observation time was 3.2 years (range 0.5–11.4 years).

Thirty-six people did not experience a decrease in the serum M-protein level: 19 (52.8%) had a detectable HIV load at last follow-up, 7 (19.4%) started ART after the age of 50, 5 (13.9%) were coinfected with HCV, 3 (8.3%) had a disseminated Mycobacterium avium complex disease and 2 (5.6%) had an IgM M-protein. Unfortunately, the retrospective nature of our study prevented us from investigating other causes of lymphocyte B stimulation, including viruses such as Epstein-Barr virus or cytomegalovirus, whose viral loads were not tested in this cohort, although Epstein-Barr virus and cytomegalovirus serological profiles showed evidence of past infection in all these patients.

In agreement with the observed trends, ART seems to have a favorable impact on the serum M-protein level. These results support the hypothesis that the therapy improves the well-known B-cell dysfunction in HIV-infected people, by lowering, first, the antigenic stimulation; consequently, the B-lymphocyte expansion; and, finally, the monoclonal paraproteinemia.2,3

Unlike the disappearance described in 66.2% of the population included in Casanova’s article,1 the M-protein remained almost always detectable in our cohort, although we obtained a similar proportion of improvements: it decreased in 66.7% of cases, becoming unquantifiable in many of them. Our results are similar to the ones obtained by Amara et al in their retrospective analysis of 25 patients and by Genet et al in their retrospective analysis of 12 patients.4,5

MG in the general population has been associated with an increased risk for progression to multiple myeloma, plasmacytoma, macroglobulinemia, and other malignant plasma cell disorders.6 According to current clinical recommendations, this is the reason why a detected MG should be monitored indefinitely in any case, even when the above-mentioned risk could be considered low (if the serum monoclonal protein is <15 g/L, IgG type and the free light chain ratio is normal and the risk for progression is low).7

Given that we adopted the same methods as the ones used by Casanova et al1 to analyze electrophoretic patterns, our results support the hypothesis that M-protein remains detectable lifelong in most of the patients on ART, who should be followed for the development of hematologic malignancies.

HIV viral load blips, which usually occur randomly in those who take the therapy regularly, could be a possible explanation for the failure to complete disappearance of the serum monoclonal spike, although they do not seem to vanish the beneficial effect produced by ART on M-protein. Another possible explanation could be represented by the onset of an irreversible impairment in B-cell function, which may persist in patients with an undetectable HIV viral load.8

Persistence of MG despite ART still requires exploration: further prospective studies with a long-term follow-up are needed to assess the risk for subsequent development of malignant plasma cell disorders in this population.

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REFERENCES

To the Editors:

Dolutegravir is an HIV integrase inhibitor with a potent antiviral activity, distinct resistance profile, and favorable pharmacokinetic profile1 recently approved for use in naive and highly active antiretroviral therapy–experienced patients. Its efficacy and safety have been demonstrated in various clinical trials conducted both in naive and experienced patients.2 In dose-ranging study, dolutegravir monotherapy has shown a potent antiviral activity, with a significant reduction in plasma HIV RNA levels from baseline to day 11 for various doses.3 Dolutegravir is approved for use in

Dolutegravir Monotherapy in HIV-Infected Naive Patients With <100,000 Copies/mL HIV RNA Load

The authors have no funding or conflicts of interest to disclose.
TABLE 1. Baseline Characteristics of the Patients, HIV RNA Level (at baseline), Number of CD4 Cells (at baseline), HIV RNA Level* After Four Week of Dolutegravir and at Last Visit, Number of CD4 Lymphocytes at Last Control, and Months on Dolutegravir Monotherapy

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Age/Gender/Sexual Orientation</th>
<th>CDC Stage</th>
<th>CD4/μL at Baseline</th>
<th>HIV RNA Copies/μL at Baseline</th>
<th>HIV RNA at Last Visit</th>
<th>HIV RNA Copies/μL at Last Visit</th>
<th>CD4/μL at Last Visit</th>
<th>Months on Dolutegravir</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>40/F/hetero</td>
<td>A2</td>
<td>248</td>
<td>20,400</td>
<td>Not detectable</td>
<td>Not detectable</td>
<td>600</td>
<td>10</td>
</tr>
<tr>
<td>2</td>
<td>36/M/homo</td>
<td>A2</td>
<td>335</td>
<td>18,400</td>
<td>&lt;20</td>
<td>Not detectable</td>
<td>471</td>
<td>9</td>
</tr>
<tr>
<td>3</td>
<td>38/F/hetero</td>
<td>A2</td>
<td>356</td>
<td>90,500</td>
<td>Not detectable</td>
<td>31</td>
<td>527</td>
<td>7</td>
</tr>
<tr>
<td>4</td>
<td>40/M/homo</td>
<td>A2</td>
<td>350</td>
<td>39,000</td>
<td>Not detectable</td>
<td>35</td>
<td>623</td>
<td>7</td>
</tr>
<tr>
<td>5</td>
<td>39/M/homo</td>
<td>A2</td>
<td>329</td>
<td>43,300</td>
<td>Not detectable</td>
<td>&lt;20</td>
<td>613</td>
<td>7</td>
</tr>
<tr>
<td>6</td>
<td>44/M/homo</td>
<td>A2</td>
<td>229</td>
<td>17,500</td>
<td>&lt;20</td>
<td>45</td>
<td>404</td>
<td>6</td>
</tr>
<tr>
<td>7</td>
<td>47/M/homo</td>
<td>A2</td>
<td>785</td>
<td>18,200</td>
<td>Not detectable</td>
<td>&lt;20</td>
<td>879</td>
<td>6</td>
</tr>
<tr>
<td>8</td>
<td>45/M/bisexual</td>
<td>A2</td>
<td>214</td>
<td>16,900</td>
<td>Not detectable</td>
<td>Not detectable</td>
<td>309</td>
<td>8</td>
</tr>
<tr>
<td>9</td>
<td>76/M/homo</td>
<td>A2</td>
<td>345</td>
<td>52,000</td>
<td>Not detectable</td>
<td>&lt;20</td>
<td>484</td>
<td>6</td>
</tr>
</tbody>
</table>

*The blood samples were collected from HIV-1 seropositive patients by venipuncture. All plasmas were extracted and quantified by the COBAS AmpliPrep/COBAS TaqMan HIV-1 test, version 2.0 (Roche, Mannheim, Germany), following the manufacturers’ instructions. The amount of HIV-1 RNA is shown as the number of copies per milliliter of plasma. The lower quantitative detection limit is determined at 20 copies per milliliter (HIV RNA <20 copies per milliliter or not detectable).

association with an abacavir/lamivudine or emtricitabine/tenofovir backbone in antiretroviral naive patients at a 50-mg once-daily dose. In 3 phase III randomized controlled clinical studies in antiretroviral naive patients, dolutegravir plus 2 nucleoside reverse transcriptase inhibitors was superior to both tenofovir/emtricitabine/efavirenz and darunavir/ritonavir regimens, and noninferior to raltegravir.3–5 We report our experience in 9 antiretroviral naive HIV-1–infected patients followed at the Infectious Diseases Outpatient Department of G.B. Rossi Hospital in Verona, Italy, who started dolutegravir monotherapy after refusing nucleoside reverse transcriptase inhibitors. They all gave written informed consent to the use of dolutegravir as only antiretroviral drug. Seven men and 2 women were all HIV monoinfected, with a mean age of 45 years (range, 36–76). Pretreatment characteristics of the patients, HIV RNA level (at baseline), number of CD4 cells (at baseline), HIV RNA level 4 weeks after starting treatment and at last visit, number of CD4 lymphocytes at the last control, residual plasma HIV RNA 3 and 6 months after the beginning of dolutegravir, and duration of dolutegravir monotherapy are indicated in Table 1.

No patients had baseline HIV resistance mutations for NRTI, NNRTI, PI, or INI. The second table shows total cholesterol, low-density lipoprotein and high-density lipoprotein cholesterol, and triglycerides levels before starting dolutegravir and at the last control. For CD4 cell count, the mean increase was 191 cells per microliter. Serum lipids increased importantly only in 1 patient (no. 1, Table 2), who had also an increase in her body weight. The treatment of HIV infection continues to be based on the combination of 3 antiretroviral drugs. Monotherapy with protease inhibitors in antiretroviral naive patients is inferior to standard antiretroviral regimens in clinical studies.6 Dolutegravir in association with 2 nucleosides is superior to efavirenz and darunavir in naive patients.3,5 Dolutegravir 50 mg daily showed a high antiviral potency with a reduction of viral load of 2.5 log10 after 10 days of monotherapy. Recently, a combination of dolutegravir and lamivudine was virologically effective in 20 treatment-naive patients in a pilot study.7 The results of our small and time-limited study suggest the feasibility of a dolutegravir monotherapy in patients with a viral load lower than 100,000 copies per milliliter. Should well powered clinical trials with long follow-up confirm our results, a dolutegravir monotherapy strategy could be used to preserve future

TABLE 2. Serum Levels of Total Cholesterol, LDL and HDL Cholesterol, and Triglycerides Before Starting Dolutegravir and at Last Control

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Total Cholesterol Pretreatment (n.v.: &lt;200 Mg/dL)</th>
<th>Total Cholesterol at Last Visit</th>
<th>LDL/HDL Pretreatment (n.v.: LDL &lt;130 Mg/dL; HDL &gt;40 Mg/dL)</th>
<th>LDL/HDL Levels at Last Visit</th>
<th>Triglycerides Pretreatment (n.v.: &lt;150 Mg/dL)</th>
<th>Triglycerides Levels at Last Visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>194</td>
<td>240</td>
<td>111/52</td>
<td>145/64</td>
<td>153</td>
<td>158</td>
</tr>
<tr>
<td>2</td>
<td>107</td>
<td>127</td>
<td>72/42</td>
<td>85/59</td>
<td>43</td>
<td>47</td>
</tr>
<tr>
<td>3</td>
<td>173</td>
<td>202</td>
<td>107/51</td>
<td>110/58</td>
<td>75</td>
<td>165</td>
</tr>
<tr>
<td>4</td>
<td>138</td>
<td>177</td>
<td>112/26</td>
<td>119/35</td>
<td>157</td>
<td>105</td>
</tr>
<tr>
<td>5</td>
<td>132</td>
<td>185</td>
<td>95/36</td>
<td>122/38</td>
<td>76</td>
<td>116</td>
</tr>
<tr>
<td>6</td>
<td>170</td>
<td>201</td>
<td>118/34</td>
<td>131/34</td>
<td>92</td>
<td>175</td>
</tr>
<tr>
<td>7</td>
<td>160</td>
<td>194</td>
<td>104/42</td>
<td>123/52</td>
<td>68</td>
<td>92</td>
</tr>
<tr>
<td>8</td>
<td>221</td>
<td>214</td>
<td>144/59</td>
<td>130/61</td>
<td>90</td>
<td>107</td>
</tr>
<tr>
<td>9</td>
<td>160</td>
<td>170</td>
<td>99/48</td>
<td>108/48</td>
<td>59</td>
<td>65</td>
</tr>
</tbody>
</table>

*LDL, low-density lipoprotein; HDL, high-density lipoprotein; n.v., normal value.
Isolated Hepatitis B Core Antibody is Associated With Advanced Hepatic Fibrosis in HIV/HCV Infection But Not in HIV Infection Alone

To the Editors:

INTRODUCTION

Isolated hepatitis B virus (HBV) core antibody (HBcAb+), defined as the presence of HBcAb in the absence of HBV surface antigen (HBsAg) and surface antibody (HBsAb), occurs in up to 34% of HIV–HCV-coinfected persons.1–6 Isolated HBcAb can indicate occult HBV viremia, (the presence of HBV viremia in the absence of HBsAg), resolved infection with low titers of HBsAb, a window period during acute infection, or a false-positive result. However, the relationship between isolated HBcAb pattern and liver disease remains unclear with some, but not all, studies describing an association with liver disease.5,7–10 Our objective was to characterize the prevalence of isolated HBcAb pattern among HIV- and HIV/HCV-infected veterans in the Veterans’ Aging Cohort Study (VACS) and to determine whether the isolated HBcAb pattern was associated with advanced fibrosis in HIV- and HCV-coinfected veterans.

METHODS

Study Design and Setting

We conducted a cross-sectional study among HIV-infected individuals in the Veterans Aging Cohort Study Virtual Cohort (VACS-VC).11 Comprised electronic medical record data from all HIV-infected veterans at Veterans Affairs (VA) medical facilities in the United States, data include hospital and outpatient diagnoses, laboratory results, and pharmacy data.12

Study Patients

The study sample included all HIV-infected individuals who enrolled in the VACS-VC between October 1996 and September 2010, had at least 180 days of follow-up, and who had all 3 HBcAb, HBsAg, and HBsAb serologies tested. We then searched for the first positive or negative HBcAb test and included only those who had subsequent HBsAb and HBsAg testing ≤12 months from the first positive or negative HBcAb result. We further evaluated those tested for whom data variables to calculate FIB-4 and aspartate aminotransferase (AST)-to-platelet ratio index (APRI) scores were available within ±12 months of the earliest complete serologic data. The following 5 serologic patterns were assessed:

- Isolated HBcAb: HBsAg negative, HBcAb positive, HBsAb negative
- Resolved HBV infection: HBsAg negative, HBcAb positive, HBsAb positive

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