option of oral administration make sildenafil an attractive alternative to conventional therapy for PHT. Further investigation is required to establish whether the decrease in PHT achieved by sildenafil has the potential to lower the risk of congestive heart failure in thalassemia patients.

To the editor:

AML, angiogenesis, and prognostic variables

A previous letter to this journal discussed the importance of correlating increased bone marrow microvessel density with known prognostic variables in acute myeloid leukemia (AML) since earlier reports have not addressed this issue. One group correlated indirect evidence of angiogenic potential (increasing VEGF protein with the traditional prognostic variables) in newly diagnosed AML with shorter overall and disease-free survival and also found VEGF protein to be an independent prognostic variable. However, no relationship between VEGF protein with the traditional prognostic variables such as white blood cell or blast count, age, cytogenetic changes, performance status, or presence of an antecedent hematologic disorder was found.

To address this issue, we collected 4 nonneoplastic control bone marrow specimens and 21 specimens that contained at least 80% AML from different treatment protocols. All samples were from the time of diagnosis unless otherwise noted in the data table. In a blinded fashion, we cultured 5 × 10⁶ cells 72 hours in 700 μL EGM (Clonetics) without human epidermal growth factor or bovine brain extract additives and 2% fetal bovine serum in 24-well plates in triplicate. The conditioned media from each well was collected, filtered, and placed over

Table 1.

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (y)/sex</th>
<th>Cytogenetics, dysplasia, relapse information</th>
<th>FAB</th>
<th>Prognostic category</th>
<th>% change in endothelial proliferation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>55/F</td>
<td>De novo, Inv(16), + 22</td>
<td>M4</td>
<td>F/I</td>
<td>− 12</td>
</tr>
<tr>
<td>2</td>
<td>50/M</td>
<td>De novo, 46XY</td>
<td>M5a</td>
<td>F/I</td>
<td>− 27</td>
</tr>
<tr>
<td>3</td>
<td>55/F</td>
<td>De novo, 46XX</td>
<td>M1</td>
<td>F/I</td>
<td>− 20</td>
</tr>
<tr>
<td>4</td>
<td>40/M</td>
<td>De novo, t(15;17), add 7(q36)</td>
<td>M3</td>
<td>F/I</td>
<td>− 32</td>
</tr>
<tr>
<td>5</td>
<td>19/M</td>
<td>Inv 16</td>
<td>M4Eo</td>
<td>F/I</td>
<td>− 42</td>
</tr>
<tr>
<td>6</td>
<td>32/M</td>
<td>De novo, + 11</td>
<td>M1</td>
<td>F/I</td>
<td>− 13</td>
</tr>
<tr>
<td>7</td>
<td>76/M</td>
<td>De novo, + 8</td>
<td>M0</td>
<td>F/I</td>
<td>− 50</td>
</tr>
<tr>
<td>8</td>
<td>67/M</td>
<td>t(15;17)</td>
<td>M3</td>
<td>F/I</td>
<td>− 41</td>
</tr>
<tr>
<td>9</td>
<td>68/F</td>
<td>De novo, + 4, + 11</td>
<td>M4</td>
<td>F/I</td>
<td>− 21</td>
</tr>
<tr>
<td>10</td>
<td>18/F</td>
<td>Relapsed, t(6;9)</td>
<td>M1</td>
<td>U</td>
<td>− 15</td>
</tr>
<tr>
<td>11</td>
<td>66/M</td>
<td>De novo, 46XY, relapse within 2 months</td>
<td>M2</td>
<td>U</td>
<td>− 53</td>
</tr>
<tr>
<td>12</td>
<td>64/M</td>
<td>+ 8, dyspoiesis</td>
<td>M1</td>
<td>U</td>
<td>+ 5.5</td>
</tr>
<tr>
<td>13</td>
<td>68/M</td>
<td>History of MDS, 46XY</td>
<td>M2</td>
<td>U</td>
<td>− 31</td>
</tr>
<tr>
<td>14*</td>
<td>31/F</td>
<td>t(11;19), relapsed within 6 months, dyspoiesis</td>
<td>M4</td>
<td>U</td>
<td>+ 35</td>
</tr>
<tr>
<td>15</td>
<td>54/M</td>
<td>11q23</td>
<td>M5a</td>
<td>U</td>
<td>− 19</td>
</tr>
<tr>
<td>16</td>
<td>83/F</td>
<td>Multiple relapses</td>
<td>M5a</td>
<td>U</td>
<td>+ 5</td>
</tr>
<tr>
<td>17</td>
<td>68/F</td>
<td>t(9;22) and – 7</td>
<td>Mixed lineage</td>
<td>U</td>
<td>+ 3</td>
</tr>
<tr>
<td>18*</td>
<td>42/M</td>
<td>Complex karyotype</td>
<td>M1</td>
<td>U</td>
<td>+ 0</td>
</tr>
<tr>
<td>19*</td>
<td>55/M</td>
<td>History of MDS</td>
<td>M5</td>
<td>U</td>
<td>− 27</td>
</tr>
<tr>
<td>20</td>
<td>61/F</td>
<td>History of CMML, complex karyotype</td>
<td>M4</td>
<td>U</td>
<td>− 12</td>
</tr>
<tr>
<td>21</td>
<td>53/F</td>
<td>History of MDS, complex karyotype</td>
<td>M2</td>
<td>U</td>
<td>− 26</td>
</tr>
</tbody>
</table>

*Sample analyzed was from time of relapse (after treatment).
FAB indicates French-American-British classification.
intermediate prognosis AML; 10005 cases (n
P
difference (versus the percent change, there is clear evidence of statistical
endothelial growth at least minimally. When this data were
unfavorable but 0 of 9 F/I cases were able to support or enhance
prognosis cases (n
relapse within 6 months of diagnosis. Favorable/intermediate
tory, or morphologic evidence of myelodysplasia, or disease
enhance endothelial proliferation.

1 × 10^4 human umbilical vein endothelial cells (Clonetics,
Walkersville, MD) for an additional 72 hours. Endothelial cell
proliferation was measured using the MTT assay. 7

AML samples were classified into 2 broad, therapeutically
relevant prognostic groups: favorable/intermediate (F/I) and
unfavorable (U) according to published criteria. 8,9 Unfavorable
cases (n = 12) were those with unfavorable cytogenetics, his-
tory, or morphologic evidence of myelodysplasia, or disease
relapse within 6 months of diagnosis. Favorable/intermediate
prognosis cases (n = 9) were those without these features.

As compared to controls (Table 1, Figure 1), 6 of 12
unfavorable but 0 of 9 F/I cases were able to support or enhance
endothelial growth at least minimally. When this data were
analyzed using the Duncan multiple means test for the prognosis
versus the percent change, there is clear evidence of statistical
difference (P < .05) between the F/I and unfavorable groups.

Other investigators have used AML culture supernatants as
we have and demonstrated enhanced endothelial growth in vitro;
however, without correlation with prognostic variables. 4,10 Our
preliminary results suggest that AML cases with unfavorable
prognostic features are more likely to enhance endothelial
proliferation in vitro than cases with favorable/intermediate
prognosis. The nature of a possible relationship between prog-
nostic variables and enhanced endothelial proliferation is intrigu-
ing. It may be that the complex karyotypic and molecular
genetic changes in unfavorable prognosis AML blasts alter the
expression of angioregulatory molecules such as VEGF, as
suggested previously. 6

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To the editor:

SENV-H viremia and liver transplantation: significant increase of the prevalence

SENV virus H (SENV-H) is a novel circular single-stranded DNA
virus that has been assumed to be associated with posttransfusion
hepatitis. 1 A recent investigation revealed that in about 2% to 10%
of healthy Japanese blood donors, SENV-H viremia can be detected
by polymerase chain reaction (PCR). 1,2 To determine the risk for
SENV-H transmission by blood and blood products, we examined
26 patients (8 women and 18 men; mean age 47) who underwent
liver transplantation (LTX) between 1995 and 1998 in a retrospec-
tive study. These patients are at high risk for acquiring transfusion-
transmitted agents due to the numerous units of blood and blood
products administered to them during surgery. All patients had liver
cirrhosis due to chronic hepatitis C virus (HCV) infection. At least
one sample from before and after LTX was available from all
patients. Additional follow-up samples were available from 12
patients over a period of up to 3 years.

SENV-H infection was investigated by nested PCR using primers
directed against a conserved region within the postulated open reading
frame 1. 3 Before LTX, SENV-H DNA was detectable in 3 (11.5%) of the
26 patients. Postoperatively, one of the initially SENV-H viremic and 11
additional patients (46%) had detectable viremia in sera drawn between
days 6 and 14 after transplantation. Additional follow-up samples were
available from 8 viremic and 4 negative patients; 6 of the viremic
patients became negative within 1 year of infection. In the other patients,
viremia became undetectable within 2 and 3 years, respectively. The 4
patients who were initially negative remained negative during the entire
follow-up period.

Since transfusion of blood and blood products is supposed to be
a major route of SENV-H transmission, 4 we examined the number of
blood products (blood plasma, erythrocyte, and thrombocyte
concentrates) administered to the patients in connection with the

Figure 1. Effect of conditioned media from AML and nonneoplastic bone
marrow samples on endothelial proliferation. AML samples from patients with
unfavorable prognostic features (defined in text) were significantly more likely to
enhance endothelial proliferation. ◇, non-neoplastic bone marrows; △, favorable/
intermediate prognosis AML; ▲, unfavorable prognosis AML.
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