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Oncology Trial Emulation Using Real-World Electronic Health Record Data: Results of the Coalition to Advance Real-World Evidence through Randomized Controlled Trial Emulation (CARE) Initiative

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Objectives

The Coalition to Advance Real-World Evidence through Randomized Controlled Trial (RCT) Emulation (CARE) Initiative seeks to advance understanding of when real-world data (RWD) can generate valid treatment effectiveness estimates by emulating RCTs using RWD. We present findings from three oncology emulations.

Methods

Following rigorous RCT and fit-for-purpose data selection, we emulated the KEYNOTE-189 (metastatic NSCLC) trial of first-line pembrolizumab+chemotherapy vs. chemotherapy in two electronic health record datasets (DS3 and DS4) and the PALOMA-2 (advanced breast cancer) trial of first-line palbociclib+letrozole vs. letrozole in DS3. Trial entry criteria were applied, as feasible. Treatment status was

based on first-line medications (using vendor-defined line of therapy algorithms) initiated during a fixed ascertainment period. Inverse probability of treatment weighting was used to control baseline confounding. Kaplan-Meier and Cox proportional hazards models were used to estimate the primary outcome(s).

Results

The KEYNOTE-189 real-world progression-free survival (rwPFS) hazard ratio (HR) emulated in DS4 was similar to the RCT finding, whereas the DS3 result was closer to the null [RCT: HR=0.52 (0.43, 0.64); DS4: HR=0.64 (0.47, 0.84); DS3: HR=0.81 (0.65, 1.00)]. The PALOMA-2 rwPFS HR emulated in DS3 was also closer to the null [RCT: HR=0.58 (0.46, 0.72); DS3: HR=0.84 (0.61, 1.23)]. KEYNOTE-189 real-world overall survival estimates in DS4 were closer to the null, whereas DS3 results crossed the null [RCT: 0.49 (0.38, 0.64), DS4: 0.89 (0.63, 1.29), DS3: 1.18 (0.95, 1.44)].

Conclusions

RWD oncology emulation conclusions may depend on: dataset features (predominantly academic vs. community, uptake of newly approved therapies, death capture), route of administration (oral vs. infusion), and real-world follow-up (frequency of visits, progression assessments). Interpretable RWE study results require understanding real-world patterns of care.