RESEARCH LETTER

Incidence Trends of Primary Cutaneous T-Cell Lymphoma in the US From 2000 to 2018: A SEER Population Data Analysis

Recent incidence patterns of cutaneous T-cell lymphoma (CTCL) in the US are not well described. We sought to describe recent incidence trends by tumor subtype, sex, age, race and ethnicity, socioeconomic status (SES), and geography.

Methods | Incidence data were derived from 18 population-based registries of the Surveillance, Epidemiology, and End Results (SEER) Program for 2000 to 2018. We included histologically confirmed cases of first primary CTCL with malignant behavior and primary site of involvement skin (C44.0-C44.9). Patient characteristics included sex, age, race and ethnicity, and geographic region (metropolitan vs nonmetropolitan counties). Area-level SES information was available from 2000 to 2016 and was categorized into quintile; Q1 lowest, Q5 highest. We used the 2000 US standard population to calculate age-adjusted annual incidence rates (IR) per million people. Annual percent change (APC) was calculated by using the weighted least squares method. Statistical calculations used SEER*Stat statistical software (version 8.3.9.2) in January 2022. The Stanford institutional review board deemed this study exempt from review and waived the requirement for patient informed consent because only deidentified data were used.

Results | We identified 14,942 new cases of CTCL from 2000 to 2018. Table 1 shows the number of cases, IR, and APC of IR of CTCL by International Statistical Classification of Diseases and Related Health Problems for Oncology (ICD-O) diagnosis. Mycosis fungoides (MF) was the most common diagnosis, followed by primary CTCL (PCTCL) and primary cutaneous anaplastic large cell lymphoma (PCALCL). The overall CTCL incidence was 8.55 per million and increased over the study period (APC, 0.61%). Among CTCL subtypes, MF had the highest incidence (5.42) and Sézary syndrome had the highest increase (APC, 3.83%). Overall, PCTCL was the only subtype with decreasing incidence over the study period (APC, −1.39%).

Table 2 shows IR and APC by tumor subtype, sex, age, race and ethnicity, SES, and geographic region. Overall, CTCL incidence was highest in men (10.06), non-Hispanic Black patients (11.68), individuals in highest SES quintiles (10.31), and patients living in metropolitan counties (8.96). Patients aged 40 years or older had a 6-times higher overall incidence rate than those younger than 40 years. Despite having a lower incidence compared with the older age group, patients younger than 40 years showed significantly higher increases in overall CTCL IR (APC, 2.87%) and in MF IR (APC, 3.67%). Other groups with significant increases in incidence included women (APC, 0.92%), non-Hispanic Black patients (APC, 1.63%), patients in the lowest SES quintile (APC, 1.87%), and individuals in metropolitan counties (APC, 0.68%).

Discussion | We observed an increased overall CTCL incidence between 2000 and 2018. These findings differ from previous North American studies, which suggested CTCL incidence stabilized after 1998, but are consistent with recent studies from Europe. These trends are likely multifactorial. Better diagnostic tools and increased awareness among physicians and patients may have led to improved CTCL detection. Physician density has been associated with higher incidence; therefore, efforts to increase access to health care may contribute to a rise in CTCL diagnosis. The incidence of PCTCL has decreased considerably since 2000, possibly owing to better classification because PCTCL is often a diagnosis of exclusion.

Table 1. Number of Cases, Age-Adjusted Incidence Rate, and Annual Percent Change of Incidence Rate of CTCL in 18 SEER Registries Between 2000 and 2018

| Subtypes (ICD-O) | Cases, no. | Frequency, % | Incidence rate (per million people) | Annual % change (95% CI) |
|------------------|------------|--------------|-------------------------------------|---------------------------|
| All CTCL         | 14,942     | 100          | 8.55                                | 0.61 (0.12 to 1.10)        |
| Mycosis fungoides (9700/3) | 8445 | 56.6 | 5.42 | 1.34 (0.89 to 1.79) |
| Sézary syndrome (9701/3) | 268 | 1.8 | 0.21 | 3.83 (2.00 to 5.69) |
| Peripheral T-cell lymphoma, not otherwise specified (9702/3) | 910 | 6.1 | 0.48 | 0.31 (~0.93 to 1.56) |
| Subcutaneous panniculitis-like T-cell lymphoma (9708/3) | 61 | 0.4 | 0.02 | NA |
| Primary CTCL (9709/3) | 3637 | 24.3 | 1.50 | −1.39 (~2.22 to −0.56) |
| Primary cutaneous anaplastic large cell lymphoma (9718/3) | 1,509 | 10.1 | 0.86 | −0.48 (~2.57 to 1.65) |
| Extranodal natural killer/T-cell lymphoma (9719/3) | 52 | 0.3 | 0.01 | NA |
| Primary cutaneous γ-δ T-cell lymphoma (9726/3) | 48 | 0.3 | 0.05 | NA |
| Adult T-cell leukemia/lymphoma (9827/3) | 12 | 0.1 | 0.01 | NA |

Abbreviations: CTCL, cutaneous T-cell lymphoma; ICD-O, International Classification of Diseases for Oncology; NA, not applicable; SEER, Surveillance, Epidemiology, and End Results.

* Significantly different from 0.
Overall, CTCL incidence by age, sex, and race and ethnicity stayed mostly consistent with previous reports. One key new finding is the more rapid increase in incidence among young patients, possibly owing to earlier diagnosis. Another hypothesis is that MF cases previously misdiagnosed as atopic dermatitis or psoriasis are discovered at a younger age in the era of biologics. Higher SES and metropolitan county were both associated with increased incidence, consistent with previous studies correlating with income and physician density. Environmental exposures may also be associated with CTCL owing to clustering of cases in industrial regions of North American cities.

To our knowledge, this is the first study to analyze CTCL incidence by SES and geography. Limitations include potential underreporting, heterogeneous classification, changes in diagnostic tools, and small sample sizes.

These findings suggest that the incidence of CTCL continues to increase in the US. Prospective data collection efforts should gather data on SES, geographic location, and health care access to better understand these differences.

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Table 2. Incidence Rate in 2018 and Annual Percent Change of CTCL, Mycosis Fungoides, Sézary Syndrome, and Primary Cutaneous Anaplastic Large-Cell Lymphoma by Sex, Age, Race and Ethnicity, SES, and Geographic Location

| Characteristics | All CTCL | Mycosis fungoides | Sézary syndrome | Primary cutaneous anaplastic large-cell lymphoma |
|-----------------|---------|------------------|----------------|-----------------------------------------------|
|                 | Rate    | APC, % (95% CIs) | Rate           | Rate                                        |
| Rate            | APC, % (95% CIs) | Rate | APC, % (95% CIs) | Rate | APC, % (95% CIs) | Rate | APC, % (95% CIs) |
| Rate            | APC, % (95% CIs) | Rate | APC, % (95% CIs) | Rate | APC, % (95% CIs) | Rate | APC, % (95% CIs) |
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| Rate            | APC, % (95% CIs) | Rate | APC, % (95% CIs) | Rate | APC, % (95% CIs) | Rate | APC, % (95% CIs) |
| Race and ethnicity |        |                  |                |                      |
| Black           | 11.68   | 1.63 (0.80 to 2.47) | 6.50 | 2.03 (0.85 to 3.23) |
| Hispanic        | 7.07    | 1.12 (−0.01 to 2.26) | 4.94 | 1.85 (0.39 to 3.33) |
| Non-Hispanic    | 7.89    | 0.14 (−0.39 to 0.68) | 4.92 | 0.88 (0.39 to 1.36) |
| SES (quintiles) | |                  |                |                      |
| Q1 (lowest)     | 7.55    | 1.87 (0.53 to 3.23) | 4.51 | 1.69 (0.13 to 3.26) |
| Q2              | 7.40    | 1.34 (0.37 to 2.32) | 4.26 | 2.12 (0.74 to 3.52) |
| Q3              | 7.47    | 0.92 (−0.15 to 2.01) | 4.10 | 1.13 (−0.10 to 2.78) |
| Q4              | 8.91    | 0.52 (−0.79 to 1.85) | 4.98 | 0.75 (−0.76 to 2.29) |
| Q5 (highest)    | 10.31   | 1.16 (0.27 to 2.06) | 6.99 | 1.96 (0.93 to 3.00) |
| Geographic location |      |                  |                |                      |
| Metropolitan    | 8.96    | 0.68 (0.16 to 2.04) | 5.76 | 1.38 (0.85 to 1.92) |
| Nonmetropolitan | 8.85    | −0.66 (−2.03 to 0.73) | 2.40 | −0.19 (−2.09 to 1.75) |

Abbreviations: APC, annual percent change; CTCL, cutaneous T-cell lymphoma; NA, not applicable; SES, socioeconomic status.

* Significantly different from 0.

** Data limited to patients diagnosed from 2000 to 2016.

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Evolution of Early-Phase Anticancer Drug Investigations in China

In recent years, China has implemented a revised drug administration law and registration regulation. The purpose is to accelerate the development of new innovative drugs. Policies, such as the “60 working day silent approval of investigational new drug applications” and “Technical Guiding Principles for the Acceptance of the Overseas Clinical Trial Data of Drugs,” have had a positive association with timelines for trial startup and marketing of new innovative drugs in China. These policies have been associated with significantly increased anticancer drug trials and more diversified anticancer therapies that benefit patients.1,2 In this article, we present our analysis of phase 1 clinical trials performed in China from 2017 to 2021.

Methods | Details of oncology phase 1 trials in solid tumors were obtained from INFORMA database (https://pharma.id.informa.com). One-hundred sixty-one trials were excluded from the 1526 identified trials based on the exclusion criteria (Methods in the Supplement). The average annual growth rates (AAGR) of trials were calculated as $Z = (X/Y)^{1/3} - 1$. The variables $X$ and $Y$ represent the trial numbers in 2021 and 2017, respectively.

Results | A total of 996 drugs were tested in phase 1 trials in China. Most drugs (461 [46%]) were immuno-oncology drugs (Figure, A), among which cell therapy (200 [20%]) constituted the largest category (Figure, B). Nine trials conducted in China during the 4-year period included first-in-class drugs with novel targets (Table). For example, GNC-035, GNC-038, and GNC-039 were the first tetra-specific antibodies targeting immune antigens; CBP-1008 was the first bispecific ligand drug conjugate.

In addition, 1359 phase 1 trials of anticancer drugs were initiated, with an AAGR of 23%. Sixty-three phase 1 trials were global multicenter trials, accounting for less than 5% of the total number. Most global multicenter trials were sponsored by Chinese pharmaceutical enterprises (32 of 48 sponsors [67%]). Haihe Biopharma sponsored the most global trials (5 [8%]), followed by BeiGene (4 [6%]), and Novartis (3 [5%]). Institutes that coparticipated with Chinese sites in global multicenter trials were mainly from the US (52 [83%]), followed by Australia (19 [30%]), Taiwan (14 [22%]), and the Republic of Korea (13 [21%]).

Furthermore, an increase of phase 1 trials with a seamless design occurred from 67 in year 1 (2017) to 123 in year 4 (2020) (AAGR, 22%). A total of 358 trials (26%) were biomarker-guided studies with an AAGR of 21%. A master-protocol design was also introduced into those biomarker-guided trials, including umbrella (2 [1%]) and basket (13 [4%]) trials.

Discussion | This cohort study examined how the reform and increasingly supportive drug registration regulation in China was associated with the acceleration of the conduct and increase in the number of early-phase trials. The focus of these...