Abstract: P699

Title: 6-YEAR TIME TO NEXT TREATMENT (TTNT) EXTRAPOLATION CURVE FOR GLOW STUDY: FIRST-LINE IBRUTINIB + VENETOCLAX (I+V) OFFERS LONG TREATMENT-FREE PERIOD FOR ELDERLY/UNFIT CLL PATIENTS

Abstract Type: Poster Presentation

Topic: Chronic lymphocytic leukemia and related disorders - Clinical

Background:

GLOW is a phase 3 trial evaluating the efficacy and safety of fixed-duration (FD) ibrutinib plus venetoclax (I+V) in elderly patients and/or those with comorbidities with previously untreated chronic lymphocytic leukemia (CLL). With a median follow-up of 46 months, this study demonstrated a significantly prolonged progression-free survival (PFS) with I+V compared to chlorambucil plus obinutuzumab (HR 0,214 [95% CI 0,138–0,334]; p<0,0001), as well as an advantage in overall survival (OS) within this population (HR 0,487 [95% CI 0,262–0,907]; p=0,021). Moreover, time to next treatment (TTNT), defined as time from the date of randomization to the start date of any subsequent anti-leukemic treatment (with patients without subsequent treatment censored at the date of the last site visit) was significantly longer with I+V (HR 0,155 [95% CI 0,072–0,333]; p<0·0001). The median TTNT was not reached in both treatment groups. The estimated 46-month TTNT rate was 91,4% for I+V and 57,3% for chlorambucil plus obinutuzumab.

Based on RESONATE-2 trial, the median duration of treatment with Bruton's Tyrosine Kinase inhibitor ibrutinib, given until disease progression, was 6 years (74 months). However, long-term evidence regarding the duration of therapeutic effect associated with this FD therapy in previously untreated elderly and/or unfit patients with CLL is still limited.

Aims:

We used parametric models to simulate 6-year TTNT for patients who started FD I+V on the basis of the GLOW trial data, to estimate the expected share of patients who will not have started a subsequent anticancer therapy approximately 5 years after end of I+V treatment.

Methods:

The extrapolation was produced by applying survival distribution functions to the TTNT Kaplan Meier (KM) data. Survival distributions (S(t)) describe the probability of not experiencing an event (i.e., start of subsequent anti-cancer therapy) by time t. Exponential, Weibull, Gompertz, log-logistic, log-normal, Gamma and Generalized Gamma parametric models were applied for this analysis in line with National Institute for Health and Care Excellence (NICE) Technical Decision Support Unit recommendation. For each distribution, the fit to observed data was assessed by the Akaike Information Criterion (AIC) and Bayes Information Criterion (BIC).

Results:

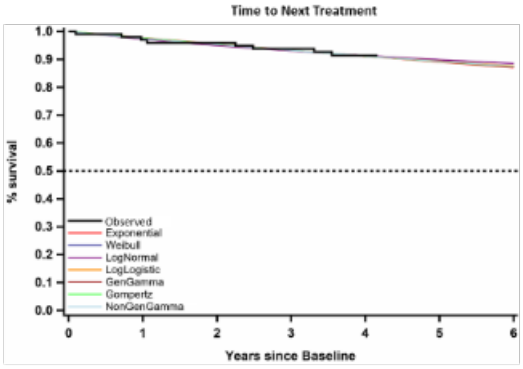
At the time of data cut-off (September 2022), there were 8 patients (7.55%) who had initiated a subsequent therapy after FD I+V. The KM curve for TTNT is provided in the figure, together with the fitted parametric models. The estimated percentage of patients free of subsequent treatment at the 6-year landmark, based on the different parametric models ranged from 87.0% to 88.5%.

Small differences in AIC and BIC values were observed between distributions, however the lowest values for both were reported for Exponential (AIC=119.3 and BIC=122.0) followed by Weibull, Log-logistic, and Gamma (all with AIC=121.3 and BIC=126.6).

Summary/Conclusion:

In conclusion, the extrapolation based on the observed TTNT data for the combined treatment of ibrutinib and

venetoclax suggests that at 6 years approximately 87% of patients treated with this combination will not require a second line of treatment. These findings suggest a promising long treatment-free period for previously untreated elderly and/or unfit CLL patients. However, caution is advised when interpreting these extrapolated results, and prospective long-term studies are needed to further validate the durability and efficacy of this therapeutic strategy in real-world clinical settings.



Survival distributions	Exponential	Weibull	Log-Normal	Log-logistic	Gen Gamma	Gompertz	Gamma
% of patients without subsequent therapy – 6 years	87.0%	87.5%	88.5%	87.6%	87.3%	87.4%	87.4%
AIC	119.3	121.3	121.4	121.3	123.3	121.3	121.3
BIC	122.0	126.6	126.8	126.6	131.3	126.7	126.6

Keywords: Chronic lymphocytic leukemia, ibrutinib