Did Novel Agents Change the Curve?

Survival Acceleration in Classical Hodgkin Lymphoma After 2016: SEER Analysis

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INTRODUCTION

Classical Hodgkin lymphoma is highly curable with frontline chemotherapy.

Over the past 15 years, treatment changed with the arrival of brentuximab vedotin for relapsed or refractory disease, programmed death-1 (PD-1) inhibitors, and frontline brentuximab vedotin plus doxorubicin, vinblastine, and dacarbazine chemotherapy for advanced disease.

It is still not clear whether these approvals produced real survival gains in the population, or whether outcomes simply improved over time for other reasons.

AIM

Using the Surveillance, Epidemiology, and End Results (SEER) database from 2005 to 2022, we measured survival trends by treatment era and looked for the year when the trend changed, in adults aged 18 years and older with classical Hodgkin lymphoma.

Follicular lymphoma served as a negative control, to separate a treatment effect from a general improvement over time.

METHOD

- We identified adults with a first-primary, microscopically confirmed classical Hodgkin lymphoma diagnosed between 2005 and 2022 in the SEER 17-registry database (November 2024 submission).
- Patients were grouped into three treatment eras: before novel agents (2005 to 2010), brentuximab vedotin (2012 to 2017), and brentuximab vedotin plus checkpoint inhibitors (2018 to 2022).
- We used adjusted Cox proportional-hazards models, sensitivity analyses, and restricted mean survival time.
- Joinpoint regression located the year when Hodgkin lymphoma-specific mortality changed direction.
- Follicular lymphoma was identified with the same criteria as a negative control; a disease-by-era comparison tested whether the trends differed.

CONCLUSIONS

- Survival in classical Hodgkin lymphoma improved substantially across successive US Food and Drug Administration approval eras, with the largest gains after the mid-2010s.
- The fall in mortality sped up around 2016, at the same time that programmed death-1 (PD-1) inhibitors and frontline brentuximab vedotin plus chemotherapy entered routine practice.
- The improvement was seen across age, race, cancer stage, and rural groups, including older adults, with the greatest benefit in patients aged 18 to 75 years.
- **The significant era by disease interaction using follicular lymphoma as a negative control supports a treatment era associated effect rather than a purely secular trend**

RESULTS

Negative control: the disease-by-era interaction was highly significant (likelihood-ratio $p < 10^{-87}$); the benefit was specific to Hodgkin lymphoma

27,250
Hodgkin lymphoma patients
first primary, 2005 to 2022

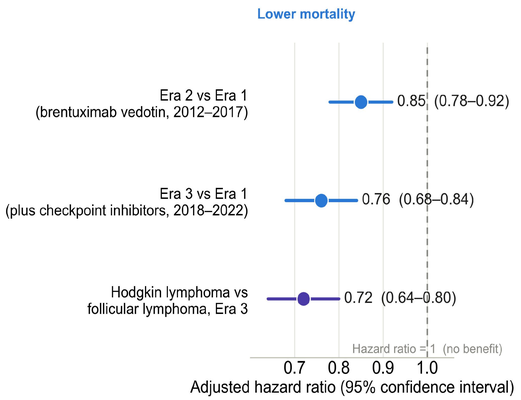
5,276
Deaths
during follow-up

0.76
Era 3 hazard ratio
versus Era 1 · 95% CI 0.68–0.84

2016
Mortality inflection point
95% CI 2012 to 2020

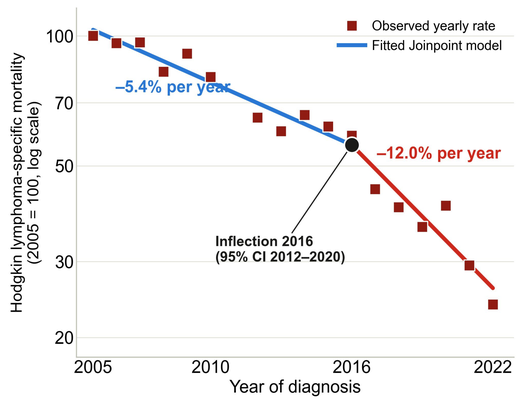
0.72
Hodgkin vs follicular lymphoma
Era 3 hazard ratio (negative control)

Survival improved across eras



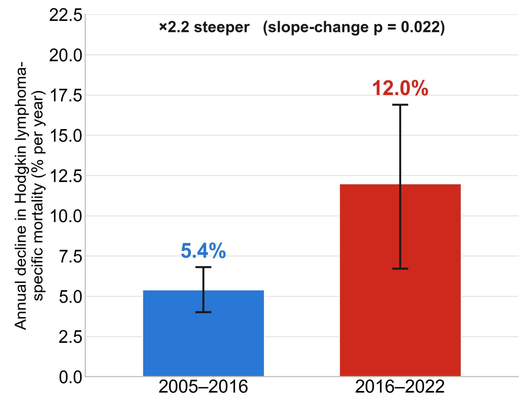
Adjusted hazard ratios versus Era 1 (before novel agents). Bottom row shows the Hodgkin lymphoma versus follicular lymphoma comparison in Era 3 (negative control).

Decline accelerated after 2016



Fitted Joinpoint model of Hodgkin lymphoma-specific mortality; single inflection point at 2016 (95% confidence interval 2012 to 2020).

The rate of decline doubled



Annual percentage decline in Hodgkin lymphoma-specific mortality before and after the 2016 inflection point.

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CONTACT INFORMATION

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