Patient imaging studies and dosimetric calculations

The patients received an intravenous injection of labeled anti-CD66 antibody as a slow intravenous push. Blood samples were obtained at 5 and 30 min; 1, 2, and 4 h; and 1, 2, 3, and 6 d after injection. Planar whole-body scintigraphies (anterior and posterior views) with a double-head $\gamma$-camera (ECAM; Siemens) were performed at 2 and 4 h and 1, 2, 3, and 6 d after injection to evaluate the distribution and elimination of the radiotracer. Scanning speed was varied to adjust for physical decay.

A region-of-interest (ROI) analysis was performed to determine the activity within the accumulating organs (kidneys, liver, red bone marrow, spleen) and the abdominal background. The red marrow uptake was defined using an ROI drawn over the L2–L4 vertebrae and a scale factor from the Reference Man model. The ROIs were drawn individually on 1 scan of each patient and copied and adjusted to the subsequent images. A background correction was performed for the red bone marrow, spleen, and kidneys, by assuming the following organ-specific fractions of the abdominal background: 0.8, 0.67, and 0.75, respectively. To obtain the counts for the remainder of the body, the sum of the organ counts was subtracted from the whole-body counts. The count distribution within the geometrically averaged image was then assumed to be proportional to the activity distribution within the body, as no transmission was performed for attenuation correction.

For bone marrow the selection between three methods were possible: patient height adjusted according to a reference man model (L2–L4 vertebrae or L4 only) or multiple ROI selections. The scale factor $f_L$ for the reference man model is calculated according to (Eq. 8 in Ref.3)

$$f_L = \frac{170}{\text{height(cm)}} \cdot \frac{1}{L}$$

with L=0.06665 when using a ROI around the L2–L4 vertebrae and L=0.02305 for a L4 ROI only. In case of multiple ROI selections the scale factor is the ratio between the total pixel number of the selected ROIs and the number of pixels in the bone marrow ROI.

Decay-corrected time-activity data for the source organs were fitted with up to 3 exponential functions. Organ residence times, which are a measure for the relative number of decays in each organ, were calculated using these results and correcting for the physical decay of the nuclide used for therapy.

Estimation of radiation-absorbed doses

The calculated residence times were applied to the appropriate phantom dosimetry model contained in the OLINDA/EXM software. Internal radiation-absorbed doses were then calculated using the method recommended by the MIRD Committee of the Society of Nuclear Medicine.

Antibody labeling

The anti-CD66 antibody (BW250/183) used in this study is described by Ringhoffer et al. The labeling with $^{111}$In or $^{90}$Y was conducted in 2 steps. First, the bifunctional chelator [2-(p-SCN-Bz)-6-methyl-diethylenetriaminepentaacetic acid [DTPA]] was attached to the antibody, and second the radioisotope was bound to the chelator. Briefly, 10 mg of antibody and 18 mg of mx-DTPA were incubated at pH 8.5 for 2 h at room temperature and 15 h at 4°C. Then excess mx-DTPA was removed using gel filtration/size-exclusion chromatography. Subsequently, fluorescence-activated cell sorting (FACS) analysis was used to test an aliquot of the antibody-chelator complex for immunoreactivity. The immunoreactivity was greater than 90%. Radiolabeling was conducted, incubating the antibody-chelator complex with yttrium chloride or indium chloride at a pH of 5.0–5.5 for 5 min ($^{90}$Y) and for 30 min ($^{111}$In) at room temperature. To evaluate the radiochemical purity, an aliquot of the labeled antibody was subjected to size-exclusion chromatography–high-performance liquid chromatography. The antibody solution was sterilized using Millipore filtration.
<table>
<thead>
<tr>
<th>Criterion</th>
<th>Number of patients</th>
<th>Leukocytes &gt; 1G/l [d+]</th>
<th>Neutrophiles &gt; 0.5 G/l [d+]</th>
<th>Platelets &gt; 20 G/l [d+]</th>
<th>Reticulocytes &gt; 10% [d+]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marrow radiation dose ≥ 40 Gy (TBI and RIT)</td>
<td>4</td>
<td>19 (8–32)</td>
<td>21 (12–32)</td>
<td>31 (19–42)</td>
<td>29 (17–52)</td>
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<tr>
<td>Marrow radiation dose &lt; 40 Gy (TBI and RIT)</td>
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<td>21 (5–31)</td>
<td>21 (12–31)</td>
<td>51 (11–125)</td>
<td>23 (14–30)</td>
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<tr>
<td>TBI containing conditioning</td>
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<td>20 (8–32)</td>
<td>22 (12–32)</td>
<td>44 (11–125)</td>
<td>23 (14–52)</td>
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<tr>
<td>Conditioning without TBI</td>
<td>6</td>
<td>19 (5–28)</td>
<td>21 (12–31)</td>
<td>49 (24–84)</td>
<td>25 (19–30)</td>
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<tr>
<td>Stem cell source BM</td>
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<td>25 (15–32)</td>
<td>25 (14–32)</td>
<td>55 (11–125)</td>
<td>22 (14–28)</td>
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<tr>
<td>Stem cell source PBSC</td>
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<td>17 (12–23)</td>
<td>39 (19–61)</td>
<td>27 (17–52)</td>
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<tr>
<td>All patient with leukemia (A1–A13)</td>
<td>13</td>
<td>20 (5–32)</td>
<td>21 (12–32)</td>
<td>47 (11–125)</td>
<td>25 (14–52)</td>
</tr>
</tbody>
</table>
Figure S1. Estimated absorbed doses of radioimmunotherapy
Box-and-whiskers plots showing median, lower and upper quartiles, sample minimum and maximum in different organs. Doses are calculated based on a pre-therapeutic dosimetry using $^{111}$In-labeled anti-CD66 monoclonal antibody and planar $\gamma$ camera measurements.

A

Group A, malignant diseases

B

Group B, non-malignant diseases
Figure 2. Reconstitution of hematopoiesis depending on disease
The ratio of patients achieving reconstitution levels post HCT are shown.

(A) Reconstitution of leucocytes (>1.0 × 10^9/L leukocytes at three consecutive days).
(B) Reconstitution of neutrophils (>0.5 × 10^9/L neutrophils at three consecutive days).
(C) Reticulocyte reconstitution (>1% reticulocytes at three consecutive days).
(D) Reconstitution of platelets (>20.0 10⁹/L platelets at three consecutive days and at least seven day after last platelet transfusion).
Figure S3. Reconstitution of hematopoesis depending on absorbed bone marrow doses by radioimmunotherapy
The ratio of patients achieving reconstitution levels post HCT are shown.

(A) Reconstitution of leukocytes (>1.0 × 10^9/L leukocytes at three consecutive days).
(B) Reconstitution of neutrophils ($>0.5 \times 10^9$/L neutrophils at three consecutive days).
(C) Reticulocyte reconstitution (>1% reticulocytes at three consecutive days).
(D) Reconstitution of platelets (>20.0 $10^9$/L platelets at three consecutive days and at least seven day after last platelet transfusion).
REFERENCES