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Donor human leukocyte antigen-G single nucleotide polymorphisms are associated with post-lung transplant mortality

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Cite this article as: Lazarte J, Ma J, Martinu T, *et al*. Donor human leukocyte antigen-G single nucleotide polymorphisms are associated with post-lung transplant mortality. *Eur Respir J* 2019; 54: 1802126 [https://doi.org/10.1183/13993003.02126-2018].

ABSTRACT Human leukocyte antigen (HLA)-G is a non-classical HLA that inhibits immune responses. Its expression is modified by single nucleotide polymorphisms (SNPs), which are associated with transplant outcomes. Our aim was to investigate the association of donor and recipient HLA-G SNPs with chronic lung allograft dysfunction (CLAD) and mortality after lung transplantation.

In this single-centre study, we examined 11 HLA-G SNPs in 345 consecutive recipients and 297 donors of a first bilateral lung transplant. A multivariable Cox proportional hazards model assessed associations of SNPs with death and CLAD. Transbronchial biopsies (TBBx) and bronchoalveolar lavage (BAL) samples were examined using quantitative PCR, ELISA and immunofluorescence.

Over a median of 4.75 years, 142 patients (41%) developed CLAD; 170 (49%) died. Multivariable analysis revealed donor SNP +3142 (GG+CG *versus* CC) was associated with increased mortality (hazard ratio 1.78, 95% CI 1.12–2.84; p=0.015). In contrast, five donor SNPs, -201(CC), -716(TT), -56(CC), G*01:03(AA) and 14 bp INDEL, conferred reduced mortality risk. Specific donor–recipient SNP pairings reduced CLAD risk. Predominantly epithelial HLA-G expression was observed on TBBx without rejection. Soluble HLA-G was present in higher concentrations in the BAL samples of patients who later developed CLAD.

Specific donor SNPs were associated with mortality risk after lung transplantation, while certain donor–recipient SNP pairings modulated CLAD risk. TBBx demonstrated predominantly epithelial, and therefore presumably donor-derived, HLA-G expression in keeping with these observations. This study is the first to demonstrate an effect of donor HLA-G SNPs on lung transplantation outcome.