Clinical Features and Contribution of Virological Findings to the Management of Kaposi Sarcoma in Organ-Allograft Recipients

Stephane Barete, MD; Vincent Calvez, MD, PhD; Catherine Mouquet, MD; Benoit Barrou, MD; Henri Kreis, MD; Jacques Dantal, MD; Richard Dorent, MD; Francois Durand, MD; Yves Dimitrov, MD; Nicolas Dupin, MD; Anne-Genevieve Marcelin, PharmD; Jean-Charles Piette, MD; Marc Olivier Bitker, MD; Camille Francès, MD

Objectives: To describe the clinical features of Kaposi sarcoma (KS) in organ-allograft recipients and to determine the contribution of human herpesvirus 8 (HHV-8) investigations to the management of KS.


Methods: We detected HHV-8 antibodies using an indirect immunofluorescence assay and the HHV-8 DNA genome using nonnested polymerase chain reaction with KS-associated herpesvirus 330233 primers in peripheral blood mononuclear cells collected at transplantation and KS diagnosis. We detected the HHV-8 genome in involved and uninvolved tissue specimens and in 10 patients' serum samples collected 1 month before the first manifestation of KS. We determined the HHV-8 double-strand DNA sequence and subtypes of open reading frame 26.

Intervention: Management of KS consisted of progressively tapering immunosuppressive therapy regardless of KS dissemination. Associated infections were treated when possible. Chemotherapy was prescribed only when a functional disability persisted, and polychemotherapy was prescribed for life-threatening disease.

Main Outcome Measures: Percentage of recipients with KS remission and stabilization, organ-graft survival, and death rates.

Results: Remission of KS was obtained in 9 (45%) of the 20 patients independently of disease dissemination, with a mean follow-up of 35 months. The kidney graft survived in 12 (67%) of the 18 patients. Only 1 patient (5%) died of KS progression. All allograft recipients had anti–HHV-8 antibodies before transplantation. We detected HHV-8 DNA in all involved tissue samples but not in serum samples 1 month before KS onset. The most prevalent subtype was HHV-8 C (9 [53%] of 17 patients) and was not associated with extradermatological extension of KS compared with subtypes A and B.

Conclusions: Virological investigations of HHV-8 contribute poorly to KS management. Prospective studies are needed to determine the role of HHV-8 virological investigations and to identify associated cofactors so as to prevent KS in organ-allograft recipients.

Arch Dermatol. 2000;136:1452-1458

HUMAN herpesvirus 8 (HHV-8), also known as Kaposi sarcoma (KS)-associated herpesvirus, is associated with 3 diseases: KS, primary effusion lymphoma, and some forms of multicentric Castleman disease. Since HHV-8 is considered the etiological agent of all clinical types of KS, virological and immunological analyses, such as detection of HHV-8 DNA in different tissue samples or anti–HHV-8 antibodies in serum samples and classification of HHV-8 subtypes, are now available. The aims of this study were to describe the clinical features and evolution of KS in a series of organ-allograft recipients and to determine the contribution of these HHV-8 investigations to patient management.

RESULTS

DESCRIPTION OF THE COHORT

Fourteen men and 6 women (male-female ratio, 2:3) received allografts. The median duration of stay in the native countries was 33.2 (range, 16-65) years. The median age at transplantation was 48 (range, 26-67) years. Ten patients (50%) experienced 1 (n=8) or 2 (n=2) acute graft rejection episodes before KS.
PATIENTS AND METHODS

ORGAN-ALLOGRAFT RECIPIENTS

Twenty solid-allograft recipients were referred to our center for KS between November 1, 1991, and May 31, 1999. The organ allografts were the kidney (n = 18), liver (n = 2), and heart (n = 1); 1 patient received both a kidney and liver. Most organ allografts were obtained from cadavers; 2 kidneys were provided by living wives. Immunosuppressive regimens consisted of double or triple therapy: prednisone and azathioprine (n = 17) or mycophenolate mofetil (n = 3) and cyclosporine (n = 12). Acute graft rejection was treated with boluses of high-dose methylprednisolone hemisuccinate combined with antithymocyte or monoclonal OKT3 antibodies.

DIAGNOSIS AND TREATMENT OF KS

Regardless of its localization, the diagnosis of KS was confirmed in all cases by its typical histologic characteristics. The dissemination of KS was evaluated with the following: chest radiography, thoracic and abdominal computed tomography, and upper gastrointestinal tract endoscopy. Lung bronchoscopy with examination of the bronchial-alveolar lavage fluid was performed only when the results of the preceding thoracic investigations were abnormal, and colonoscopy was done only when the upper gastrointestinal tract was involved. Associated infections were systematically sought.

In the absence of life-threatening disease caused by KS (respiratory insufficiency or clinical gastrointestinal manifestations), the therapeutic strategy consisted of progressively tapering immunosuppressive therapy, regardless of KS dissemination. This progressive reduction of immunosuppressive therapy was modulated according to organ-allograft function and KS evolution. Our aim was not to obtain KS remission but to stabilize the disease and to preserve good allograft function, especially in liver and heart recipients. Remission was defined as the disappearance of all KS lesions; progression, a 2-fold increase in the number of KS lesions; and stabilization, the persistence of KS lesions without progression. Isolated skin lesions were treated with cryotherapy when they caused aesthetic problems. Monochemotherapy with bleomycin sulfate (7.5 mg/wk) was prescribed for persistent functional disability 6 months after the first reduction of immunosuppressive therapy. Polychemotherapy (doxorubicin hydrochloride, 30 mg/m²; bleomycin sulfate, 10 mg/m²; and vincristine sulfate, 2 mg every 3 weeks) was prescribed for life-threatening disease due to KS. High doses of intravenous immunoglobulins were prescribed for 2 patients with KS progression.

VIROLOGICAL HHV-8 ASSAYS

Human IgG antibodies directed against HHV-8 were detected in serum samples at 1:100 dilution with an indirect immunofluorescence assay on latent nuclear antigen 1 in BCP-1 cells derived from primary effusion lymphoma as previously described. Of the 20 recipients, 18 serum samples (90%) were tested just before transplantation, and all serum samples were tested at the time of KS diagnosis.

Nonnested polymerase chain reaction (PCR) with KS 330 primers was used to detect HHV-8 DNA in peripheral blood mononuclear cells (PBMCs) collected before transplantation (n = 5) and at the time of KS diagnosis (n = 10) and in the following tissues involved and uninvolved with KS: involved skin (n = 19), distant normal skin (n = 14), previously involved skin after KS remission (n = 6), involved lymph nodes (n = 5), uninvolved lymph nodes (n = 1), involved liver (n = 1), and bronchoalveolar lavage fluid (n = 1). Positive and negative controls were included in each PCR, with 40 amplification cycles conducted in a thermal cycler (Perkin Elmer 9600; Perkin Elmer LLC, Norwalk, Conn). β-Globin gene amplification was performed using PCR to exclude the possibility of a PCR inhibitor. Viral HHV-8 DNA were subtyped after phenolchloroform DNA extraction from skin biopsy samples (n = 13) and lymph nodes (n = 4) with KS. Direct nonnested PCR 233-base pair fragments were sequenced (ABI 377; Applied Biosystems Inc, Foster City, Calif) after PCR open reading frame 26 amplification with KS 330 primers. The 17 sequences were aligned with CLUSTAL W (available at: http://members.tripod.com/~moenicka/clustalw.html) using computer software (Sequence Navigator, Perkin Elmer LLC). Subtypes A, B, C, and variants were determined with the 4 key subtype designator positions within 9 polymorphic nucleotides, as described by Zong et al.4

Molecular epidemiologic findings with HHV-8 DNA subtyping enabled determination of prevalence of HHV-8 subtypes in organ-allograft recipients. Fisher exact test was used to compare extradermatological KS dissemination at diagnosis according to the HHV-8 subtype.

Phylogenetic relationships between HHV-8 subtypes were analyzed, and a phylogenetic tree was constructed with maximum likelihood using a package of programs for inferring phylogenies (PHYLIP; available at: http://evolution.genetics.washington.edu/phylip.html) in tree-drawing software (TreeView; available at: http://taxonomy.zoology.gla.ac.uk/rod/treeview.html).
patients and sometimes as vegetative tumors (n=3). They were localized to 1 limb in 3 patients and diffuse in 16 patients.

Extradermatological localization of KS was observed in 11 patients (Table 1). In the gastrointestinal tract, KS lesions did not cause clinical manifestations; they were localized in the stomach (n=9), duodenum (n=1), and colon (n=3), with multiple localization in 4 patients. In the 5 patients with suspected KS on computed tomographic scans of the chest, 2 had histologically confirmed endobronchial KS lesions. In the 3 others, the diagnosis of pulmonary KS was made by excluding other possible diagnoses.

**EVOLUTION OF KS**

Remission was observed in 9 of the 18 kidney-allograft recipients. Two of them had extensive cutaneous KS, which disappeared without any reduction of immunosuppressive therapy once pulmonary tuberculosis had been treated (Figure 1). The time between the first reduction of immunosuppressive therapy and remission was 11.2 (range, 4-20) months. In 5 of these 9 patients, kidney function remained stable. Four resumed dialysis treatment; of these, 3 had chronic kidney rejection prior to KS.

Stabilization was obtained in 9 patients: 6 received kidneys; 1, a heart; and 2, liver grafts. Of these 9, 3 had visceral involvement at KS diagnosis. The mean ± SD time between the first reduction of immunosuppressive therapy and KS stabilization was 3.6 ± 2.0 months. Of these 9 patients, 2 were treated secondarily with bleomycin sulfate (mean dose, 90 mg) due to KS-associated functional disability (leg edema or foot lesions). Treatment was stopped when the functional disability disappeared. One patient resumed dialysis treatment 1 year later because of chronic graft rejection. Others retained good organ function, with a mean follow-up of 21 (range, 16-32) months. Visceral and skin KS progressed suddenly in 1 of these patients 12 months after KS stabilization and concomitant with the development of a fatal pancreatic adenocarcinoma.

The progression of KS despite reduced immunosuppressive therapy was noted for 2 allograft recipients. High doses of intravenous immunoglobulins failed to stop the progression. One patient was treated with a cumulative dose of bleomycin sulfate, 105 mg, which was stopped 14 weeks later because of the development of lung fibrosis. Despite pulse therapy with high-dose methylprednisolone given for lung fibrosis, chronic kidney rejection led to end-stage renal failure. Kaposi sarcoma stabilized after removal of the kidney allograft and reduction of the dose of methylprednisolone. In the other patient with visceral KS treated with iterative chemotherapy, KS progressed; the patient had white lungs in the chest radiographic results and died after 68 months of follow-up.

**VIROLOGICAL AND IMMUNOLOGICAL HHV-8 ASSAYS**

All tested organ-allograft recipients had antibodies to HHV-8 in serum samples collected before transplantation (n=18) and at the time of KS diagnosis (n=20). The 2 living donors were also seropositive for HHV-8.

The results of PCR using PBMC DNA were negative for the HHV-8 genome at the time of transplanta-
tion (5 of 5) and positive for the HHV-8 genome at KS diagnosis (5 of 10). No relationship could be established between KS dissemination and PCR results positive for HHV-8 in PBMC. Furthermore, the results of PCR for HHV-8 performed with 1 mL of ultracentrifuged serum from 10 patients 1 month before KS onset were all negative for HHV-8.

The results of PCR were positive for HHV-8 in all KS-involved tissues (skin \(n=19\), lymph nodes \(n=5\), and liver \(n=1\)) and in 1 uninvolved lymph node. The results were negative for HHV-8 in all distant normal skin (\(n=14\)) and in all previously involved skin after remission of KS lesions (\(n=6\)). The presence of the HHV-8 genome was not detected in bronchoalveolar lavage fluid of a patient with pulmonary KS.

The distribution of HHV-8 subtypes and countries of origin of 17 patients are reported in Table 2. Subtype C occurred in 9 patients (53%) from sub-Saharan Africa, where a new C variant occurred in 1 patient (6%); subtype B’ occurred in 5 patients (29%) from North Africa (\(n=2\)), Europe (\(n=2\)), and Madagascar (\(n=1\)); and subtype A occurred in 2 patients (12%) from North Africa and Europe. The HHV-8 subtype C/C variant (10 patients [59%]) was the most prevalent and was not associated with extradermatological KS localization compared with HHV-8 subtypes A and B’. Extradermatological KS sites were present at diagnosis in 5 of 7 patients with subtype A or B’ and in 4 of 10 patients with subtype C/C variant; the difference was not statistically significant (\(P=.33\)).

A phylogenetic tree representing the divergence according to variation of nucleotides among the different subtypes was constructed (Figure 2). In agreement with a previous analysis, we also found that subtype B’ was more distant from subtypes A and C than A and C were from each other.

**COMMENT**

Dermatological and KS visceral lesions in organ-allograft recipients do not differ significantly from those of other epidemiological forms of KS. Unilateral or bilateral lymphatic leg edema was frequently (7 [35%] of 20) observed at an early stage of the disease, occurring 6 months before other KS skin lesions. This frequency of early lymphatic edema was recently explained by HHV-8 tropism for lymphatic endothelial cells.

As in other types of KS, disease severity depends on the patient’s extent of immune deficiency. Unlike patients with KS associated with acquired immunodeficiency syndrome (AIDS), peripheral blood lymphocyte counts, especially helper T lymphocytes (CD4), are not a reliable marker for assessing the transplant recipient’s degree of immune deficiency; therefore, the application of Krown’s criteria can be excluded. Several prognostic factors have to be taken into account for KS prognosis in organ-allograft recipients. Higher death rates (25% to 86%) in kidney recipients were previously reported for those with extradermatological KS. In our series, only 1 of the 10 kidney-transplant recipients with early visceral involvement died after 68 months of follow-up.

The detrimental effect of KS visceral dissemination on graft survival is also likely, as only 5 of 10 kidney recipients with visceral KS had graft survival, while 7 of 8 patients with only skin KS retained good kidney function. Another major prognostic factor for graft loss is the presence of a previous ongoing kidney rejection, present in 3 of 5 transplant recipients who resumed dialysis treatment vs 0 of 12 who retained good kidney function. In another series, all 4 patients with previous ongoing kidney rejection resumed dialysis treatment. The presence of prior or concomitant opportunistic infections was not associated with a poor prognosis since 5
of the 7 patients with such infections experienced KS remission without chemotherapy (Table 1). When tuberculosis was concomitant with the onset of KS (n=2), complete remission was obtained with antibiotics alone.

Management of KS in organ-allograft recipients poses a dilemma: to achieve KS remission, immunosuppressive therapy must be reduced, but to do so increases the risk of losing the graft. There is consensus that immunosuppressive therapy must be tapered to the lowest level consistent with adequate allograft function. However, drastic reduction of immunosuppressive therapy is inconceivable for vital organs, such as the liver or heart, because of the high risk of acute graft rejection. For all the kidney recipients in the present study, immunosuppressive therapy was progressively tapered even when the patients had visceral involvement (10 [55%] of 18). In the Cincinnati, Ohio, registry,10 KS remission after reducing immunosuppressive therapy alone occurred in 17% of the 213 patients with mucocutaneous involvement and 16% of the 143 patients with visceral involvement. Compared with the remission rate (9 [50%] of 18) reported in the present study, these values were probably underestimated because the long mean intervals between reducing immunosuppressive therapy and KS stabilization (3.6 months) or remission (11.0 months) were never taken into account in previous studies.12,13 Our aim was to obtain stabilization rather than remission of KS that was neither life-threatening nor disabling. Initially, KS appears to be a benign and reversible polyclonal hyperplasia,14 although monoclonality has been reported during late KS stages.15

Unlike 1 patient with iatrogenic KS associated with polymyositis,16 high-dose intravenous immunoglobulins did not stop KS progression in 2 of our patients. To our knowledge, no controlled therapeutic trials evaluating several antiviral drugs (cidofovir, foscarnet sodium, and ganciclovir sodium) that inhibit HHV-8 replication in vitro17 have been published for organ-allograft recipients with KS.

### Table 2. Comparison of Open Reading Frame (ORF) 26 Sequence Variability of Human Herpesvirus 8 DNA in Kaposi Sarcoma (KS) Samples and Origin of Recipients*

<table>
<thead>
<tr>
<th>Patient No./Sex</th>
<th>Allograft Source</th>
<th>ORF 26 (233 Base Pairs)</th>
<th>Subtype Origin</th>
<th>Extradermatological KS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/F</td>
<td>AIDS-KS, Lymph</td>
<td>C C G C G A A C G A</td>
<td>United States</td>
<td>...</td>
</tr>
<tr>
<td>2/M</td>
<td>Kidney, Skin, Lymph node</td>
<td>C T G C G A T A C G A</td>
<td>Algeria</td>
<td>+</td>
</tr>
<tr>
<td>3/M</td>
<td>Heart, Skin, Lymph node</td>
<td>A T T C G G T C C G B</td>
<td>France</td>
<td>-</td>
</tr>
<tr>
<td>4/M</td>
<td>Kidney, Lymph node</td>
<td>A T T C G G T C C G B</td>
<td>Portugal</td>
<td>+</td>
</tr>
<tr>
<td>5/F</td>
<td>Kidney, Skin, Lymph node</td>
<td>A A T G G T G T C C G B</td>
<td>Algeria</td>
<td>-</td>
</tr>
<tr>
<td>6/M</td>
<td>Kidney, Skin, Lymph node</td>
<td>A A T G G T G T C C G B</td>
<td>Mauritania</td>
<td>+</td>
</tr>
<tr>
<td>7/M</td>
<td>Kidney, Skin, Lymph node</td>
<td>A A T G G T G T C C G B</td>
<td>Madagascar</td>
<td>+</td>
</tr>
<tr>
<td>8/M</td>
<td>Lung, Skin, Lymph node</td>
<td>A T T C G G T C C G C</td>
<td>Algeria</td>
<td>+</td>
</tr>
<tr>
<td>9/M</td>
<td>Kidney, Lymph node</td>
<td>A A T G G T G T C C G C</td>
<td>Central African Republic</td>
<td>-</td>
</tr>
<tr>
<td>10/M</td>
<td>Kidney, Skin, Lymph node</td>
<td>A A T G G T G T C C G C</td>
<td>Senegal</td>
<td>-</td>
</tr>
<tr>
<td>11/M</td>
<td>Kidney, Lymph node</td>
<td>A A T G G T G T C C G C</td>
<td>Senegal</td>
<td>+</td>
</tr>
<tr>
<td>12/F</td>
<td>Kidney, Skin, Lymph node</td>
<td>A A T G G T G T C C G C</td>
<td>Senegal</td>
<td>-</td>
</tr>
<tr>
<td>13/F</td>
<td>Kidney, Skin, Lymph node</td>
<td>A A T G G T G T C C G C</td>
<td>Cameroon</td>
<td>-</td>
</tr>
<tr>
<td>14/M</td>
<td>Kidney, Lymph node</td>
<td>A A T G G T G T C C G C</td>
<td>Cameroon</td>
<td>+</td>
</tr>
<tr>
<td>15/M</td>
<td>Kidney, Lymph node</td>
<td>A A T G G T G T C C G C</td>
<td>Cameroon</td>
<td>+</td>
</tr>
<tr>
<td>16/M</td>
<td>Kidney, Skin, Lymph node</td>
<td>A A T G G T G T C C G C</td>
<td>French Guiana</td>
<td>-</td>
</tr>
<tr>
<td>17/F</td>
<td>Kidney, Skin, Lymph node</td>
<td>A A T G G T G T C C G C</td>
<td>C variant Ivory Coast</td>
<td>-</td>
</tr>
</tbody>
</table>

*Ellipses indicate not applicable; AIDS-KS, Kaposi sarcoma associated with acquired immunodeficiency syndrome; plus sign, presence; minus sign, absence; and C, new mutation to determine C variant subtype.
†Four key subtype designator positions according to Zong et al.4

![Figure 2. Phylogenetic tree of subtypes A/A', B', and C/C variant in open reading frame (ORF) 26 of human herpesvirus 8 isolated from 17 allograft recipients with Kaposi sarcoma.](image-url)
At present, HHV-8 virological investigations contribute poorly to KS management. In the present study, the results of PCR were always positive for HHV-8 in KS samples and in 1 uninvoluted KS lymph node. Although bronchoalveolar lavage fluid has been reported to be useful for HHV-8 detection using PCR in pulmonary KS associated with AIDS and in 1 case of iatrogenic KS, no negative result has been reported previously.

The serological indirect immunofluorescence assay on BCP-1 cells (with chronic HHV-8 but not Epstein-Barr virus) that we used targeted antibodies directed against latent nuclear antigen 1 and has been used in numerous epidemiological studies to determine HHV-8 seroprevalence with high specificity and sensitivity, which varied according to the epidemiological form of KS. In our experience, in all the patients with iatrogenic or sporadic KS, the indirect immunofluorescence assay results were positive for HHV-8 at diagnosis.

We detected HHV-8 DNA in the PBMC of only 5 of the 10 patients in the present study, but it was detected in as many as 78% in another series. No correlation could be established between nonquantitative detection of HHV-8 DNA in the results of PCR and visceral dissemination of KS at diagnosis. Although a decreasing quantitative detection of HHV-8 DNA in the PCR results has been correlated with KS remission in patients with AIDS receiving highly active antiretroviral therapy and in patients with iatrogenic KS with reduced immunosuppressive therapy, whether the results of PCR on PBMC DNA from allograft recipients with HHV-8 prior to transplantation predict KS remains to be determined in prospective studies. Moreover, 1 month before KS onset, no HHV-8 DNA could be detected by PCR in the serum samples of 10 patients. Thus, this method, unlike PCR performed in PBMCs in individuals infected with human immunodeficiency virus, had no predictive value for the future development of KS and appeared not to be useful for early KS diagnosis. These observations are in accordance with the fact that PCR detection of the HHV-8 genome in serum samples is very rare and mainly achieved during clinical exacerbation of Castleman disease. However, lack of detection of HHV-8 in serum samples 1 month prior to KS does not necessarily mean that replication is not occurring prior to development of KS and more sensitive assays and/or evaluation at points closer to onset of the disease may need to be assessed to evaluate this hypothesis.

In contrast to the results of Boralevi et al obtained in patients with AIDS, the marked aggressiveness of subtype A was not obvious in our series. However, the small number of organ-allograft recipients included in our analysis could be a limiting factor; thus, the aggressiveness of subtype A cannot yet be excluded in this context.

A future goal is to prevent KS in organ-allograft recipients. To do so, HHV-8 investigations will have to be able to identify patients at high risk of subsequently developing KS and the cofactors associated with this risk. In the series of Regamey et al, KS was observed only in patients with seroconversion to HHV-8 within the first year after transplantation. In contrast, all our patients and 10 of the 11 organ recipients in another series who developed KS had HHV-8 seropositive results prior to transplantation. Thus, reactivation of HHV-8 is mainly associated with KS in organ-allograft recipients. This reactivation is also supported by the similarity between the observed HHV-8 subtypes and those prevalent in the patients' respective countries of origin. Immunosuppressive therapy alone given for transplantation is not sufficient to lead to KS development in organ-allograft recipients previously infected with HHV-8. Indeed, we previously demonstrated that only 28% of 32 kidney recipients positive for HHV-8 at the time of transplantation subsequently developed KS.

In recipients positive for HHV-8, bacterial and/or Pneumocystis carinii infection were significantly associated with KS development.

In conclusion, a more precise modulation of immunosuppressive therapy as a function of KS severity and organ rejection would probably improve the prognosis of KS in organ-allograft recipients. Remission of KS is not a goal to be sought at any price. At present, HHV-8 virological investigations do not contribute to the management of KS. To prevent KS in this context, the investigations will have to be improved to better evaluate the risk of HHV-8 reactivation and the associated cofactors must be identified. Then, new treatments can focus on ways to prevent KS while preserving organ function.

Accepted for publication July 13, 2000.

From the Departments of Internal Medicine (Drs Barete, Piette, and Frances), Renal Transplantation (Drs Mouquet, Barrou, and Bither), Virology (Drs Barete, Calvez, Dupin, and Marcelin), and Heart Transplantation (Dr Dorent), Pitié-Salpêtrière Hospital and the Department of Renal Transplantation, Necker Hospital (Dr Kreis), Paris; the Department of Renal Transplantation (Dr Danial), Hôtel-Dieu Hospital, Nantes; the Department of Liver Transplantation, Beaujon Hospital, Clichy (Dr Durand); the Unit of Renal Transplantation, Civil Hospital, Strasbourg (Dr Dimitrov), France.

This study was supported by grant 1999 from the Association Pour la Recherche Contre le Cancer, Villejuif, France. Dr Barete is a fellow of the Fondation pour la Recherche Médicale, Paris, France.

We thank Francis Angleraud, Jean Pierre Lagarde, MSc, and Catherine Milliancourt, MSc, for their technical assistance and Patrick Moore, MD, PhD, and Yuan Chang, MD, for providing BCP-1 cells.

Corresponding author: Stéphane Barete, MD, Service de Virologie CERVI, Groupe Hospitalier Pitié-Salpêtrière, 83, Boulevard de l'Hôpital 75651, Paris, Cedex 13, France (e-mail: stephane.barete@psl.ap-hop-paris.fr).

REFERENCES

4. Zong JC, Metroka C, Reitz MS, Nicholas J, Hayward GS. Strain variability among
Kaposi’s sarcoma–associated herpesvirus (human herpesvirus 8) genomes: evidence that a large cohort of United States AIDS patients may have been infected by a single common isolate. J Virol. 1997;71:2505-2511.


