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MEETING ABSTRACT

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A neutralizing monoclonal antibody (mAb A24) directed against the transferrin receptor induces apoptosis of tumor T lymphocytes from ATL patients

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Adult T-cell leukemia/lymphoma (ATL) is an aggressive lymphoid proliferative disease that exists under diverse clinical forms ranging from chronic to acute. In contrast to resting T cells, human T-cell lymphotropic virus type 1 (HTLV-1) infected cells constitutively express high levels of surface transferrin receptor (TfR). Interestingly this expression is higher in acute than in chronic forms. We have characterized a new monoclonal antibody (mAb A24) directed against the human TfR that blocks the proliferation and induced apoptosis through mitochondria depolarization of ATL cells *ex vivo*. We determined that A24 binds TfR with an equilibrium constant (Kd) of 2.7 nM and competes with transferrin for binding to TfR. Interestingly A24 exhibits a higher affinity than transferrin when TfR are highly expressed. A24 inhibited [⁵⁵Fe]-transferrin uptake through TfR endocytosis via the clathrin adaptor protein-2 complex pathway followed by transport to lysosomal compartments. In monkey administration of single and repeated doses of A24 did not induce significant toxicity except a slight decreased of haemoglobin level, increased of transferrin and decreased of iron serum levels. Interestingly in lymph nodes, apoptosis was observed in germinal center in zone of high proliferation of B and T cells. Therefore, A24 might be a safe and effective treatment of ATLL particularly acute forms.

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