**SUPPORTING INFORMATION**

**Table S1:** Morphologic subtypes of PTLD included in the study

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**Table S4:** Cancer risk following first PTLD diagnosis by latency period (≤ 6 months, or > 6 months after PTLD)

**Table S5:** Risk of selected cancers following first PTLD diagnosis according to cancer stage

**Figure S1:** Distribution of the time from PTLD to cancer diagnosis according to cancer stage

**Table S1:** Morphologic subtypes of PTLD included in the study

|  |  |
| --- | --- |
| **Morphologic subtype of PTLDa** | **No. of PTLD diagnoses**b |
| **Any PTLD** | 3,591 |
|  |  |
| **Any lymphoid malignancy** | 3,045 |
| **NHLs** |  |
| *B-cell NHLs* |  |
| Diffuse large B cell lymphoma | 1,418 |
| Burkitt lymphoma | 134 |
| Marginal zone lymphoma | 61 |
| CLL/SLL | 55 |
| Follicular lymphoma | 46 |
| Lymphoplasmacytic lymphoma | 14 |
| *T-cell NHLs* |  |
| Peripheral T-cell lymphoma, NOS | 55 |
| T-cell NHLs, Other/NOS | 121 |
| *NHL, Others/NOS* | 482 |
| **Hodgkin lymphoma** | 152 |
| **Plasma cell neoplasms** | 198 |
| **Acute lymphocytic leukemia** | 19 |
| **Lymphoid neoplasm, Others/NOS** | 290 |
|  |  |
| **Polymorphic PTLD** | 566 |
| **PTLD, NOS** | 115 |
|  |  |

**Abbreviations:** CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma; NHL, non-Hodgkin lymphoma; NOS, not otherwise specified; PTLD, post-transplant lymphoproliferative disorder

a First diagnosis of a PTLD type. A transplant recipient could have multiple types of PTLD but only the first diagnosis of any PTLD, any lymphoid malignancy, polymorphic PTLD, and PTLD NOS are considered. During follow-up, 3,591 recipients were diagnosed with PTLD of any type [lymphoid malignancy only, n=2,917; polymorphic PTLD only, n=448; PTLD not otherwise specified only, n=92; multiple PTLD types, n=134].

b Number of transplant recipients with at least one type of PTLD diagnosis

**Table S2:** Cancer risk following first lymphoid neoplasm or polymorphic PTLD diagnosis

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Cancers** | **No. of cancers** | **First lymphoid malignancya** | | **First polymorphic PTLDa** | |
| **No. with PTLD\*** | **aHR (95% CI)** b | **No. with PTLD\*** | **aHR (95% CI)** b |
|  |  |  |  |  |  |
| All non-PTLD cancers | 11,968 | 226 | 1.5 (1.3 - 1.8) | 44 | 2.9 (1.8 - 4.7) |
|  |  |  |  |  |  |
| Colon | 719 | 17 | 2.3 (1.3 - 4.0) | 2 | … |
| Lung | 2,057 | 26 | 1.0 (0.6 - 1.7) | 5 | 2.1 (0.5 - 8.5) |
| Melanoma | 580 | 8 | 1.5 (0.7 - 3.5) | 5 | 4.7 (0.7 - 33.3) |
| Female breast | 741 | 8 | 0.9 (0.3 - 2.4) | 3 | … |
| Prostate | 1,706 | 35 | 0.9 (0.5 - 1.5) | 6 | 3.6 (0.9 - 14.6) |
| Kidney | 1,142 | 26 | 2.3 (1.4 - 3.9) | 2 | 2.4 (0.3 - 17.0) |
| Thyroid | 342 | 13 | 6.3 (3.3 - 11.9) | 1 | … |
| Non-lymphocytic leukemiac | 510 | 13 | 2.6 (1.4 - 5.0) | 1 | 3.2 (0.5 - 22.9) |
| Miscellaneousd | 828 | 12 | 1.6 (0.8 - 3.0) | 7 | 4.8 (1.2 - 19.1) |
|  |  |  |  |  |  |

**Abbreviations:** aHR, adjusted hazard ratio; CI, confidence intervals; CNS, central nervous system; PTLD, post-transplant lymphoproliferative disorder

a Refers to the first occurrence of first lymphoid malignancy or first polymorphic PTLD in the SRTR or linked cancer registry. The “No. with PTLD” column refer to number of PTLD cases that were diagnosed before non-PTLD cancers.

b Hazard ratios were obtained from Cox regression models with age as the time scale, PTLD diagnosis as a time-dependent variable, and adjusted for the following variables decided *a priori*: sex, race/ethnicity, year of transplant, transplanted organ, and time since transplantation (as a time-dependent variable). Risk for specific cancers could not be evaluated in detail due to the small number of individuals with polymorphic PTLD.

c Non-lymphocytic leukemia includes myelodysplasia and myeloproliferative neoplasms.

d Miscellaneous includes cancers of other gastrointestinal tract sites (n=96), other respiratory tract organs (n=68), male breast (n=31), other female genitalia (n=82) other male genitalia (n=97), eye (n=30), other endocrine glands (n=15), leukemia NOS (n=24), and unknown/uncertain primary cancers (n=385).

Underlined estimates were considered statistically significant based on two-sided p < 0.05.

“…” indicates that the model did not converge

**Table S3:** Cancer risk following first PTLD diagnosis, stratified by transplanted organs

|  |  |  |  |
| --- | --- | --- | --- |
| **Cancers**  Transplanted organs | **No. of cancers** | **No. of PTLD cases**a | **aHR (95% CI)** b |
| **All non-PTLD cancers** | 11,968 | 272 | 1.6 (1.4 - 1.9) |
| Kidney | 6,462 | 114 | 1.9 (1.5 - 2.4) |
| Liver | 2,167 | 55 | 1.4 (1.0 - 2.0) |
| Heart and/or Lung | 2,931 | 92 | 1.4 (1.1 - 1.9) |
| Other/Multiple | 408 | 11 | 1.9 (0.8 - 4.2) |
|  |  |  |  |
| **Colon** | 719 | 18 | 2.1 (1.2 - 3.6) |
| Kidney | 347 | 4 | 1.9 (0.7 - 5.0) |
| Liver | 186 | 8 | 2.4 (1.0 - 5.8) |
| Heart and/or Lung | 158 | 6 | 2.5 (0.9 - 6.8) |
| Other/Multiple | 28 | 0 | … |
|  |  |  |  |
| **Lung** | 2,057 | 32 | 1.1 (0.7 - 1.7) |
| Kidney | 872 | 8 | 0.8 (0.3 - 2.3) |
| Liver | 393 | 11 | 1.4 (0.6 - 3.2) |
| Heart and/or Lung | 757 | 13 | 1.1 (0.6 - 2.2) |
| Other/Multiple | 35 | 0 | … |
|  |  |  |  |
| **Melanoma** | 580 | 12 | 1.6 (0.8 - 3.5) |
| Kidney | 335 | 9 | 2.8 (1.1 - 6.7) |
| Other organsc | 245 | 3 | 0.8 (0.2 - 3.2) |
|  |  |  |  |
| **Female Breast** | 741 | 12 | 0.8 (0.3 - 2.1) |
| Kidney | 460 | 4 | … |
| Liver | 149 | 5 | 1.7 (0.6 - 5.5) |
| Heart and/or Lung | 94 | 3 | 1.0 (0.1 - 7.3) |
| Other/Multiple | 38 | 0 | … |
|  |  |  |  |
| **Prostate** | 1,706 | 39 | 0.9 (0.5 - 1.6) |
| Kidney | 916 | 16 | 1.1 (0.5 - 2.5) |
| Liver | 238 | 4 | 0.7 (0.2 - 2.6) |
| Heart and/or Lung | 523 | 19 | 0.9 (0.4 - 2.2) |
| Other/Multiple | 29 | 0 | … |
|  |  |  |  |
| **Kidney** | 1,142 | 29 | 2.3 (1.4 - 3.7) |
| Kidney | 873 | 22 | 3.4 (2.0 - 5.8) |
| Other organsc | 269 | 7 | 0.6 (0.2 - 2.6) |
|  |  |  |  |
| **Thyroid** | 342 | 14 | 5.5 (2.9 - 10.4) |
| Kidney | 237 | 8 | 6.5 (2.8 - 14.7) |
| Other organsc | 105 | 6 | 4.3 (1.6 - 12.0) |
|  |  |  |  |
| **Non-lymphocytic leukemiad** | 510 | 15 | 2.8 (1.6 - 5.0) |
| Kidney | 254 | 5 | 3.0 (1.1 - 8.2) |
| Other organsc | 256 | 10 | 2.7 (1.3 - 5.5) |
|  |  |  |  |

**Abbreviations:** aHR, adjusted hazard ratio; CI, confidence intervals; CNS, central nervous system; PTLD, post-transplant lymphoproliferative disorder

a Refers to the first occurrence of any type of PTLD in the SRTR or linked cancer registry

b Hazard ratios were obtained from Cox regression models with age as the time scale, PTLD diagnosis as a time-dependent variable, and adjusted for the following variables decided *a priori*: sex, race/ethnicity, year of transplant, and time since transplantation (as a time-dependent variable).

c “Other organs” indicate any organ transplanted other than kidney.

d Non-lymphocytic leukemia includes myelodysplasia and myeloproliferative neoplasms.

Underlined estimates were considered statistically significant based on two-sided p < 0.05.

“…” indicates that the model did not converge

**Table S4:** Cancer risk following first PTLD diagnosis by latency period (≤ 6 months, or > 6 months after PTLD)

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Cancers** | **No. of cancers** | **Overall** | | **≤ 6 months** | | **> 6 months** | |
| **No. with PTLD** | **aHR (95% CI)** a | **No. with PTLD** | **aHR (95% CI)** a | **No. with PTLD** | **aHR (95% CI)** a |
|  |  |  |  |  |  |  |  |
| All non-PTLD cancers | 11,968 | 272 | 1.6 (1.4 - 1.9) | 97 | 4.0 (3.0 - 5.2) | 175 | 1.2 (1.0 - 1.5) |
| Colon | 719 | 18 | 2.1 (1.2 - 3.6) | 7 | 6.4 (2.6 - 15.3) | 11 | 1.5 (0.7 - 3.0) |
| Lung | 2,057 | 32 | 1.1 (0.7 - 1.7) | 12 | 2.9 (1.4 - 6.0) | 20 | 0.8 (0.5 - 1.4) |
| Melanoma | 580 | 12 | 1.6 (0.8 - 3.5) | 2 | 1.5 (0.2 - 10.9) | 10 | 1.7 (0.7 - 3.7) |
| Female breast | 741 | 12 | 0.8 (0.3 - 2.1) | 7 | 4.8 (1.5 - 14.8) | 5 | 0.2 (0.03 - 1.6) |
| Prostate | 1,706 | 39 | 0.9 (0.5 - 1.6) | 11 | 2.0 (0.7 - 5.3) | 28 | 0.8 (0.4 - 1.5) |
| Kidney | 1,142 | 29 | 2.3 (1.4 - 3.7) | 11 | 3.9 (1.4 - 10.3) | 18 | 2.0 (1.1 - 3.5) |
| Thyroid | 342 | 14 | 5.5 (2.9 - 10.4) | 5 | 13.8 (5.2 - 37.2) | 9 | 3.9 (1.7 - 8.8) |
| Non-lymphocytic leukemiab | 510 | 15 | 2.8 (1.6 - 5.0) | 8 | 17.7 (6.5 - 47.7) | 7 | 0.7 (0.1 - 4.9) |
|  |  |  |  |  |  |  |  |

**Abbreviations:** aHR, adjusted hazard ratio; CI, confidence intervals; PTLD, post-transplant lymphoproliferative disorder

a Hazard ratios were obtained from Cox regression models with age as the time scale, PTLD diagnosis as a time-dependent variable, and adjusted for the following variables decided *a priori*: sex, race/ethnicity, year of transplant, transplanted organ, and time since transplantation (as a time-dependent variable).

b Non-lymphocytic leukemia includes myelodysplasia, and myeloproliferative neoplasms.

Underlined estimates were considered statistically significant based on two-sided p < 0.05.

**Table S5:** Risk of selected cancers following first PTLD diagnosis according to cancer stage

|  |  |  |  |
| --- | --- | --- | --- |
| **Cancers** | **No. of cancers** | **No. with PTLDa** | **aHR (95% CI)** b |
| **Kidney** |  |  |  |
| Overall | 1142 | 29 | 2.3 (1.4 - 3.7) |
| Combined stagec |  |  |  |
| Localized/Stage I | 710 | 18 | 2.3 (1.1 - 4.0) |
| Regional/Distant/Stage II-III | 224 | 4 | 0.7 (0.04 - 3.1) |
| Unstaged/Missing | 208 | 7 | 4.2 (1.5 - 9.2) |
|  |  |  |  |
| **Thyroid** |  |  |  |
| Overall | 342 | 14 | 5.5 (2.9 - 10.4) |
| Combined stagec |  |  |  |
| Localized/Stage I | 208 | 9 | 6.2 (2.6 - 12.4) |
| Regional/Distant/Stage II-III | 80 | 4 | 4.7 (0.8 - 15.3) |
| Unstaged/Missing | 54 | 1 | 3.5 (0.2 - 16.6) |
|  |  |  |  |
| **Colon** |  |  |  |
| Overall | 719 | 18 | 2.1 (1.2 - 3.6) |
| Combined stagec |  |  |  |
| Localized/Stage I | 218 | 9 | 3.6 (1.4 - 7.5) |
| Regional/Distant/Stage II-III | 405 | 8 | 1.7 (0.7 - 3.5) |
| Unstaged/Missing | 96 | 1 | 1.0 (0.1 - 4.7) |
|  |  |  |  |
| **Melanoma** |  |  |  |
| Overall | 580 | 12 | 1.6 (0.8 - 3.5) |
| Combined stagec |  |  |  |
| Localized/Stage I | 318 | 8 | 2.0 (0.7 - 4.5) |
| Regional/Distant/Stage II-III | 138 | 2 | 1.0 (0.1 - 4.4) |
| Unstaged/Missing | 124 | 2 | 1.2 (0.1 - 5.6) |
|  |  |  |  |

**Abbreviations:** aHR, adjusted hazard ratio; CI, confidence intervals; PTLD, post-transplant lymphoproliferative disorder

a Refers to the first occurrence of any type of PTLD in the SRTR or linked cancer registry

b Hazard ratios were obtained from Cox regression models with age as the time scale, PTLD diagnosis as a time-dependent variable, and adjusted for the following variables decided *a priori*: sex, race/ethnicity, year of transplant, and time since transplantation (as a time-dependent variable).

c Combined stage variable was created by assigning cancer stage according to the date of cancer diagnosis as follows: SEER summary stage 1977 (cancers diagnosed between 1987-2000), SEER summary stage 2000 (2001-2004), AJCC 6th edition (2004-2010), and AJCC 7th edition (2010+). SEER summary stages were either localized, regional, distant, or unstaged. AJCC stages were stage I, II, or III.

**Figure S1:** Distribution of the time from PTLD to cancer diagnosis according to cancer stage.

**Figure S1 legend:** This figure illustrates the distribution of time since PTLD diagnosis to kidney (Panel A) or thyroid (Panel B) cancer diagnosis, according to cancer stage at diagnosis. The time from PTLD to cancer diagnosis is plotted on the y-axes, while the combined stage has been shown on the x-axes. Combined stage variable was created by assigning cancer stage according to the date of cancer diagnosis as follows: SEER summary stage 1977 (cancers diagnosed between 1987-2000), SEER summary stage 2000 (2001-2004), AJCC 6th edition (2004-2010), and AJCC 7th edition (2010+). SEER summary stages were either localized, regional, distant, or unstaged. AJCC stages were stage I, II, or III.

**Abbreviations:** PTLD, post-transplant lymphoproliferative disorder