Transportability of Overall Survival Estimates from the United States to Germany in EGFRm advanced NSCLC Patients Post-Tyrosine Kinase Inhibitor (TKI) Treatment

MSR205

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BACKGROUND

- Lung cancer, particularly advanced non-small cell lung cancer (aNSCLC), continues posing a significant mortality burden in both the United States (US) and Germany[1,2].
- While advances in targeted therapies have improved outcomes, access to treatment and mutation prevalence vary between these countries[3-6].
- These differences highlight the growing need for market-specific real-world evidence (RWE) to support payer and regulatory decisions.
- However, despite the increasing role of RWE in decision-making, limited access to local, high-quality real-world data (RWD) often hinders the generation of robust RWE to complement clinical evidence.
- In response, the potential to use international fit-for-purpose data instead has raised questions about the transportability of evidence across countries (that is, applying RWE from a source population to a different target population).
- The relative maturity and comprehensiveness of RWD in the US makes it a valuable case for assessing cross-country transportability.

OBJECTIVE

- This study evaluated whether RWE generated in the US can be meaningfully applied to a target population in Germany.
- Particularly, it assessed the transportability of real-world overall survival (rwOS) estimates between two distinct populations of patients diagnosed with aNSCLC with epidermal growth factor receptor mutations (EGFRm) who had previously been treated with EGFR tyrosine kinase inhibitors (TKIs).
  - The US study cohort was derived from Electronic Medical Records (EMR) data (Flatiron Health) while German cohort was derived using statutory health insurance data (AOK Plus).

STUDY DESIGN

- Adult patients diagnosed with EGFRm aNSCLC between 2016 and 2023, who received first- or second-line (LoTs) EGFR TKI therapy followed by a subsequent treatment were eligible.
  - The start of the subsequent LoT to EGFR TKI therapy was defined as the index date.
- G-computation was used to adjust for baseline differences in age, sex, metastatic sites, number of prior LoTs, time since diagnosis (Table 1), index treatment (Figure 1), and index year between US (Flatiron Health EMR) and German (AOK Plus claims data) cohorts.
- Model parameters were estimated from US data and used to predict a survival curve standardized to the German cohort's baseline covariates.
  - rwOS was measured from index date until death.
  - This predicted rwOS was compared to the observed rwOS in Germany to assess comparability.

STUDY POPULATION AT BASELINE

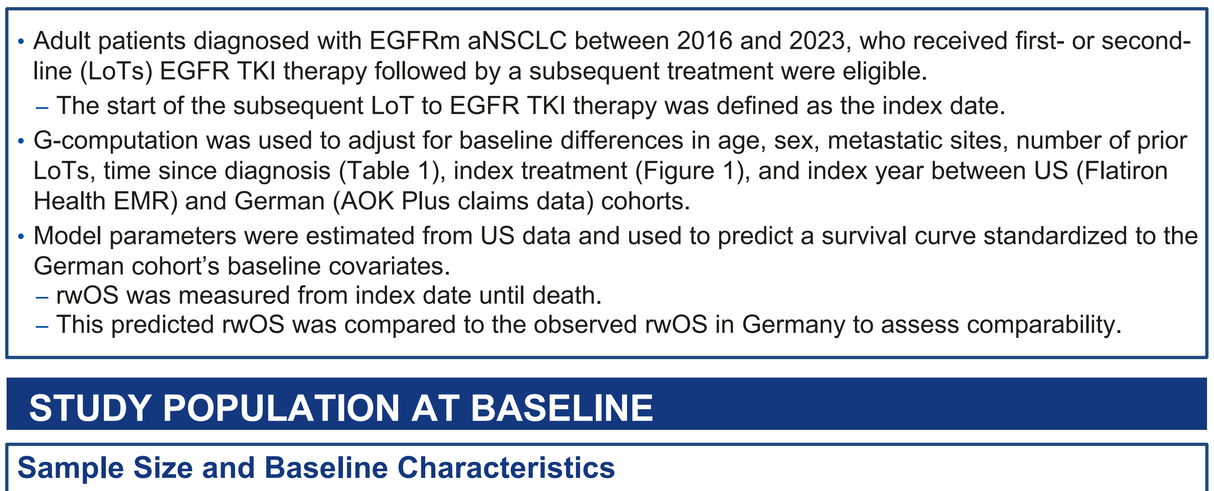
Sample Size and Baseline Characteristics

- The final US and German cohort consisted of 1,407 and 84 patients, respectively.
- Standardized mean differences (SMDs) were calculated to ensure that the cohorts have similar risk at baseline (defined as SMDs ≤0.2).
- Most patients were indexed at 2LoT, implying an exposure to EGFR TKI in their 1LoT.

Table 1: Baseline Demographic and Clinical Characteristics

Variable	Measure	Flatiron	AOK PLUS	SMD
Total Patients	**Number**	1,407	84	
Index line = LoT 2	**Number (%)**	1202 (85%)	64 (76%)	0.2
Index line = LoT 3	**Number (%)**	205 (15%)	20 (24%)	-0.2
Age at start of index treatment (years)	**Mean (SD)**	68.04 (10.82)	66.87 (12.93)	0.1
Sex (at index)				
Males	**Number (%)**	442 (31%)	28 (33%)	-0.05
Females	**Number (%)**	965 (69%)	56 (67%)	0.05
Total number of metastatic sites	**Mean (SD)**	1.95 (1.34)	1.69 (1.02)	0.2
Time to start of index treatment (in months)	**Median (IQR)**	0.23 (0.03, 0.73)	0 (0, 1.11)	-
Time to discontinuation (in months)	**Median (IQR)**	4.87 (1.83, 12.33)	2.97 (1.23, 7.56)	-
Time from diagnosis to start of index treatment (in months)	**Median (IQR)**	13.93 (8.27, 22.57)	13.59 (6.62, 20.62)	-

Figure 1: Index Treatment



The treatment category was based on a pre-determined regimen hierarchy. The graph above represents the regimen order (left to right). Osimertinib is the only approved 3rd Generation EGFR TKI.

RESULTS

Primary Model Survival Outcomes

- The primary model included clinical variables available in both databases. Higher-order derivatives and two-way interactions were included to allow for a flexible model.
- The observed OS curves for the US (Figure 2, green) and German (Figure 2, blue) cohorts did not overlap, showing a 6.2-months difference in median OS.
- For the German cohort, the predicted OS curve (Figure 2, red) closely aligned with the observed OS curve (Figure 2, blue). The difference in median OS was 3.3 months.
- Due to limited availability of clinical variables in the AOK Plus data, the transportability model could not adjust for some key baseline characteristics such as performance and smoking status and mutation type.

Table 2: Observed and Predicted Primary Model Outcomes

	Flatiron	AOK PLUS	
	Observed	Observed	Predicted using Flatiron coefficient
Total patients	1,407	84	
Median survival (months)	16.33	10.05	13.39
Lower 95% CI	15.03	6.87	11.52
Upper 95% CI	17.57	14.68	15.73

Figure 2: Comparing Predicted Survival in AOK Plus German Population with Observed Survival in Flatiron US and AOK Plus German Populations

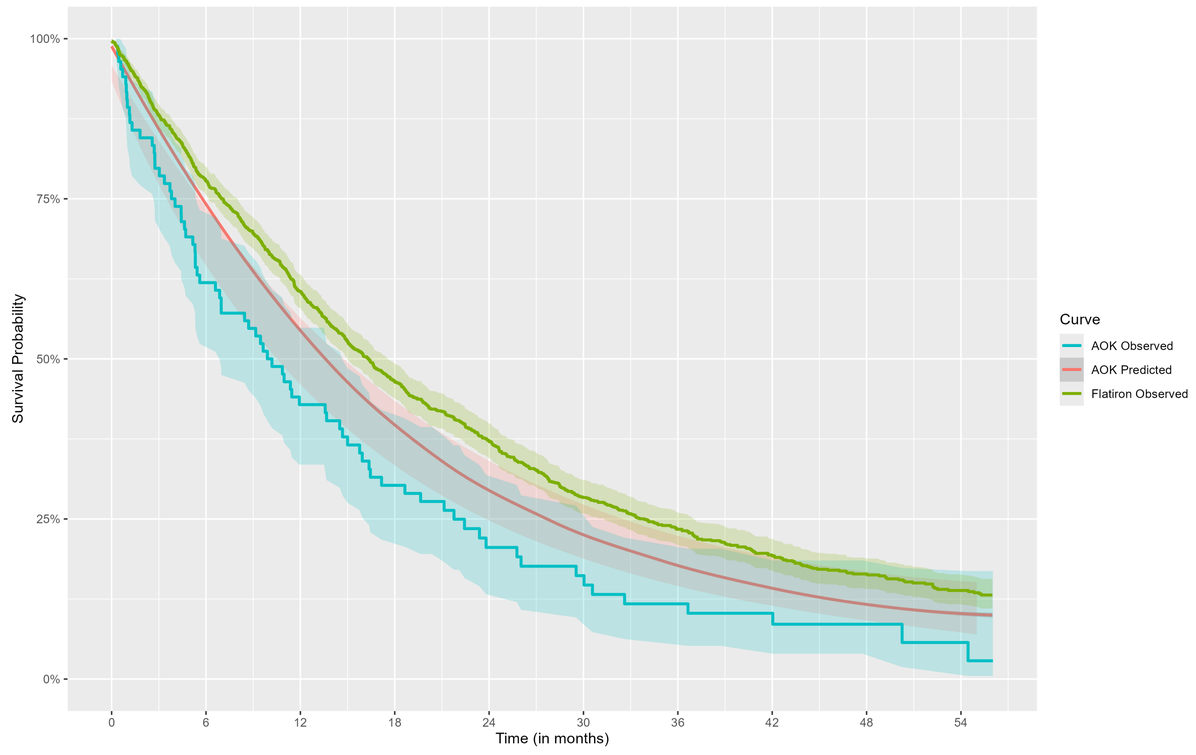
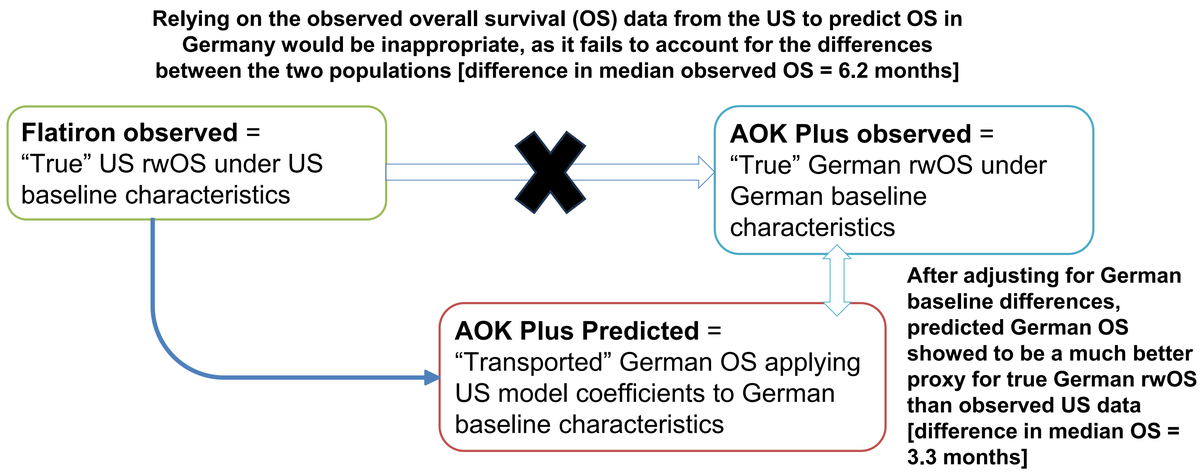


Figure 3: Interpretation of Results



CONCLUSION

- In this transportability analysis, applying model coefficients estimated from the US cohort to baseline covariate data from the German cohort produced a predicted survival curve that aligned more closely with the observed German survival curve than with unadjusted model.
- These findings illustrate the potential for using US real-world data to estimate survival outcomes for German aNSCLC patients, but only when appropriate cohort adjustments are made to account for the differences between populations.
- Due to small sample size and lack of measured clinical variables in German claims data, additional analysis is planned using German registry data to evaluate if it further improves transportability.

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