The revised manuscript has adequately addressed the concerns raised by the reviewers. The inclusion of HLA-C genotyping is an important addition and has added additional findings.

The authors describe a study investigating the association of HLA-B and HLA-C alleles and KIR genotypes with outcomes of TB, HIV-1 infection and immune reconstitution inflammatory syndrome (IRIS). Patients were from Rio de Janeiro, Brazil - followed from 2006 to 2016 - and constituted 4 groups of patients: Grp1 - TB+/HIV+ (n=88; 11 with IRIS), Grp2 - HIV+ (n=24), Grp3 - TB+ (n=24) and Grp4 - healthy individuals (n=26).

The following findings were reported:
With TB as an outcome, KIR2DS2 associated with risk, while HLA-B*08 and female gender. The absence of KIR2DL3 (KIR2DL2 homozygosity) and HLA-C*07 associated with protection against TB in HIV-infected patients.
With IRIS as an outcome - HLA-B*41, KIR2DS2, KIR2DS1 + HLA-C2, KIR2DL3 + HLA-C1/C2 absence, KIR2DL1 + HLA-C1/C2 absence, and CD8 count ≤ 500 associated with an increased risk of IRIS in TB/HIV coinfected patients. Associations of HLA-B*41, KIR2DS2 and KIR-HLA-C pairs with IRIS have previously not been reported.

It needs to be very clear what is meant by KIR2DL3 + HLA-C1/C2 absence, KIR2DL1 + HLA-C1/C2 absence, as this can be very confusing to the reader. See comment for line 307 below.

Specific comments and suggested edits:

- line 36: KIR "alleles" should be "genes" to not confuse with allelic variants at KIR loci.
- line 46: 500 "cells/ul" missing units
- line 57: repetition of "worldwide"
- line 58,60,62,64: inconsistent use of "HIV" and "HIV-1" - should use "HIV-1" throughout the document
- line 60,63: inconsistent use of "." or "," in numbers "69.500" should be "69,000" - check consistency throughout document.
- line 74: cytotoxic T-lymphocyte responses (CTL) - abbreviation in wrong place - cytotoxic T-lymphocyte (CTL) responses
- line 75: repeated definition for CTL
- line 76: add "serving as" before "ligands"
- line 112: "specific single nucleotide polymorphisms (SNPs)" - add definition in full
- line 127: spelling "enrolment"
- line 129: use "and", not "&"
line 137: n = 26, inconsistent with spacing "n=26"
line 143,146: superscript mm3 = mm3
line 154: singular not plural: "one non-nucleoside reverse transcriptase inhibitor"
line 162: repetition with respect to previous sentence
line 170: It is unusual to use "skin colour" rather than "Caucasian, Black or Mixed ancestry" to define individuals racial background?
line 184: Authors used 4-digit level for HLA typing in methods, but only 2-digit resolution is reported in results. It is more informative to use 4-digit.
line 190: A mention should be made that Bw4 80I and 80T epitopes were combined and HLA-A Bw4 was not included.
line 197: "were verified" change to "was determined"
line 216: "KIR alleles" should be KIR genes"; "estimated" change to "determined"
line 223: "Allelic frequencies" do you mean "HLA allele frequencies"

line 232,233: One may be introducing a bias by including HIV+ individuals in the TB+ and TB- group. Were the groups combined to increase sample size? The higher numbers of HIV positive patients because of the TB+HIV+ TB group in the "TB combined group" vs the smaller numbers in the HIV group in the "non-TB group" could affect the outcomes. There should be some explanation for combining of different phenotypes within these groups, as one ideally would not do this. If the statistics used considers this adequately (you have adjusted for HIV as a possible confounder etc) then this should be stated in the text as well. It is appreciated that sample numbers are what they are and cannot be added to at this stage. The grouping of different phenotype groups should be more clearly justified and how you have accounted for the heterogeneity between groups and interpretation of the findings when you combine different groups. In Table 2 you show various comparisons of combined and specific groups (HIV patients with and without HIV) - does this help with teasing out the relationships found in the combined groups.

line 237,238: Unusual way to define individuals ethnic background. Can the individuals be assigned Caucasian, Black and Mixed Ancestry based on the skin colour?

line 253: Using 2-digit resolution may not be the best since some functional differences exist at the 4-digit level. Eg. B*58:01 and B*58:02 have opposite effects of disease progression in HIV-1 infected patients.

line 264: HLA-C and REDOME sentence should be moved to the next paragraph.
line 270: "HLA-B*03" should be "HLA-C*03"

line 279: Most publications that mention KIR genotypes use the nomenclature e.g. "Bx6" meaning all 16 KIR genes were present. It may be better to put Bx in front of the number instead of GID #6, to avoid confusion that a different genotyping nomenclature system was used.

line 291: inconsistency - in other places the 95% CI ranges are omitted, but here they are included.

line 294: Can absence of KIR2DL3 be stated as KIR2DL2 homozygous. Gene association studies make sense with respect to the presence of a gene, not the absence.

line 307: It is confusing to write "KIR2DL3 + HLA-C1/C2 absence". Does this mean both KIR and ligands must be absent or can it be absence of KIR, but presence of ligands or vice versa? This could be seen as presence of KIR2DL2 homozygous and either C1 or C2 homozygous was significant.
KIR2DL1 + HLA-C1/C2 absence - unlikely this can be absence of KIR2DL1 as a gene as have very high percentages across the groups (most individuals will have at least one copy). Do you mean absence of HLA-C1/C2 only? What is meant needs to be explicitly stated so the reader understands.

line 309: superscript mm³ = mm³
line 325: "accelerating" change to "improving"
line 334: Conesa-Botella et al - take out "and collaborators"
line 339: Pean et al - take out "and colleagues"
line 343: submitted "for" publication

line 355: "To the best of our knowledge, HLA-B*08.." See Indian study Shankarkumar et al 2009, JAIDS, vol 51, number 5, August 15, page 640. There is mention of HLA-B*08 in this study that should be discussed.

line 367: KIR2DL2 homozygosity instead of KIR2DL3 absence. KIR2DL2 recognises C1 ligands with a higher affinity than KIR2DL3 - this might be a contributing factor.

line 383: mm³ = mm³; interesting that CD8 cell count was significant and not CD4; no discussion on why CD4 count below 50 cells/mm³ was not significant (was it also non-significant at 100 cells/mm³?).

line 384: HLA-B*41 molecules or allotypes - not "antigens"
line 426: remove "responses" not part of the definition
line 434: "8" no"18"

Table 1: Was there a rationale for choosing 500 as the cut-off for CD8 analysis? Would a different cut-off have yielded different statistical results? It would be good to include a rationale for this choice.

Table 3: It is surprising not to see any associations of CD4 count < 50 cells/mm³ in the TB-IRIS cases. Low CD4 count (<100 cells/mm³ has been seen as a hallmark of developing IRIS. Would a cut-off of 100 cells/mm³ have shown an association?

Supplementary tables:
Viral load cut-off set at 20,000 copies/ml? Rationale for this choice? What happens if 10,000 copies is used as cut-off?
Correct: "All de groups" heading of Supplementary Table S4 - to "All the groups"

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes
Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

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