Our results suggest that a high Lactobacillaceae abundance prior to the onset of aGvHD may point to a preventive effect, as these patients survived. A human clinical trial of Lactobacillus rhamnosus GG prebiotic gavage to HSCT patients at time of engraftment demonstrated no protection against GvHD [1]. This could mean that Lactobacillaceae may not play a key role in aGvHD development, at least not the particular Lactobacillus rhamnosus strain under the conditions used in this group of patients. However, the administered probiotic did not alter the abundance of Lactobacillus spp. in the patients’ guts [1], suggesting that the strain was not able to establish and proliferate in the host environment in this situation. An intrinsic increase of Lactobacillaceae prior to aGvHD onset, as observed here, therefore might still play a role in reducing aGvHD. A recent study related to the use of a probiotic given to infants to prevent sepsis suggested that the time point of application of a specific Lactobacillus sp. strain as a synbiotic played a critical role in positive clinical outcomes [2]. Furthermore, a study on gut microbial immunomodulation emphasized the importance of characterizing bacteria at the strain-level, because individual strains can have different modulatory effects on the immune system [3]. Therefore, it would be of great interest to determine the identity and predicted function of the specific Lactobacillus spp. strains in our patients, and in particular, in those who exhibited an early high abundance of Lactobacillus spp., as compared with those who experienced an expansion of Lactobacillus spp. after aGvHD and who later died.

Interestingly, Enterococcus was not among the most relevant taxa identified by our multivariate analyses. Intestinal domination of Enterococcus spp. was not clearly associated with adverse outcomes in our subgroup of 30 patients, in contrast to previous findings [4–6]. It should be noted that these previous observations were made in adult allo-HSCT patients and were dependent on
the type and amount of antimicrobial treatment. In addition, to elucidate this discrepancy further, we are currently characterizing *Enterococcus* isolates from fecal samples of our patient group, to gain insight into bacterial strain-level differences.

**Supplementary references**


