Population coverage of HLA-A*02:01, *02:05, *02:06 across selected cancer types in the United States

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Nashita Patel,[1] Charlotte Carroll,[2] Ken Culver,[3] Shibani Pokras[2]*

[1] Value Evidence and Outcomes, GlaxoSmithKline, Brentford, London, UK;
[2] Value Evidence and Outcomes, GlaxoSmithKline, Collegeville, PA, USA;
[3] Global Medical Affairs, GlaxoSmithKline, Collegeville, PA, USA
*Corresponding author.

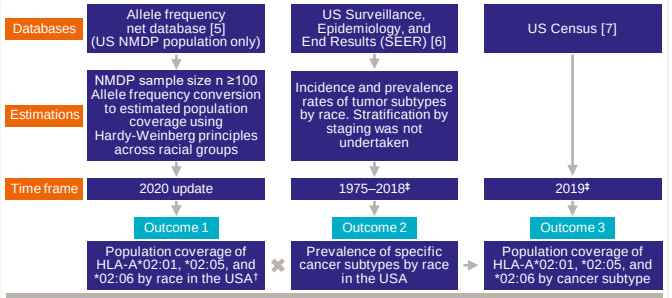
Background

- GSK is investigating an autologous T-cell receptor (TCR) T-cell therapy for solid tumors that recognizes the cancer testis antigen, NY-ESO-1, presented by specific human leukocyte antigen (HLA)-A*02 subtypes.
- Race has been consistently identified as a predictive factor associated with the development of most diseases, including cancer. Consequently, different races may have differing risks in the development of subtypes of cancer [1, 2].
- Since the prevalence of HLA subtypes are associated with race [3,4], greater understanding of the coverage of HLA-A*02:01, *02:05, and *02:06 subtypes across the US population and cancer subtypes may facilitate an estimation of the size of eligible populations suitable for certain T-cell therapies requiring specific histocompatibility.

Aim

The aim of this study was to estimate the number of US patients with HLA-A*02:01, *02:05, and *02:06 subtypes across selected cancer subtypes, accounting for racial variation in the US population in 2020.

Methods



All outcomes were stratified by race[§]: "White," "Black," "Asian/ Pacific Islander," "American Indian/ Alaskan,[¶]" and "Other."
Cancer subtypes included: invasive lung, invasive and in-situ bladder, multiple myeloma, invasive ovarian,[#] invasive gastric, and invasive esophageal.
Limitations and assumptions

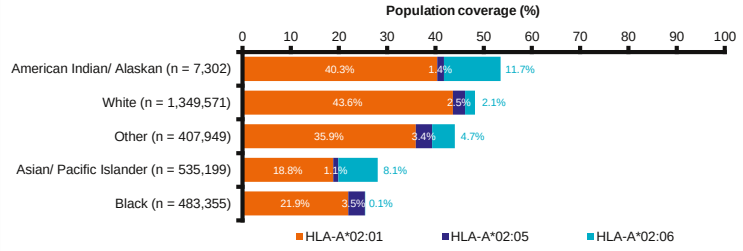
- Population coverage was calculated utilizing the Hardy-Weinberg assumptions of the allele carrier rate in heterozygotes and homozygotes within a given population. Assumptions include: a large population, random mating within a given population, no genetic mutation, no gene flow (ie, immigration/emigration), and random reproductive success.
- Census data and allele frequency were assumed to be reflective of the US population or geographic region, respectively; rates of change in disease trends and population growth were assumed to be constant.
- Predictive and prognostic clinical characteristics including histological subtypes were not accounted for in this analysis.

"White" included US NMDP European Caucasian, North American Amerindian, Middle Eastern, or North Coast of Africa. "Black" included US NMDP African, African American population 2, Black South or Central American, or Caribbean Black. "Asian/Pacific Islander" included US NMDP Chinese, Filipino, Japanese, Korean, South Asian Indian, South East Asian, Hawaiian, other Pacific Islander or Vietnamese. "Native American" included Alaskan Native or Aleut or American Indian South or Central America. "Other" included Caribbean Hispanic, Hispanic South or Central American, or Mexican or Chicano. These definitions of race were consistent across all 3 outcomes. †Estimated utilizing Hardy Weinberg principles and allele frequencies extracted from the allele frequency net database; ‡The 2020 estimates for outcome 2 and outcome 3 assumed constant disease trends and population growth from the data collection time frame; §The Hispanic population was included as a proportion of each category, where appropriate; ¶For the purposes of outcome 2 and outcome 3, "American Indian & Alaskan population" were combined with "Other"; #Estimates were based on United States female population only.
US NMDP, US National Marrow Donor Program.

Results

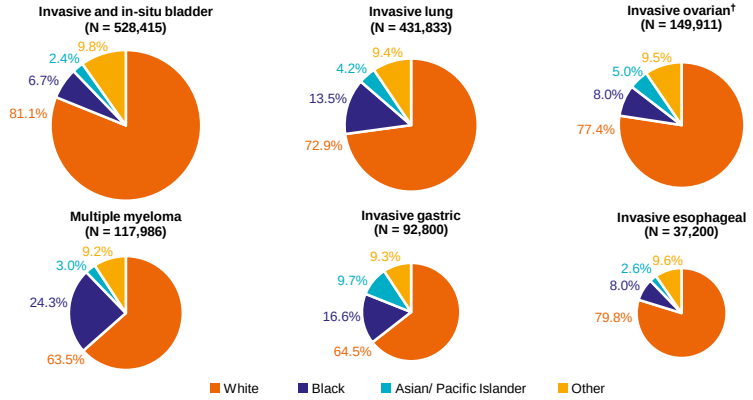
Estimated distribution by race of HLA-A*02:01, *02:05, and *02:06 subtypes in the overall US population, %

- HLA-A*02:01 was the most common subtype, regardless of race.



US racial distribution of selected cancer subtypes, %

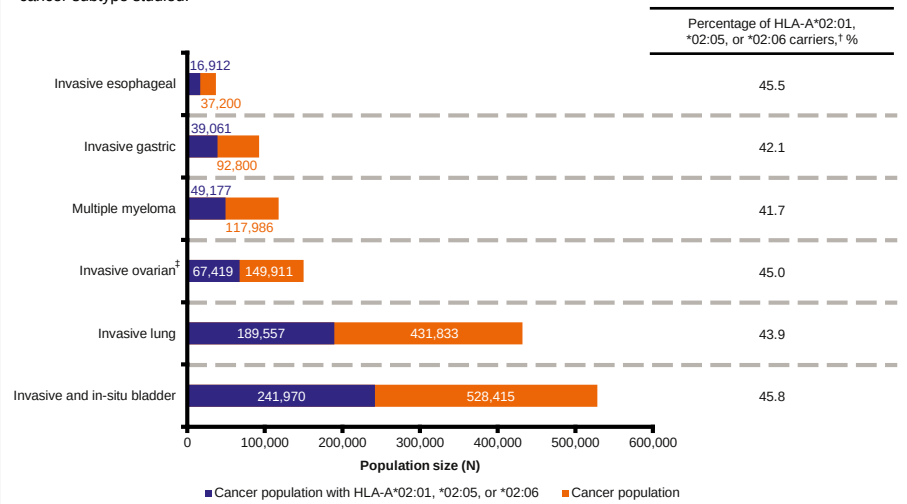
- White patients were estimated to make up the greatest proportion of patients among the cancer subtypes studied, reflecting the racial distribution of the US. The proportion of Black and Asian/ Pacific Islander patients was highest in multiple myeloma and invasive gastric cancer, respectively, among the cancer subtypes studied.



American Indian/ Alaskan patients were combined with "Other" for the purposes of these analyses due to a lack of SEER prevalence rates for this population. Percentages for each cancer type may not sum 100% due to rounding of data. Pie charts are sized in proportion to their respective cancer subtype N value. †Estimates are based on the US female population only.

Estimated overall proportion of HLA-A*02:01, *02:05, or *02:06–positive population in the US in 2020 accounting for racial variation, n (%)

- The overall proportion of patients who are carriers of HLA-A*02:01, *02:05, or *02:06 subtypes was estimated to be between 41.7% (multiple myeloma) and 45.8% (invasive and in-situ bladder) in the US accounting for the racial variations in each cancer subtype studied.



†Population percentage of HLA-A*02:01, *02:05, or *02:06 carriers calculated using the overall cancer population as the denominator for each cancer type; ‡Estimates were based on United States female population only.

Conclusions

- The estimated proportion of cancer patients who carry HLA-A*02:01, *02:05, or *02:06 was estimated to be between 41.7% and 45.8%, and is an important consideration when estimating the population size of eligible patients for T-cell therapies requiring specific HLA-A*02 histocompatibility.
- The proportion of patients with specific HLA-A*02 subtypes is similar across selected cancers, accounting for racial variation in the development of cancer subtypes and the US population.
- As this study utilized conceptual modelling, findings from this study should be validated with individual-patient data.

Disclosures

NP, **CC**, and **SP** are employees of and own stocks/shares in GlaxoSmithKline (GSK). **KC** is an employee of GSK, a former employee of Novartis, and owns stocks/shares in GSK.

Acknowledgments

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