Aim and objectives

We present two consecutive patients treated in our Hospital in 2022 who developed clinically acute myeloid leukemia (AML) during or after ICI treatment for solid tumors. Patient 1 is a man with a previous history of metastatic lung adenocarcinoma treated with pembrolizumab, which was stopped due to complete response (CR) 5 months before diagnosis of AML in April 2022. Patient 2 is a woman, with a previous history of ductal breast cancer treated with adjuvant chemoradiotherapy; she also developed a metastatic V600E BRAF-mutated melanoma, treated with BRAF/MEK inhibitors. Finally after two months of pembrolizumab, she developed AML in April 2022.

Materials and Methods

In both Patients 1 and 2, peripheral blood (PB) and bone marrow blood testing confirmed Core Binding Factor (CBF) AML, according to the presence of (inv16)(p13;q22) in 80% and 70% of blasts in the PB, respectively. According to ESMO AML Guidelines, therapy with gemtuzumab ozogamycin associated with standard chemotherapy was recommended for both patients.

Results

Patient 1 achieved a CR after induction and consolidation therapy; patient 2 performed cytarabine-based consolidation therapy due to leukemia-aberrant immunophenotype. At current follow-up (9 months after diagnosis) both patients are alive: in patient 1 negative CBF was confirmed and patient 2 had PD treated with the association azacitidine + venetoclax.

Conclusion and Relevance

A case of AML after 3 cycles of pembrolizumab for the treatment of non-small cell lung cancer and 5 cases of mieloid neoplasia after treatment with ICIs were recently reported. Hyperprogression of subclinical myeloid malignancies could be a potential explanation, since a myeloid clone with acquired driver mutation(s) could obtain an extra proliferation advantage from functional myeloid PD-1 knockout after ICI. Abberant PD-1 expression was observed in 8–26% of CD34+ blasts in myelodysplastic syndromes, chronic myelomonocytic leukemia and AML. Moreover chemotherapy and BRAF inhibitor exposure, together with short exposure to pembrolizumab in Patient 2, suggest a major role of previous therapies in the development of AML.

The correlation between ICI and myeloid neoplasias is still uncertain.

References and/or Acknowledgements