For rare diseases like B-cell precursor acute lymphoblastic leukemia (B-ALL), trials frequently present limitations including small samples and single-arm design.

The BLAST trial is an open-label, multicenter, single-arm, phase 2 study that evaluated the efficacy of blinatumomab in patients with minimal residual disease (MRD) B-ALL in hematological complete remission (CR).

Blinatumomab resulted in complete MRD response in 111 of 514 patients who were associated with an overall survival (OS) of 36.5 months.6

The cost-effectiveness of blinatumomab vs chemotherapy was demonstrated from a US healthcare payer perspective using a partitioned survival analysis framework.

Partitioned Survival Models (PSMs)

– Are relatively simple, transparent, and require relatively few assumptions

– But are unable to link MRD response or survival and model explicitly the impact of subsequent treatment/interventions such as hematopoietic stem cell transplant (HSCT)

– Markov cohort models (MCMs)

– Can include intermediate endpoints affecting survival

– But require more assumptions and more parameter estimates

In the context, we propose to assess the value of using a PSM that only relies on relapse-free survival (RFS) and OS evaluating the cost-effectiveness of blinatumomab vs chemotherapy.

METHODS

– Clinical data from BLAST study (blinatumomab) and historical control study (chemotherapy) adjusted using inverse probability of treatment weighting were used to populate both cost-effectiveness models.

– In the PSM, RFS and OS were based on parametric distributions fit to patient level failure-time data from the BLAST trial and the historical control study.

– MRD response was included to estimate its consequences on resource use, but its impact on survival was not modelled.

– HSCT was included in the model to estimate its impact on costs and utilities, but its potential impact on survival was not included.

– To validate PSM findings, an MCM, which explicitly estimated the contribution of MRD and HSCT on survival, was developed.

– Time to HSCT, time to relapse conditional on HSCT, time to death conditional on HSCT were added to the model.

– All survival functions were derived according to MRD response; RFS response was applied only to the blinatumomab group since it was not available in the historical cohort.

– Transition probabilities for HSCT, relapse, and death were estimated using BLAST.

We evaluated the sensitivity of both models around parameters and assumptions.

RESULTS

CONCLUSIONS

– In both models, blinatumomab is cost-effective vs chemotherapy in ALL patients with MRD for US healthcare payers.

– Whether to use PSM vs MCM likely depends on a number of factors including sample size, duration of follow-up, nature of the clinical problem, strength of the association between intermediate and final outcomes, and availability of long-term observational data.

– In the context of blinatumomab, the PSM structure is simple, widely accepted, and can be based on a limited amount of data with few assumptions. However, it cannot explicitly account for treatment effects on survival mediated by MRD response or HSCT.

– However, MCM requires more assumptions due to limited data for estimating transition probabilities.

– MRD response was available only for one treatment arm

– The link between HSCT and survival independent of treatment was not well established from the BLAST trial

– Based on these elements, PSM is recommended as the primary approach to estimate the cost-effectiveness on blinatumomab in ALL.

REFERENCES


DISCLOSURE

– The study was funded by Amgen.