

## LETTER TO THE EDITORS

## European survey on the management of tuberculosis in solid-organ transplant recipients and candidates

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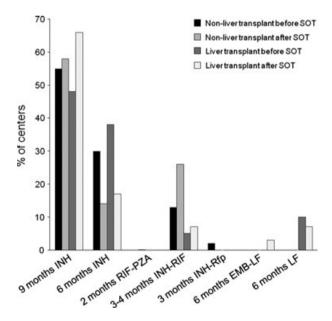
Dear Sir,

The risk of tuberculosis (TB) among solid-organ transplant (SOT) recipients is estimated to be 20–74 times higher than in the general population [1–4]. Management of TB in SOT recipients is challenging because of a potential increased toxicity of anti-tuberculous therapy and a higher risk for drug interactions between immunosuppressive and anti-tuberculous drugs [3]. We performed a survey among European transplant centres with the aim to determine the variability on the management of TB in SOT recipients and candidates and to identify factors associated with nonadherence to existing guidelines [5,6].

From October to December 2011, an internet-based survey was sent to 150 transplant clinicians registered at the European Society for Organ Transplantation or at the Study Group for Infections in Compromised Hosts of the European Society of Clinical Microbiology and Infectious Diseases. The survey consisted of 20 questions on demographics, diagnosis, and therapy of latent (LTBI) and active TB in SOT recipients [7–10].

Overall, 55/150 (37%) transplant programs from 19 European countries completed the survey. Most responders (89%) worked in countries with low incidence of TB (<20 cases/100 000 population) and they were infectious diseases specialists (60%). The majority of responders (67%) were aware of the published guidelines on the management of TB in SOT recipients. Screening for LTBI in SOT candidates was performed systematically in 60% of the centers, selectively in patients with risk factors for TB in 31% of the centers, and 9% of the centers did not perform screening. Predictors for systematic screening were awareness of guidelines (OR 8.27; 95% CI 2.12–32.35; P = 0.002) and to have  $\geq 1$  case of active TB per year (OR 5.76; 95% CI 1.12– 29.5; P = 0.04). Methods for diagnosis of LTBI included tuberculin skin test (TST) alone (48%), interferon-γ release assay (IGRA) alone (30%), TST and IGRA simultaneously (16%) and TST first followed by IGRA in case of TST positivity (6%). Most centers (73%) initiated treatment of LTBI prior to transplantation in nonliver transplant candidates, but only 38% of centers did so in liver transplant candidates. Depending on the transplanted organ, between 7% and 18% of the centers reported not to treat patients with LTBI. All of them were located in countries with low incidence of TB. Isoniazid was the preferred drug for treatment of LTBI (77%) (Fig. 1). A majority of programs (67%) estimated their incidence of post-transplant active TB to be low/very low (1 case every 2–3 years or less). For treatment of active TB, 61% of centers used a regimen including rifamycins in case of localized nonsevere TB, and 95% used rifamycins in the case of severe disseminated TB.

We found a wide variation in the practices between European countries regarding the management of TB in transplant candidates and recipients. This reflects the variable estimation of the risk for the development of TB after transplantation. These results highlight the need of



**Figure 1** Drugs used for therapy of latent tuberculosis infection (LTBI) according to the type of organ transplant and timing of therapy. EMB, ethambutol; INH, isoniazid; LF, levofloxacin; LTBI, latent tuberculosis infection; PZA, pyrazinamid; RIF, rifampicin; Rfp, rifabutine; SOT, solidorgan transplant.

additional research in the field of TB in SOT recipients. Moreover, current clinical guidelines should be better implemented to improve and/or harmonize the pre- and post-transplant management of these patients.

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## **Conflicts of interest**

MS has received kits free of charge by Cellestis and Oxforimmunotec to study the performance of IGRA responses in immunocompromised patients. MS has a patent application entitled "*In vitro* process for the quick determination of a patient's status relating to infection with Mycobacterium tuberculosis" (international patent number WO2011113953/A1).

## References

1. Torre-Cisneros J, Doblas A, Aguado JM, *et al.* Tuberculosis after solid-organ transplant: incidence, risk factors, and clin-

- ical characteristics in the RESITRA (Spanish Network of Infection in Transplantation) cohort. *Clin Infect Dis* 2009; **48**: 1657.
- Canet E, Dantal J, Blancho G, Hourmant M, Coupel S. Tuberculosis following kidney transplantation: clinical features and outcome. A French multicentre experience in the last 20 years. Nephrol Dial Transplant 2011; 26: 3773.
- 3. Subramanian A, Dorman S. Mycobacterium tuberculosis in solid organ transplant recipients. *Am J Transplant* 2009; **9** (Suppl. 4): S57.
- 4. Ou SM, Liu CJ, Teng CJ, *et al.* Impact of pulmonary and extrapulmonary tuberculosis infection in kidney transplantation: a nationwide population-based study in Taiwan. *Transpl Infect Dis* 2012; **14**: 502.
- Aguado JM, Torre-Cisneros J, Fortun J, et al. Tuberculosis in solid-organ transplant recipients: consensus statement of the group for the study of infection in transplant recipients (GESITRA) of the Spanish Society of Infectious Diseases and Clinical Microbiology. Clin Infect Dis 2009; 48: 1276.
- Bumbacea D, Arend SM, Eyuboglu F, et al. The risk of tuberculosis in transplant candidates and recipients: a TBNET consensus statement. Eur Respir J 2012; 40: 990.
- 7. Kim SH, Lee SO, Park JB, *et al.* A prospective longitudinal study evaluating the usefulness of a T-cell-based assay for latent tuberculosis infection in kidney transplant recipients. *Am J Transplant* 2011; 11: 1927.
- 8. Manuel O, Humar A, Preiksaitis J, *et al.* Comparison of quantiferon-TB gold with tuberculin skin test for detecting latent tuberculosis infection prior to liver transplantation. *Am J Transplant* 2007; **7**: 2797.
- 9. Fabrega E, Sampedro B, Cabezas J, *et al.* Chemoprophylaxis with isoniazid in liver transplant recipients. *Liver Transplant* 2012; **18**: 1110.
- Meyers BR, Papanicolaou GA, Sheiner P, Emre S, Miller C. Tuberculosis in orthotopic liver transplant patients: increased toxicity of recommended agents; cure of disseminated infection with nonconventional regimens. *Transplantation* 2000; 69: 64.