Figure 7. Relationship between Mtb-specific IFN-γ CD4 T-cell signature, tuberculosis (TB) disease score and treatment outcome. (a) Correlation between TB disease score PC1 and Mtb-specific CD4 T-cell signature PC1 at baseline. Active TB (aTB)/HIV− participants are depicted in blue (n = 30), aTB/HIV− (viraemic) in yellow (n = 10), aTB/ HIV+ (aviraemic) in orange (n = 20). Linear regression and 95% confidence band are depicted. Correlation was tested by a two-tailed non-parametric Spearman rank test. (b) Comparison of the Mtb-specific CD4 T-cell signature PC1 at baseline (Pre-anti-tubercular treatment [ATT]) and 24 weeks post-ATT initiation (Post-ATT) according to time to Mtb culture conversion. PC1 values obtained from latent tuberculosis infection participants are shown with open circles. Statistical comparisons were performed using a Wilcoxon rank test for paired samples or a Mann–Whitney test for unpaired samples.

measuring particular Mtb-specific CD4 T-cell maturation and activation markers can be applied not only in the diagnosis of TB, 15,18–20 but also in the assessment of TB disease severity at presentation which is indicative of prognosis, irrespective of HIV co-infection.

be required to confirm this, we did find that this was indeed the case in the a small number of participants (n = 5) experiencing treatment failure/relapse in our cohort.

Translation of whole blood assay-based approaches into diagnostic and treatment monitoring tools requires use of simplified flow cytometry panels. Upon focusing our analyses solely on HLA-DR expression, our data concur with previous findings from our group and others that a 4-colour panel (including CD3, CD4, IFN-γ and HLA-DR) could discriminate latent from aTB15,18–20 and could also be useful to monitor the response to treatment, as recently suggested by Ahmed et al.29 Here, we show for the first time that this approach: (1) could identify those at highest risk of poor treatment outcomes, (2) could gauge the extent of TB disease severity and (3) importantly, exhibit comparable performance in HIV-infected persons, who are at highest risk of TB disease.