**METHODS**

We developed a life-time Markov cohort model in TreeAge Pro 2014 with 28-day cycle length and 5 health states, i.e. on treatment, rituximab maintenance (R-M) (90% of patients receive R-M for maximum of 2 years), stable disease, progression and death (see Table 1 for the model structure). Additionally, we modelled adverse events (AEs) of the treatment, and four sub-states during progression: 1) patients on observation during progression, 2) the next line of treatment during progression (imunochemotherapy/transplantation: CHOP-R 50.0%, CVP-R 25.0%, Fludarabin-R 16.6%, Dallplatin-R 8.3% and 15% patients receive autologous bone marrow transplant), 3) 2-year R-M period (80% of patients receive R-M in the subsequent line) and 4) post-R-M period. This treatment sequence was identified based on discussion with local clinical experts that it maximally reflects the Czech clinical practice [2].

Probability of progression was derived from the Kaplan-Meier curves from RCT [1] and extrapolated using survival analysis. Based on Asake information criterion, concordance with real clinical practice and visual fit, we used log-normal distribution for modelling of both interventions’ (B-R, CHOP-R) disease progression (Figure 2). Probabilities of AEs come from the RCT too [1]. Hazard ratio of 0.55 was applied during stable disease to probability of progression if patient underwent R-M, which is the literature data – Table 2 [10]. Utility/quality of life (QoL) data was derived from literature and equal to 0.805 (without progression), 0.618 (in progression) [4], 0.018 (an adverse event utility decrement) [5]. Due the lack of data about specific mortality, we used general Czech population mortality adjusted with specific mortality of patients in progressive disease. This approach is in line with previously published models in this disease area [4]. Resource use and costs were calculated from the healthcare payer’s perspective, based on expert opinion of Czech hematology/oncology clinical specialists [2] and using the current unit costs based on legislation and code lists. Costs and outcomes were discounted by 3.5% and converted to EUR from CZK using exchange rate of 27.44 CZK/ EUR [6]. Table 1 summarizes the model settings.

Probabilistic sensitivity analysis (PSA) was performed with 1,000 iterations using a willingness to pay (WTP) threshold equal to 3-times GDP per capita in the Czech Republic (40,100 EUR/QUALY) [7], the PSA setting is shown in Table 2. Lastly, scenario analyses of key model parameters (discount rate and time horizon) were performed.

**RESULTS**

Over a life-time horizon, B-R compared to CHOP-R brings additional 1.21 QALY (7.47 vs. 6.26) and 1.31 LYG (9.74 vs. 8.43), discounted. The incremental total costs were 1,368 EUR (total life time costs for B-R and CHOP-R were 43,080 EUR and 41,712 EUR, respectively). ICUR and ICER thus equal to 1,133 EUR/QALY and 1,044 EUR/ LYG (see Table 3).

The results of scenario analysis reveal high robustness of the model results (Table 4). When using the discount rate equal to 0% and 5%, the ICUR was equal to 567 and 1,466 EUR/ QALY, respectively. When using the time horizon equal to 20 and 10 years, the ICU was equal to 1,261 and 2,997 EUR/QUALY, respectively.

The results of scenario analyses highlight the importance of life-time horizon and WTP in the model results. The probability of progression was 55% in the Czech scenario and 45% in the UK one, but the results of the model analysis were similar with differences in costs and outcomes. The PSA revealed high robustness of the model results (Table 2).

**CONCLUSIONS**

Intervention of B-R proved that it is a highly cost-effective therapy in patients with follicular NHL stage III and IV in the Czech Republic. The higher costs of initial bendamustine treatment are in the long-term horizon offset by substantial savings of progression costs. There is 100% probability of B-R being cost-effective at the selected WTP threshold (3-times GDP per capita).

Consequently, the scenario analysis confirmed the results from the base-case scenarios when the changes in key parameters changed the final ICUR result only very slightly. The limitation of our analysis could be the absence of the Czech local utility data, as the UK published QoL data were used as the proxy. On the other hand, the results are still more than positive in terms of the cost per LYG.