Representation of Sex at Birth in Real-World Evidence, Randomized Clinical Trial, and Surveillance, Epidemiology, and End Results (SEER) Cancer Patient Registry Data by Cancer Type

Poster #RWD13

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Background

- In randomized clinical trials (RCTs) for oncology, individuals assigned female at birth have historically been underrepresented.[1-2]
- However, the significance of this variance and extent to which it impacts the representativeness of cancer research data sets have not been established.[1-2]

Objective

- To assess female sex representation across corresponding RWE, RCT, and SEER cohorts from a parallel time period.

Methods

- From RWE studies assessing first-line (1L) cancer treatment, we selected tumor types on which recent RCTs had also been conducted in the 1L setting and built SEER patient cohorts around their eligibility criteria.

Table 1. Selected studies

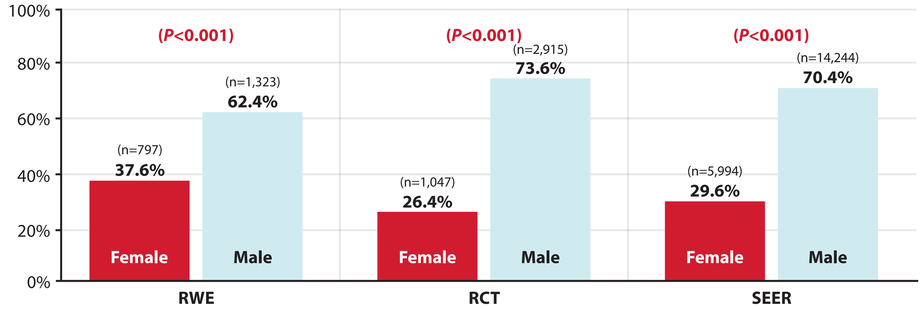
Tumor Type	RWE Study	Corresponding RCT Study(ies)
Advanced Non-small Cell Lung Cancer	Real-World Observational Study of Current Treatment Patterns and Outcomes in Recurrent or Locally Advanced/ Metastatic NSCLC	Keynote 407[3]
Advanced Hepatocellular Carcinoma	Comparative Effectiveness and Safety of Atezolizumab plus Bevacizumab in First-Line versus Alternative Treatments for Advanced Hepatocellular Carcinoma	IMBrave150[4]
Advanced Melanoma	Treatment Patterns and Outcomes of Advanced Melanoma Patients	Checkmate 067[5]
Advanced Renal Cell Carcinoma	Treatment Patterns and Outcomes of Advanced Renal Cell Carcinoma (aRCC) Patients	Checkmate 214[6], Keynote 426[7]

- Sex at birth for patients with advanced lung, liver, kidney, or melanoma skin cancers (2 studies) was compared across 5 RWE chart review studies (completed between 2020-2022), 5 corresponding RCTs (reported between 2014-2021), and the most recently available SEER data for the diagnoses (2017-2019).[8]
- Statistical comparisons were made using 2-sided chi-square tests.

Results

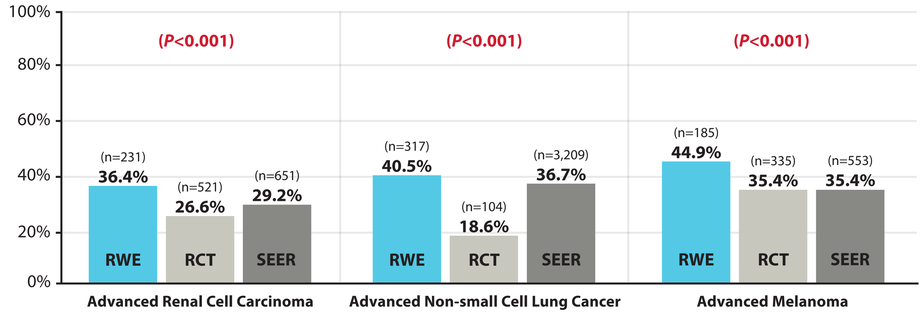
- Sex at birth was collected for 26,325 patients (RWE: n=2,120, 8.1%; RCT: n=3,962, 15.1%; SEER: n=20,238, 76.9%).
- Aggregated across the populations studied, female representation was 37.6% in RWE, 26.4% in RCT, and 29.6% in SEER studies (**Figure 1**).
- Female representation was significantly higher in RWE than RCT ($P<.001$) and in RWE than SEER studies ($P<.001$) (**Figure 1**).
- Within advanced renal cell carcinoma, female representation was significantly higher in RWE (36.4%) compared with RCT (26.6%, $P<.001$) and SEER (29.2%, $P=<.001$) studies (**Figure 2**).
- Female representation was also significantly higher in advanced non-small cell lung cancer RWE studies (40.5%) than in RCTs (18.6%, $P<.001$) and in advanced melanoma RWE studies (44.9%) than in RCTs (35.4%, $P=.001$)) (**Figure 2**).

Figure 1. Female vs. Male Representation in RWE vs. RCT vs. SEER Studies, %



P-values compared across the two subgroups using t-tests, with pooled means and standard deviations for RCTs. Study completed with advanced melanoma, lung, liver, or kidney tumors. Bolded red font indicates statistical significance ($P\leq0.05$).

Figure 2. Female Representation in Advanced Renal Cell Carcinoma, Advanced Non-small Cell Lung Cancer, and Advanced Melanoma, %



P-values compared across the two subgroups using t-tests, with pooled means and standard deviations for RCTs. Study completed with lung, liver, melanoma, or kidney cancers. Bolded red font indicates statistical significance ($P\leq0.05$).

Conclusions

- Participants assigned female at birth remain underrepresented in RCTs, which drive inferences about the safety and efficacy of interventions, clinical decision-making, and payer reimbursement.
- Despite limitations including different study periods and unique sex distributions associated with some cancer types, female representation was highest in RWE studies and lowest in RCTs.
- Well-conducted RWE studies may fill gaps left by RCTs for improving representation and generalizability to female patients with cancer.

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Abbreviations: 1L, first-line; RCT, randomized clinical trial; RWE, real-world evidence; SEER, Surveillance, Epidemiology, and End Results.