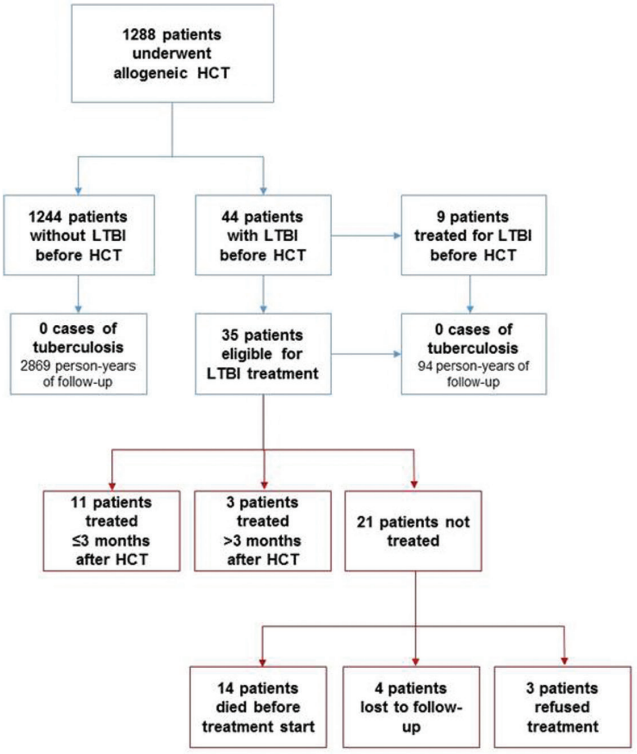

Figure 1. Study Population Outcomes.
Summary of latent tuberculosis infection (LTBI) outcomes of all patients who received allogeneic hematopoietic-cell transplants (HCT) at Dana-Farber Cancer Center from January 2010 to January 2015.

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1577. Evaluation of a Routine Screening Program with Tuberculin Skin Testing on Rates of Detection of Latent Tuberculosis Infection and Prevention of Active Tuberculosis in Patients with Multiple Myeloma at a Canadian Cancer Center

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Background. Due to chemotherapy induced T-cell dysfunction, patients being treated for multiple myeloma (MM) are at high risk for reactivation of LTBI; however, the optimal screening strategy in this patient population has not been well described. The objective of this study was to assess the number of patients treated for LTBI both before and after the introduction of a consistent tuberculosis skin test (TST) screening program for patients with MM at our cancer center.

Methods. We carried out a retrospective observational study of adult patients treated at our cancer hospital for MM with autologous hematopoietic stem cell transplantation and who also had a TST results available from January 1, 2013–December

31, 2014. Baseline demographic characteristics, results of TST and LTBI therapy were collected. This cohort was compared with a pre-intervention cohort of sporadically tested patients from January 1, 2008–December 31, 2009.

Results. During the post-intervention period, 170 patients with MM had a TST. At the time of TST, 113 (66.4%) patients had a lymphocyte count ≥1.0 × 10^9/L. Fourteen patients (8.2%) had positive Results. There were also 16 patients with radiographic evidence of prior granulomatous disease on either CXR or chest CT In these 16 patients, 12 (75%) with positive radiographic findings had negative TST Results. Notably, 7//12 (58.3%) had a lymphocyte count ≤1.0 × 10^9/L at the time of testing. Eleven patients with positive TST results and two with positive radiographic results alone were treated for LTBI. There was one case of active TB diagnosed in a patient with a negative TST. There were no TSTs performed in the pre-intervention cohort and no cases of active TB were documented.

Conclusion. A significant portion of our MM patients may benefit from LTBI therapy. A targeted program combining evaluation of host risk factors, imaging findings and screening tests would optimize LTBI diagnosis and management and may be effective in preventing the development of active TB.

Disclosures. **All authors:** No reported disclosures.

1578. Back to Bactrim–Utilizing Preferred Prophylaxis Strategies in Immunocompromised Hosts Via a Trimethoprim-Sulfamethoxazole Rechallenge Program

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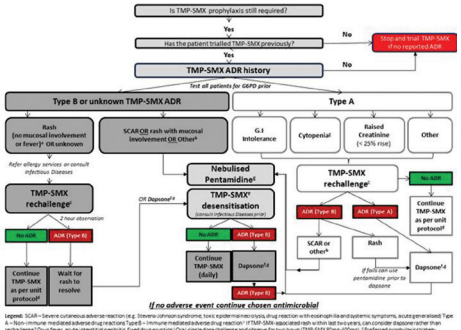
Background. Trimethoprim sulfamethoxazole (TMP-SMX) is the preferred agent for *Pneumocystis jirovecii* pneumonia prophylaxis in immunocompromised hosts (ICH). However, TMP-SMX is frequently avoided due to an adverse drug reaction (ADR) history. We report on a novel multicentre programmatic approach to TMP-SMX ADRs in ICH.

Methods. We reviewed ICH with a reported TMP-SMX ADR referred to the conjoint antibiotic allergy services at Austin Health (Melb, Aus) and Peter MacCallum Cancer Centre (Melb, Aus) between April 2015 and May 2018. ICH were defined as patients with a history of cancer, transplantation, autoimmune condition or prednisolone use > 20 mg day for 1 month. Patients were assessed and managed as per the TMP-SMX ADR protocol (Figure 1).

Results. Eighteen patients were assessed, of which 16 (89%) underwent allergy testing (6;89% patch testing [PT] and/or 9;56% oral rechallenge [OC]) and 2 (11%) successful desensitization. Of those that underwent allergy testing, 10 (63%) were cancer patients, four (25%) solid-organ transplant recipients, one (6%) HIV and one (6%) multiple sclerosis. The median age was 59 (IQR 49.5, 65) and predominate phenotypes were severe cutaneous adverse drug reactions (4; 22%) and maculopapular exanthema (MPE) (11; 61%). Eighty-nine percent (8/9) of OC patients tolerated TMP-SMX challenge. One patient experienced a recurrence of a mild self-resolving localized rash following TMP-SMX OC. Of those seven patients that did not undergo OC, two (29%) were PT positive and five (72%) histories of severe or recent T-cell-mediated allergy. Three of the seven patients who did not undergo OC received and tolerated dapsone.

Conclusion. A novel TMP-SMX ADR protocol was able to identify ICH with severe allergy phenotypes and provide alternative antibiotic sulphonamide therapeutic options, whilst safely rechallenging the majority with low-risk TMP-SMX ADR histories.



Disclosures. **All authors:** No reported disclosures.

1579. Evaluation of MATCH: an Electronic Individual Patient-Focused Management System Aimed at Preventing Cytomegalovirus Disease Following Solid Organ Transplantation

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Background. Cytomegalovirus (CMV) infection is common among solid-organ transplant (SOT) recipients and may cause CMV disease, if not promptly treated. Strategies to prevent CMV disease include chemoprophylaxis and pre-emptive monitoring and treatment of emerging subclinical infection. To optimize the implementation of these strategies as part of routine care, we developed and implemented a proactive and patient-tailored CMV management system for SOT patients (the MATCH program) in our center. Two key performance characteristics of success of MATCH are diagnosing CMV at low levels and avoiding CMV disease at diagnosis; these characteristics are assessed here before (2007–2010), during (2011–2012) and after (2013–2015) the implementation of the MATCH program.

Methods. In MATCH, SOT recipients follow a personalized, yet standardized, plan for monitoring, prophylaxis and pre-emptive therapy depending on underlying risk for CMV infection. The plan is composed in accordance with the recipient's a priori risk as to CMV IgG serostatus and is continually updated during the post-transplant course according to patient´s current situation. Each individual patient plan is produced and implemented by a rule-based artificial intelligence (AI) platform, harvesting relevant real-time data from electronic medical records. Via predefined algorithms, plans and revisions are created and alerts are generated in case of missed planned monitoring for or molecular detection of CMV infection. Prior to its implementation, prevention of CMV disease was left at the discretion of the individual physician.

Results. A total of 603, 357, and 531 patients received an SOT before, during and after implementing MATCH, resp., of whom 88 (14.6%), 56 (15.7%) and 119 (22.4%) developed CMV infection within the first year of transplantation (Table 1). Among those with CMV infection, the % with high viral load decreased as did the % with CMV disease at the time of diagnosis of CMV infection during and after the implementation of MATCH relative to before (Figure 1).

Conclusion. The implementation of a rule-based AI platform guiding routine prevention of CMV disease among SOT recipients was associated with improved CMV-specific outcome, indicating its ability to identify the CMV infection sooner after onset and before causing disease.

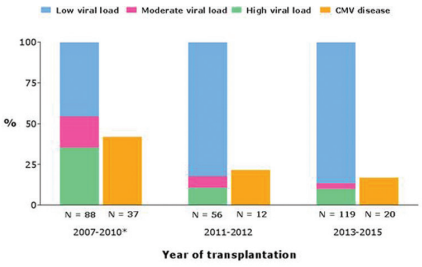

Figure 1. Prevalence of grouping of CMV viral load and CMV disease at diagnosis of CMV infection within the first year of transplantation before, during and after implementation of the MATCH program. Groupings of CMV viral load were decided prior to the analyses as rough trends for risk of CMV disease as follows: green = high viral load (>27,300 IU/mL), pink = moderate viral load (9,100 - 27,300 IU/mL) and blue = low viral load (<9,100 IU/mL).

Table 1. Characteristics of SOT-recipients with a first episode of CMV infection within the first year of transplantation before, during and after implementation of the MATCH-programme.

Year of transplantation	2007-2010 (before implementation)	2011-2012 (during implementation)	2013-2015 (after implementation)
Recipients with a first episode of CMV infection, N(% of total no. of SOT)	88 (14.6)	56 (15.7)	119 (22.4)
Sex, N(%)			
Male	60 (68.2)	28 (50.0)	69 (58.0)
Female	28 (31.8)	28 (50.0)	50 (42.0)
Median age at transplantation (IQR), years	52 (38-59)	53 (41-59)	49 (38-58)
Transplant type, N(%)			
Heart	3 (3.4)	3 (5.4)	6 (5.0)
Kidney	43 (48.9)	25 (44.6)	41 (34.5)
Kidney-Pancreas	0	0	2 (1.7)
Liver	20 (22.7)	10 (17.9)	34 (28.6)
Lung	22 (25.0)	18 (32.1)	36 (30.3)
Donor/recipient CMV IgG serostatus at transplantation, N(%)			
D+/R-	25 (28.4)	27 (48.2)	53 (44.5)
D+/R+	23 (26.2)	22 (39.3)	44 (37.0)
D-/R+	3 (3.4)	3 (5.4)	17 (14.3)
D-/R-	1 (1.1)	0	3 (2.5)
Unknown	36 (40.9)	4 (7.1)	2 (1.7)
Median viral load of the first positive CMV PCR (IQR), IU/mL	11,421 (2,821 - 55,283)	637 (328 - 3,822)	637 (273 - 2,002)

Disclosures. **All authors:** No reported disclosures.