Gut microbiota and B cell receptor (BCR) inhibitors for the treatment of lymphoid malignancies: retrospective recognition of different enterotypes correlated to clinical response or irAEs occurrence. A cross-sectional study.

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The gut microbiota (GM) composition strongly influences the state of dysbiosis and thus our healthy/disease status. Accumulating knowledge support the role of GM composition in lymphomagenesis: dysbiosis seem to act as superantigen and chronically stimulate cells of the immune system, leading to expansion of B cells [1-2]. Moreover, robust evidences regarding the ability of the GM in modulating response to immunotherapy are found in patients affected by melanoma[3].

The aim of the study was to examine the GM composition in a population of patients with chronic lymphocytic leukemia, mantle cell lymphoma and Waldenström macroglobulinemia/lymphoplasmacytic lymphoma treated with BCRi for at least 12 months by using Next Generation Sequencing (NGS) techniques, in order to recognize different enterotypes possibly related to either clinical responses or to a treatment failure (R VS NR),

8 patients were enrolled. The average age of patients was 62 yo and 50% male. The hematologic diagnosis was chronic lymphatic leukemia in all patients and 50% were treated with Ibrutinib and 50% with Idelalisib. Enterotype 1 (E1, *Bacteroides*) was the mainly represented (50%), followed by E3 (*Ruminococcus*) (38%) and E2 (*Prevotella*).The probability of treatment response was estimated as 37.5% for E1 and 25% for E3. In contrast, the probability of not responding to therapy is 12.5% in both patients with E1 and those with E3. The probability that an adverse event might not occur was estimated as 35% in E1 and 25% in E3. As observed in Gopalakrishnan et al study, *Faecalibacterium prausnitzii* is a abundant species in patients responsive to BCRi therapy.

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