Temporal Patterns Of Lymphoma Mortality Before And After FDA Approval Of CAR T-cell Therapies In The US (1999–2023)

M. Fatima [1], A. Raza [2], F. Kalpina [3], I. Shahid [1], F. Fatima [2], I. Ahmed [1], A. Siddiqua [4]

1. King Edward Medical University, Lahore, Pakistan
2. Services Institute of Medical Sciences, Lahore, Pakistan
3. Dow University of Health Sciences, Karachi, Pakistan
4. Quaid-e-Azam Medical College, Bahawalpur, Pakistan

Background

CAR T-cell therapy is an adoptive cellular immunotherapy in which a patient's T-lymphocytes are genetically modified to recognize and attack cancer cells. It was first approved by the FDA in 2017 for blood cancers like leukemia and lymphoma. This approval marked a pivotal advancement in lymphoma treatment, offering a novel option for patients with relapsed or refractory disease where conventional therapies had failed.

Aim

This study aims to explore changes in trends and patterns in lymphoma mortality in the US from 1999 to 2023, before and after chimeric antigen receptor (CAR) T-cell therapy approval.

Methods

We used the Centers for Disease Control and Prevention Wide-ranging Online Data for Epidemiological Research to extract Age-adjusted mortality rates (AAMRs) per 100,000 adults for lymphoma mortality in the US from 1999-2023. The AAMRs were analyzed using Joinpoint Regression to evaluate annual percentage change (APC) in mortality. The study period was divided into two eras, pre- and post-2017, corresponding to CAR T-cell therapy's FDA approval.

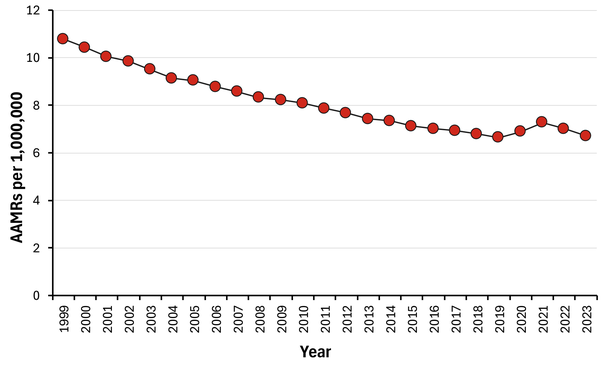
Discussion

While lymphoma mortality in the US declined overall from 1999 to 2023, the rate of decline significantly slowed after the 2017 FDA approval of CAR T-cell therapy. This paradox, despite CAR T-cell therapy's high efficacy in trials, reflects limited real-world population impact due to access barriers. First, CAR T-cell therapy remains predominantly a third-line intervention accessible to a small subset of eligible patients. Only 30-40% of eligible patients receive it.[1] Second, non-relapse mortality (NRM) associated with CAR T-cell therapy remains substantial at approximately 5%, with infections (56% of NRM), particularly COVID-19 (27% of infectious NRM), representing the leading causes of death.[2] Third, despite impressive initial response rates, approximately 30-60% of CAR T-cell recipients eventually relapse, creating a population of heavily pretreated patients with limited salvage options and poor prognosis.[3] This highlights the need for earlier integration, broader accessibility, and improved post-treatment strategies to maximize the population-level impact of CAR T-cell therapy on lymphoma mortality.

Results

From 1999-2023, lymphomas caused 684,627 deaths in US adults, with a decreasing trend [APC: -1.93% (-2.06 to -1.83)]. The AAMR was higher in the pre-2017 era [8.41 (95% CI: 8.39 – 8.44)] than in the post-2017 era [6.87 (6.84 – 6.91)]. However, the overall decline in mortality was significantly higher in the pre-approval era with an APC of -2.49% (-2.6 to -2.37) than in the post-approval era [-0.24% (-0.74 – 0.10)]. Both sexes exhibited similar trends, with males showing a greater AAMR than females in both eras [(10.8 vs. 6.61) and (9.15 vs. 5.14), respectively]. The decline in mortality was also greater in females than males in both eras [(-2.78% vs. -2.3%) and (-0.45 vs. -0.01%), respectively]. A similar trend in AAMRs was observed across racial and ethnic groups, except non-Hispanic whites, which showed a greater mortality burden in the post-approval era (8.93 vs. 11.5). Only non-Hispanic American Indians/Alaska Natives showed the same decline in the pre- and post-approval era (-1.63% vs. -1.63%), while all other races experienced a lesser decline in mortality in the post-approval era.

Trends in Lymphoma Mortality in the US,1999-2020



Conclusion

Overall lymphoma mortality in US adults declined from 1999 to 2023 but slowed markedly after 2017. Males showed consistently higher mortality than females. Most racial and ethnic groups saw smaller declines post-2017, except non-Hispanic American Indians/Alaska Natives.

References

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The authors declare no conflict of interest

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