**Data Appendix**

Article: **Cost-effectiveness of Venetoclax plus Obinutuzumab versus Chlorambucil plus Obinutuzumab for the First-Line Treatment of Adult**

**Patients with Chronic Lymphocytic Leukemia - An extended societal view**

Authors: **Ngoc Do, M.S., Frederick Thielen, Ph.D.**

This Appendix provides a description of each tab in our Excel model used to output the results represented in our article.

***Overview of the Project:***

* Research question: “Is Venetoclax plus Obinutuzumab (VenO) cost-effective compared to Chlorambucil plus Obinutuzumab (ClbO) for previously untreated CLL patients under the Dutch societal perspective setting?”
* Research population: Adults who have a mean age of 71, have untreated CLL with coexisting conditions.
* Intervention: Venetoclax in combination with Obinutuzumab
* Comparator: Chlorambucil in combination with Obinutuzumab
* Perspective: Extended societal perspective
* Time horizon of the model: 29 years
* Cycle duration: 28 days

***Descriptions of the Excel model tabs:***

* **Project information**: an introduction of the research project including the research question, intervention, comparator, the model structure, and so on.
* **Analysis:** the model outcomes including incremental costs, incremental effects, and incremental cost-effectiveness ratios - ICERs (discounted and undiscounted) are presented in this tab.
* **Parameters**: All parameters’ descriptions, their deterministic and probabilistic values, as well as sources of where the parameter values taken from, are presented in this tab.
* **VenO**: Costs and health effects pertaining to patients receiving Venetoclax in combination with Obinutuzumab (VenO) are formulated and calculated in this tab.
* **ClbO**: Costs and health effects pertaining to patients receiving Chlorambucil in combination with Obinutuzumab (ClbO) are formulated and calculated in this tab.
* **Extrapolation**: empirical survival data are extrapolated to 29 years more in the future using four standard parametric distributions (i.e. exponential, Weibull, log-logistic, and log-normal). From here, statistical tests including Akaike’s information criterion (AIC) and Bayesian Information Criterion (BIC) values were calculated as one of the criteria to select the best parametric distribution to use for fitting the survival curves.
* **Background mortality**: In order to avoid long-term survival extrapolation to surpass general population mortality, a correction for the life expectancy of the general Dutch population was carried out in our model. The 2018 (the latest year with complete data) Dutch life table (gender-specific) from the human mortality database was incorporated into the model through this tab.
* **PF state calculation**: Intermediate calculations for Progression Free Disease State related costs such as drug acquisition costs, premedication costs, chemotherapy administration costs, follow-up costs are presented here before the values are linked to the parameters and treatment tabs.
* **PD state calculation**: Intermediate calculations for Progression Disease State related costs such as drug acquisition costs, premedication costs, chemotherapy administration costs, follow-up costs are presented here before the values are linked to the parameters and treatment tabs.
* **TLS**: Intermediate calculations for prevention and treatment of Tumour Lysis Syndrome (TLS), a principal adverse reaction associated with treatments for CLL patients are carried out in this tab.
* **Indirect medical costs**: Intermediate calculations for indirect medical costs including end of life costs and future medical costs are presented in this tab. All these future medical costs used here were taken from the iMTA PAID tool (version 3.0), which is available online (https://imta.shiny apps.io/PAID3/).
* **Direct non-medical costs**: Intermediate calculations for direct non-medical costs including informal care costs and transportation costs are presented in this tab.
* **Indirect non-medical costs**: Intermediate calculations for indirect non-medical costs including future non-medical costs are presented in this tab. All future non-medical costs used here were taken from the iMTA PAID tool (version 3.0), which is available online (https://imta.shiny apps.io/PAID3/).
* **DSA**: One-way deterministic sensitivity analysis is presented here using an Excel macro adapted from Hart et al1 to examine which parameter is the most influential factor for the ICER.
* **PSA**: By using Monte Carlo simulations with 2,000 iterations, we explored the joint parameter uncertainty in this tab.
* **Scenario analysis**: this tab lists 22 scenarios tested in the model and their corresponding results (ICERs).
* **VOI**: with an Excel macro embedded, this tab calculates Expected Value of Perfect Information (EVPI), representing the maximum value one can expect to gain if uncertainty from all model parameters was eliminated.
* **CE plane**: Results (i.e. ICER) of the 2,000 PSA iterations are depicted in the cost-effectiveness (CE) plane.
* **CEAC**: The probability of VenO being cost-effective at different WTP thresholds is visualized in the cost-effectiveness acceptability (CEAC) curve.
* **EVPI**: EVPI curves are visualized in this tab using the results calculated from the VOI tab.
* **TTNT, PFS, OS curves**: for each treatment arm, all fitted and empirical survival curves are presented in one plot to serve as the visual test to choose the best-fitted parametric distribution.
* **Combined graphs**: All the chosen fitted survival curves (progression free survival, overall survival, time-to-the-next treatment curve, and general population overall survival curve) are plotted in the same plot for each treatment arm.

**Reference:**

* 1. Hart R, Burns D, Ramaekers B, et al. R and Shiny for Cost-Effectiveness Analyses: Why and When? A Hypothetical Case Study. *Pharmacoeconomics*. Jul 2020;38(7):765-776. doi:10.1007/s40273-020-00903-9