Ann Hematol (2010) 89:425–426
DOI 10.1007/s00277-009-0815-6

LETTER TO THE EDITOR

Treatment of 5q-syndrome with lenalidomide in an HIV-positive patient under cART

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Received: 15 July 2009 / Accepted: 6 August 2009 / Published online: 25 August 2009

Dear Editor,

Lenalidomide has emerged as standard treatment for 5q-syndrome [1]. In normal cell cultures, lenalidomide enhances T cell proliferation [2], and in cells isolated from HIV-positive (HIV+) and CMV+ patients, lenalidomide enhances CD8+ cytotoxic T cell activity against viral antigens [3]. There are no in vivo data on lenalidomide in HIV+ patients.

We are reporting on a 52-year-old HIV+ patient with an undetectable viral load for the past 10 years on combined antiretroviral therapy (cART) who developed 5q-syndrome and was successfully treated with lenalidomide. In 1989, he was diagnosed with HIV and had been on cART since 1996 after mono- and bi-therapies. He had suffered and recovered from multiple complications (CMV-retinitis, Kaposi sarcoma, cryptococcal meningitis, oesophageal candidiasis, disseminated *Mycobacterium genavense* infection and anal squamous cell carcinoma (T1N0M0)). In February 2007, persistent pancytopenia and dependency on red blood cell transfusions for a month motivated a bone marrow (BM) biopsy revealing a 5q-syndrome (karyotype: 46,XY,del(5)(q13-14q33)[7]/46,XY[3]). In August 2007 lenalidomide was started (10 mg for 21 days every 28 days) according to recommendations on the use of lenalidomide in MDS without dose reduction at any time [4]. He became transfusion independent 18 days after treatment start. After two cycles, complete normalisation of peripheral blood counts was achieved (Fig. 1), and phlebotomy therapy was initiated for iron overload. After five cycles, BM examination revealed complete cytological and partial cytogenetic remission (5q deletion in eight of 50 metaphases). HIV viral load remained undetectable before lenalidomide and 1, 2, 3, 4, 8, 12 and 24 weeks after the start of lenalidomide.

CD4+ cells had reached a steady state between 137 and 206 cells/mm^3 before lenalidomide. They rose to 235 cells/mm^3 2 months after starting lenalidomide and remained stable between 230 and 240 cells/mm^3. CD8+ cells were between 314 and 393 cells/mm^3 before and reached stable levels over 500 cells/mm^3 6 weeks after treatment began (527–1,195 cells/mm^3). Lymphocyte counts rose from 0.9 to 1×10^9/l to stable levels between 1.2 and 2.5×10^9/l 3 months after treatment was initiated (Figs. 1 and 2).

Before lenalidomide treatment, plasma concentrations of atazanavir (ATV) and lopinavir (LPV) were 1,767 and 13,903 ng/ml 5 h after last drug intake. On days 23 and 28 of cycle 2 of lenalidomide treatment, plasma levels 11.5 h after last drug intake were 2,728 and 2,180 ng/ml for ATV and 7,728 and 5,791 ng/ml for LPV, respectively. At day 20

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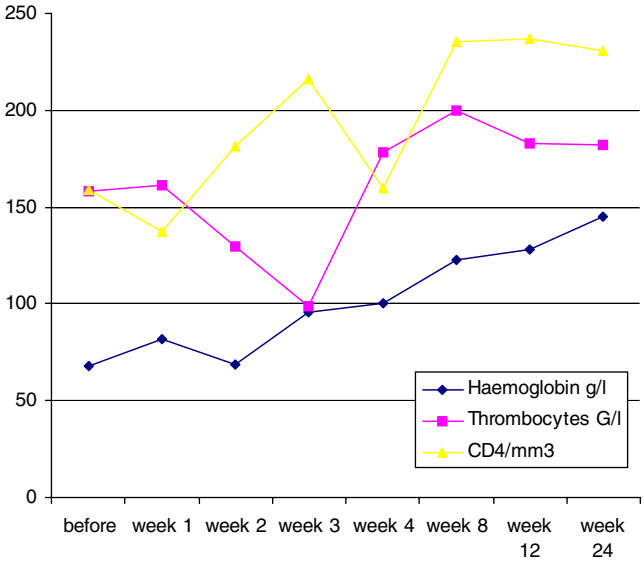

Fig. 1 Changes in haemoglobin, thrombocytes and CD4 counts

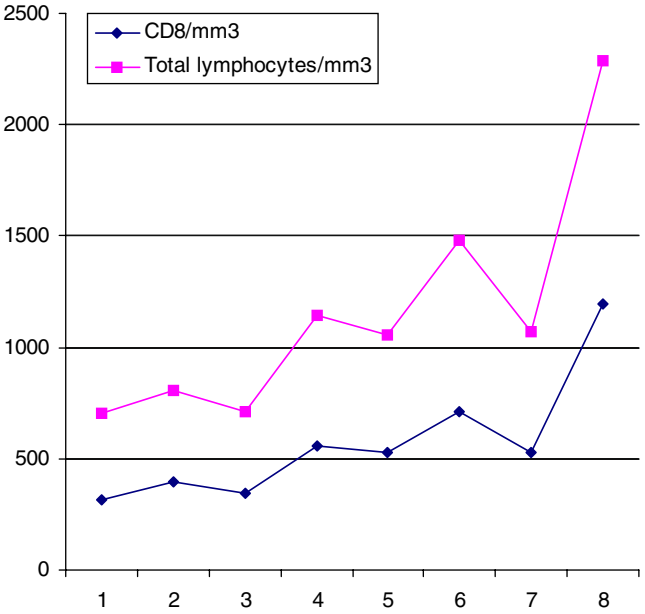

Fig. 2 Changes in CD4 and total lymphocyte counts

of cycle3, ATV and LPV plasma concentrations were 2,370 and 8,378 ng/ml 11.75 h after last drug intake.

This is the first report on lenalidomide administration to an HIV+ patient with 5q-syndrome without interruption of cART. Plasma levels of ATV under lenalidomide treatment were slightly increased (changing from percentile 40 to 80 in the reference pharmacokinetics curve), whereas plasma concentrations of LPV were not affected. Follow-up examination of CD4+ cells as well as HIV viral load did not demonstrate a negative impact of lenalidomide. On the contrary, CD4+ cells showed a tendency to rise to stable levels over 230 cells/mm^3. The CD4+ cell rise might be due to the fact that lymphocytes could have been part of the MDS clone. Another reason could be an immunomodulatory effect. No rise in viral load was observed, as demonstrated in patients treated with thalidomide [5, 6].

Although a 5q-syndrome rarely occurs in HIV+ patients, our observation is of interest as it suggests that HIV+ patients with other pathologies known to respond to lenalidomide, such as multiple myeloma for instance, could also benefit from this treatment. As thalidomide has proven to be helpful in HIV+ patients for wasting syndrome, ulcers and Kaposi's sarcoma but is sometimes impossible to continue due to adverse events, lenalidomide could also be an alternative treatment in these diseases.

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