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Blood 142 (2023) 5965

The 65th ASH Annual Meeting Abstracts

ONLINE PUBLICATION ONLY

616.ACUTE MYELOID LEUKEMIAS: INVESTIGATIONAL THERAPIES, EXCLUDING TRANSPLANTATION AND CELLULAR IMMUNOTHERAPIES

VISTA a Potential New Immuno-Oncology Target in Acute Myeloid Leukemia

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V-domain Immunoglobulin Suppressor of T cell Activation (VISTA/PD-1H) is a B7 family member highly expressed on circulating and intra-tumoral myeloid cells. VISTA is a negative checkpoint protein that inhibits anti-tumor T cell responses. In multiple solid tumors, VISTA expression is associated with poor overall survival and is also described as a potential mediator of resistance to anti-CLTA-4 and anti-PD1 therapies. VISTA expression was also investigated in hematological tumors and described as highly expressed on blasts including leukemic stem cells from AML patients. Therefore, VISTA is a unique and potentially new target for cancer immunotherapy in this indication.
Kineta has developed a fully human monoclonal antibody targeting VISTA, KVA12123, currently evaluated in a Phase 1/2 clinical trial alone and in combination with pembrolizumab in cancer patients with advanced solid tumors. We also believe that VISTA could be a promising target for AML patients. Therefore, we have tested in vivo, in a Kasumi-3 AML disseminated tumor model, the efficacy of our antibody alone or in combination with standard of care therapy, cytarabine and doxorubicin. Like leukemic cells in AML patients, the Kasumi-3 cell line exhibits a high level of VISTA expression on its cell surface. Female NOD-scid mice were first inoculated with Kasumi cells via tail vein injection, and tumor engraftment was evaluated at different time points in the blood, spleen and bone marrow to monitor engraftment using CD34, CD33, CD45 and HLA-DR cell surface expression markers. Then, when tumor burden was high, standard of care treatment (5 doses of 16mg/kg AraC by IV injections and 3 doses of 0.5mg/kg Dox by IV injections) was initiated in indicated groups for 5 cycles, before starting treatment with KVA12 for the rest of the study. Tumor engraftment was tested after chemotherapy alone to evaluate the efficacy before starting treatment with our antibody. Our results showed that untreated mice had higher number of Kasumi-3 cells in the blood when compared to chemotherapy treated mice. Two backbone versions of our antibody were then tested, a human IgG1 - KVA12123 and a human IgG4 - KVA12402, at 30mg/kg IP injections twice a week for 5 weeks. Our data showed that KVA12123 and KVA12402 as single agents and in combination with chemotherapy reduced Kasumi-3 tumor load in the blood, spleen and bone marrow within the groups and significantly improved survival when compared to IgG1 control groups.
These data all together indicate that anti-VISTA targeted therapy should be evaluated in myeloproliferative disorders like AML alone or in combination with standard of care.

Disclosures Guillaudeux: *Kineta Inc.:* Current Employment, Current equity holder in publicly-traded company. **Sridhar:** *Kineta Inc.:* Ended employment in the past 24 months. **Frazier:** *Kineta Inc.:* Ended employment in the past 24 months. **Ovechkina:** *Kineta Inc.:* Current Employment, Current equity holder in publicly-traded company. **Iadonato:** *Kineta Inc.:* Current Employment, Current equity holder in publicly-traded company, Membership on an entity's Board of Directors or advisory committees, Patents & Royalties.

https://doi.org/10.1182/blood-2023-186927