Supplementary Online Content

Nimgaonkar V, Hubbard RA, Carpenter EL, Mamtani R. Biomarker testing, treatment uptake, and survival among patients with urothelial cancer receiving gene-targeted therapy. *JAMA Oncol*. Published online May 12, 2022. doi:10.1001/jamaoncol.2022.1167

eMethods.

This supplementary material has been provided by the authors to give readers additional information about their work.

Supplementary eMethods:

Regression to Determine Rates of Uptake:
To compare the rates of uptake of erdafitinib and atezolizumab within the first 6-months of approval, we identified patients starting a new line of therapy (after having received platinum-based chemotherapy first-line) within 180 days of each drug's approval (the period from April 12, 2019- October 8, 2019 for erdafitinib, and the period from May 18, 2016- November 13, 2016 for atezolizumab). Within this population, we estimated the following linear regression model, commonly referred to as the linear probability model,

$$P(Y = 1|T, Z) = \beta_1 T + \beta_2 (T \times Z),$$

where
Y= binary indicator representing initiation of a drug of interest (atezolizumab or erdafitinib)
T= continuous variable for time in days from drug approval event
Z= period when drug was started (Atezolizumab period = 0, Erdafitinib period = 1)

In this model, β_1 represents the rate of change in the probability of initiating atezolizumab and $\beta_1 + \beta_2$ represents the rate of change in the probability of initiating erdafitinib. The model does not include an intercept or period main effect in order to reflect an assumed probability of drug initiation of 0 prior to approval.

Coefficients were multiplied by 100 to yield the rate of uptake of each drug in percentage points in the all-comer population. Using the law of total probability, the all-comers rate of uptake can be used to estimate the rate of uptake among the population with a susceptible FGFR alteration according to the following equation

$$P(Y = 1|T, Z = 1, F = 1) = \frac{P(Y = 1|T, Z = 1) - P(Y = 1|T, Z = 1, F = 0)P(F = 0|T, Z = 1)}{P(F = 1|T, Z = 1)}$$

where F is a binary indicator representing a susceptible FGFR alteration. Assuming no patients with F= 0 initiate erdafitinib, this can be simplified to

$$P(Y = 1|T, Z = 1, F = 1) = \frac{P(Y = 1|T, Z = 1)}{P(F = 1|T, Z = 1)}$$

We estimated $P(F = 1|T, Z = 1)$ using the previously reported frequency of susceptible FGFR alterations (20%),[1] and obtained an estimate of the rate of uptake in this population by dividing the rate of uptake in all comers by this quantity.

This approach to calculating uptake in the population expected to harbor a susceptible FGFR alteration was used to avoid the selection bias which would result from conducting the analysis among individuals observed to receive FGFR testing and have a susceptible FGFR alteration, as this population is expected to overrepresent those with FGFR mutations who were also willing and able to start treatment with erdafitinib.

Clinical Trial Survival Curve Reconstruction:

To compare the survival of patients receiving erdafitinib in this real-world cohort with those receiving erdafitinib post-chemotherapy in Study BLC2001, we utilized a method previously published by Liu et al.[4] to reconstruct individual patient data from a published survival curve. The *IPDfromKM* package in R was used to reconstruct data from Figure S5 in the published clinical trial results of Siefer-Radke et al.[3]

The quality of clinical trial curve reconstruction was assessed through the root mean squared error (RMSE), max absolute error, mean absolute error between the estimated and read-in survival probabilities as well as the Kolmogorov-Smirnov test. RMSE was 0.012, mean absolute error was 0.007, and max absolute error was 0.006 (recommended thresholds from Liu et al. are RMSE <0.05, mean absolute error < 0.02, and max absolute error <0.05). The p-value for the Kolmogorov-Smirnov test was 0.9996.

For the overall survival analysis of the real-world population, the index date was the date of erdafitinib initiation, the event date was the recorded date of death, and the censor date was the date of last recorded structured activity in the Flatiron dataset.