E4.ADULT T-CELL LEUKEMIA/LYMPHOMA, A CHALLENGE OF DIAGNOSIS AND TREATMENT

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Adult T-cell leukemia/lymphoma is an aggressive neoplasia, characterized by proliferation of activated peripheral T-cell lymphocytes, promoted by HTLV-I (human T-cell lymphotropic virus I) retrovirus infection.

The endemic areas for HTLV-I infection, which also have the largest experience with ATLL, are Japan, Carribean, Central and South America, Tropical Africa, and also Romania. The incidence of infection in Europe in low. The studies show that there are around 20 million HTLV-I positive adults and children worldwide, out of which 1-4% will develop ATLL, in around 30-50 years after the infection. The primary event is the viral trigger, but the lymphoproliferation becomes subsequently independent from the viral stimulation.

ATLL has four major clinical presentations: acute-leukemic, lymphomatous, chronic and smouldering. The first two forms are the most frequent and the most aggressive, with poor prognosis, a medium survival of months, severe immunosuppression and intrinsic chemoresistance – poor response to classical CHOP regimen, the conventional therapy still widely used in Europe; this response in frequently followed by relapse.

Although there are no wide trials, the studies of the Japan Clinical Oncology Group (JCOG) proposed combined chemotherapy regimens with higher efficiency such as LSG15 - VCAP-AMP- VECP. This protocol had a complete response (CR) significantly higher than CHOP-14, but a similar rate of overall response (OR), with a higher toxicity for LSG15. The 3-years survival is superior for LSG15 (24 vs 13% for CHOP-14). Still, because vindesine and ranimustine and not available usually (including in Romania), some authors propose Hyper-CVAD regimen, although with a lower efficiency.

Recent studies introduce humanized monoclonal antibody anti-CCR4 mogamulizumab, added to LSG15 regimen, with a higher rate of CR (~50%) and OR (~85%), especially efficient for acute and lymphomatous forms, with a longer median survival (~8.6 months), without an increase of toxicity. On the other hand, mogamulizumab is not widely available outside Japan.

The treatment of acute and lymphomatous forms must include prophylactic intrathecal chemotherapy, because there is a 10-25% incidence of CNS involvement.

Other treatment options may include antiviral therapy with interferon and zidovudine, especially for leukemic forms, but also for chronic and smouldering ones, for which long term survival is notably improved. Nevertheless, since the HTLV-I retrovirus is usually latent in ATLL patients, the efficiency of the antiviral therapy probably has a different mechanism.

There are also some small studies which discuss a (limited) efficacy in ATLL for other therapies, such as: alemtuzumab, arsenic trioxide with or without interferon, all-trans-retinoic acid, pralatrexate (anti-folate), bortezomib, forodesine (purine nucleoside phosphorylase inhibitor), histone deacetylase inhibitor, or lenalidomide.

In spite of all these, for acute and lymphomatous forms, allogeneic stem transplantation remains the only option with a better rate of long term response.