The Incidence of New Malignancy in Patients with Acute Leukemia Treated with Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) 1971 – 2006.

A Retrospective National Cohort Study.

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Background

• HSCT patients have an increased risk of new malignancy following treatment.

• New malignancies include:
  - Post-transplant lymphoproliferative disorders (PTLD)
  - Myelodysplastic syndrome (MDS)/Acte myeloid leukemia (AML)
  - Solid cancer
  - Donor-derived hematological malignancies

Risk of new malignancy

- Genetic predisposition
- Age
- Gender
- Life style factors
- Infections
- Treatment exposures

Conditioning regimen (TBI, chemotherapy)
- Relapse therapy
- Immunosuppression
- Chronic GvHD
- Age
- Gender

Pre-HSCT

HSCT

Post-HSCT
Risk factors of Relapse and New Malignancy after allo HSCT
Purpose

- To describe the incidence of new malignancy (excl. PTLD) among patients treated for acute leukemia by allogeneic HSCT in the Danish population.
Methods

• Retrospective Danish national cohort study
• Diagnosed with acute leukemia
• Allogeneic HSCT (April 14th. 1971- Jan. 1st. 2006)
• Follow up Dec. 14th 2011
Data Collection

- One allogeneic HSCT center (team 10186)
  National data base

- Civil Registration System

- National clinical data base e.g. pathology

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## Characteristic

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No. of patients (n=460)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>276</td>
<td>60</td>
</tr>
<tr>
<td>Female</td>
<td>184</td>
<td>40</td>
</tr>
<tr>
<td>Age at HSCT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median age (min-max)</td>
<td>21.4 y. (0.6y. - 59.5y.)</td>
<td></td>
</tr>
<tr>
<td>Disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALL</td>
<td>247</td>
<td>53.7</td>
</tr>
<tr>
<td>AML</td>
<td>213</td>
<td>46.3</td>
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<tr>
<td>Stem cell source</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BM</td>
<td>381</td>
<td>82.8</td>
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<tr>
<td>PBSC</td>
<td>77</td>
<td>16.7</td>
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<td>UCB</td>
<td>2</td>
<td>0.4</td>
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<tr>
<td>Donor – recipient relationship</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Related</td>
<td>252</td>
<td>54.8</td>
</tr>
<tr>
<td>Unrelated</td>
<td>208</td>
<td>45.2</td>
</tr>
<tr>
<td>TBI (8.5 – 12 GY)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>98</td>
<td>21.3</td>
</tr>
<tr>
<td>Yes</td>
<td>362</td>
<td>78.7</td>
</tr>
</tbody>
</table>
Results

• Allogeneic HSCT for Acute leukemia n=460
• Person-years at risk = 3.18 y.

• Diagnosed with PTLD n=6

• Diagnosed with a new malignancy n=28 (6%)
  – hematologic cancer (leukemia/MDS) n=1 (4%)
  – solid cancer n=27 (96%)
## Results – New solid cancer

<table>
<thead>
<tr>
<th>Site</th>
<th>Number (n=27)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNS</td>
<td>6</td>
<td>22</td>
</tr>
<tr>
<td>Skin</td>
<td>6</td>
<td>22</td>
</tr>
<tr>
<td>Lung</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Pancreas</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Oral cavity</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Thyroid</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Cervix</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Uterine corpus</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Ovarian</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Esophagus</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Prostate</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Breast</td>
<td>1</td>
<td>4</td>
</tr>
</tbody>
</table>
Results – time

HSCT  ➔  New malignancy

- Median time = 4457 days (12.21 y.)
- Range 666 days (1.8 y.) – 8877 days (24.3 y.)
Cummulative incidence
Risk of Secondary Malignancy after Allo SCT for Acute Leukemia

N:96 Minus TBI for conditioning

N:454 Total

%
Risk of Secondary Malignancy after Allo SCT for Acute Leukemia

%}

N:111 Ch GvHD ≤ 1y

N:343 No Ch GvHD

Years

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Risk of Secondary Malignancy after Allo SCT for Acute Leukemia

N: 349 Patients over 10 years at time of SCT

N: 105 Patients under 10 years at time of SCT

p = 0.24
Results - Risk factors new malignancy

Of the 28 patients with a new malignancy:

- \( n = 24 \) (86%) conditioned with TBI
- \( n = 9 \) (32%) chronic GvHD
- \( n = 12 \) (42%) this was the primary cause of death
Conclusions

• In the Danish cohort the patients with acute leukemia (n=460), 28 patients were diagnosed with a new malignancy following allogeneic HSCT.
• New malignancy as primary cause of death in the total cohort (n=460) = 2.6%
• Median time to new malignancy = 12 years

• No significant difference was identified between patient age at HSCT, the use of conditioning regimen with or without TBI and the development of chronic GvHD.

• **Strength:** Centralized access to patient information regarding hospitalization, pathology and vital status = complete data

• **Limitations:** Only patients diagnosed with acute leukemia treated with myeloablative allogeenic HSCT is included.
Thank you