

COST-EFFECTIVENESS OF KTE-X19 FOR ADULT PATIENTS WITH RELAPSED/REFRACTORY B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA (R/R B-ALL) IN THE USA

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BACKGROUND

- Following standard chemotherapy or hematopoietic stem cell transplantation, relapsed/refractory (R/R) adult acute lymphoblastic leukemia (aALL) can be particularly challenging to treat.
- In the US, there are currently three treatments recommended broadly for patients with R/R aALL, including blinatumomab (BLIN), inotuzumab ozogamicin (INO), and salvage chemotherapy (CHEMO)¹. however, survival remains poor (less than 8 month median OS) with these options highlighting the need for new therapeutic strategies.²⁻⁵
- KTE-X19 is an anti-CD19 chimeric antigen receptor T-cell therapy which demonstrated potential to deliver long-term clinical benefits in adult patients with R/R aALL in the pivotal ZUMA-3 trial (NCT02614066).⁶

OBJECTIVE

- To estimate the incremental cost-effectiveness ratio of KTE-X19 versus current treatments: blinatumomab (BLIN), inotuzumab ozogamicin (INO), and salvage chemotherapy (CHEMO) for the treatment of R/R aALL patients adopting a US payer perspective.

METHODS

Model Perspective

- The model was conducted from a US commercial payer perspective that considered only direct medical costs.
- Health outcomes and costs were calculated over a lifetime horizon (59 years; patients enter model at age 41 years and were followed 100 years of age), discounted annually at 3%.

Model Structure

- The model structure used a decision-tree (KTE-X19) [three-state (event-free survival (EFS), progressed disease (PD),), death) and a weekly cycle length (Figure 1a). followed by partitioned-survival model with.
- For patients receiving KTE-X19, the decision tree component of the model accounted for outcomes for-patients intended for infusion: patients will receive bridging chemotherapy before infusion (pre-infusion period).
 - Patients who did not proceed to infusion but survived the pre-infusion period are assumed to incur costs and experience survival as a weighted sum of comparator therapies.
- Patients who did not receive infusion due to adverse events (AEs) are assumed to receive CHEMO; the remaining non-infused patients are equally distributed across receiving the three therapies in the model. (Figure 1b).

METHODS

Survival Extrapolation

- Clinical data were sourced from pivotal trials (ZUMA-3, TOWER, INO-VATE).⁴⁻⁶
 - A mixture-cure modeling (MCM) methodology was used to extrapolate EFS and overall survival (OS) for comparator therapies.
 - Parametric survival curves were used to extrapolate EFS for KTE-X19; patients event-free at 2 years were assumed to achieve long-term remission and followed general background mortality. An MCM methodology was used for extrapolating KTE-X19 OS.
- Patients without disease progression after two years were assumed to experience long-term remission. Patients achieving long-term remission were assumed to experience survival and quality of life similar to the general population.

Model Inputs

- Costs included-in the model included drug-related, administration (including infusion/injection costs, physician visits, and hospitalization), monitoring/resource use, subsequent treatment, allogeneic stem cell transplant (allo-SCT), AEs, and end-of-life costs.
 - Rates of allo-SCT use were sourced directly from clinical trials and assumed as a one-time cost at the beginning of the model due to lack of timing of allo-SCT in the comparator aggregate data.
- Utilities used in the model included health state utilities, disutilities due to drug infusion, and disutilities due to adverse events and allo-SCT and were sourced from the ZUMA-3 trial and published literature.

Costs, resource use, utilities and disutilities were sourced from published literature (Marketscan claims analysis), databases (Medicare fee schedules adjusted to commercial rates, Redbook) and pivotal trial publications.

Model Outcomes

- The model estimated expected life years (LYs), quality-adjusted life years (QALYs), total costs, and pairwise incremental cost-effectiveness ratios (ICERs).
- Deterministic, probabilistic sensitivity, and scenario analyses were performed.

Model Updates

RESULTS

Cost Outcomes

- Treatment costs (drug-related and administration cost), subsequent treatment costs and allo-SCT costs were the main contributors to the total costs for each treatment (Table 1).

Table 1. Lifetime Cost Outcomes (discounted)

COST COMPONENT	KTE-X19	BLIN	Δ vs KTE-X19	INO	Δ vs KTE-X19	CHEMO	Δ vs KTE-X19
Drug-related costs	\$359,939	\$425,229	-\$65,290	\$290,958	\$68,981	\$13,188	\$346,751
Administration costs	\$201,830	\$77,326	\$124,503	\$1,607	\$200,222	\$120,725	\$81,105
Monitoring costs	\$6,817	\$5,315	\$1,503	\$1,812	\$5,005	\$2,180	\$4,638
Subsequent tx costs	\$66,290	\$71,066	-\$4,776	\$25,260	\$41,030	\$73,234	-\$6,944
allo-SCT cost	\$75,724	\$101,414	-\$25,689	\$200,745	-\$125,021	\$95,483	-\$19,759
AE costs post index hospitalization	\$56,482	\$24,625	\$31,856	\$9,909	\$46,573	\$20,009	\$36,472
End-of-life costs	\$22,285	\$24,643	-\$2,358	\$25,660	-\$3,375	\$27,004	-\$4,719
Total costs	\$789,366	\$729,618	\$59,748	\$555,950	\$233,417	\$351,822	\$437,545

RESULTS (CONT'D)

Cost-Effectiveness Outcomes

- Using a lifetime horizon, incremental total Lys and QALYs of X19 were 2.86 and 2.48 vs BLIN; 4.01 and 3.31 vs INO; 5.65 and 4.68 vs CHEMO respectively. Total lifetime incremental costs of X19 were \$59,748, versus BLIN; \$233,417, versus INO; and \$437,545 vs CHEMO, respectively. (Table 2).
- Incremental costs and incremental QALYs resulted in an ICER of \$24,108/QALY, \$70,616/QALY, and \$93,539/QALY, as compared to BLIN, INO and CHEMO, respectively (Table 2).

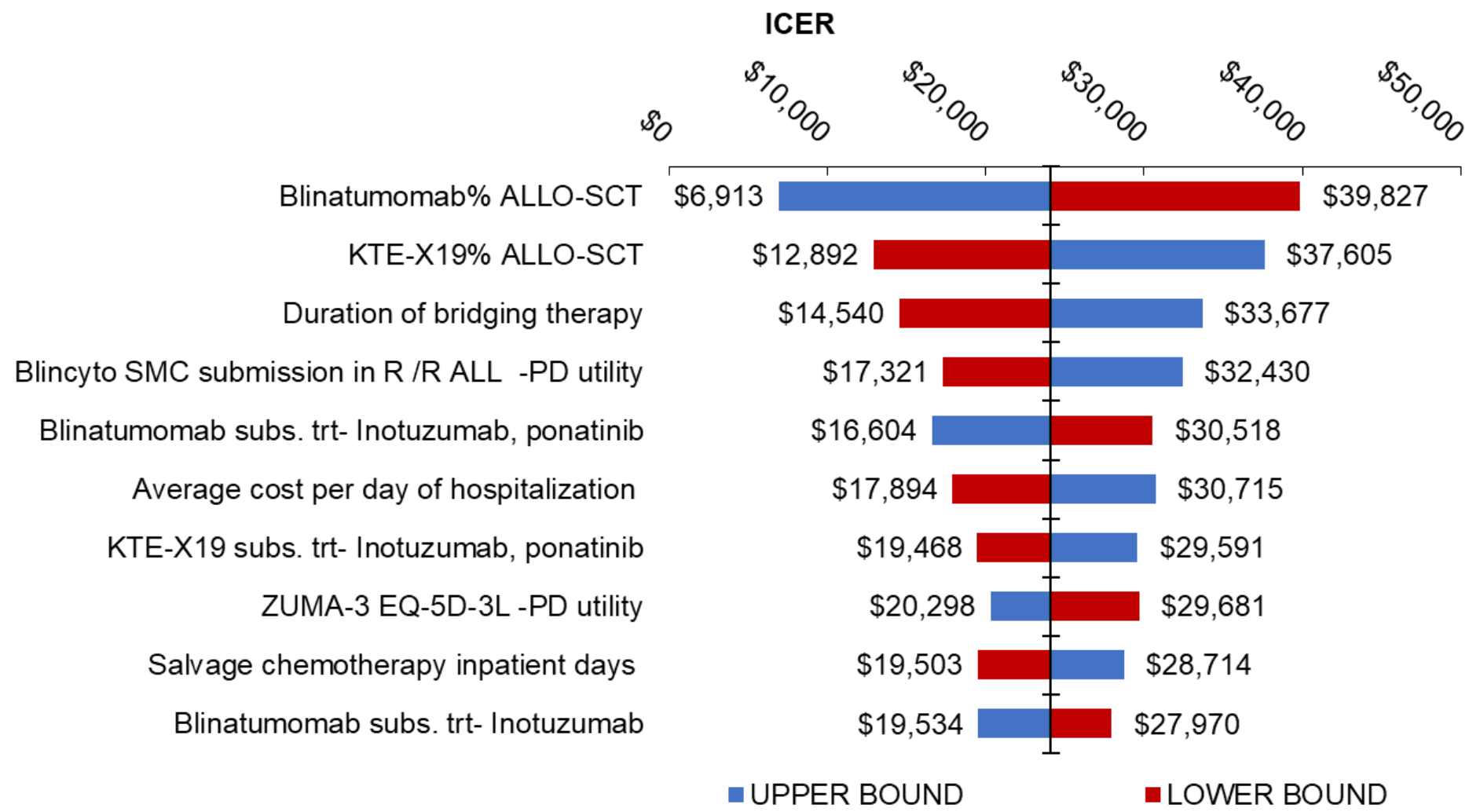
Table 2. Cost-Effectiveness Outcomes (discounted)

DRUG	TOTAL COST	TOTAL LY	TOTAL QALYs	INCR. COSTS	INCR. LY	INCR. QALY	ICER (\$/QALY)
KTE-X19	\$789,366	7.84	6.03	Ref	-	-	-
BLIN	\$729,618	4.98	3.55	\$59,748	2.86	2.48	\$24,108
INO	\$555,950	3.83	2.73	\$233,417	4.01	3.31	\$70,616
CHEMO	\$351,822	2.19	1.35	\$437,545	5.65	4.68	\$93,539

One-Way Sensitivity Analyses

- In one-way and probabilistic sensitivity analyses, a standard error of 20% was assumed across all inputs point estimates, with lower / upper bounds are calculated as 2.5% and 97.5% quantile values of those distributions (Normal, Gamma or Beta distribution based on the parameter).
- Results were robust in one-way sensitivity analyses; as compared to BLIN (Figure 3), key model drivers were rates of allo-SCT use, duration of bridging therapy for KTE-X19, health state utilities, and subsequent treatment composition. Similar drivers were observed for INO and CHEMO.

Figure 3. One-Way Sensitivity Analysis Results vs. BLIN



Probabilistic Sensitivity Analyses

- In probabilistic sensitivity analyses, KTE-X19 was projected to be ~77%, ~74% and ~74% likely to be cost-effective as a willingness-to-pay threshold of \$150,000/QALY vs. BLIN, INO or CHEMO, respectively.

RESULTS (CONT'D)

Scenario Analyses

- Scenario analyses examined the impact of model time horizon, discount rate, AE costs, excess mortality for patients with long-term remission from literature based standardized mortality (SMR) scenarios, and utility values (Table 3). In all scenarios, KTE-X19 was cost-effective vs. BLIN. Similar trends were observed in comparisons against INO and CHEMO.

Table 3. Scenario Analysis Results vs. BLIN

#	SCENARIO	ICER, KTE-X19 vs. BLIN
0	Base case scenario	\$24,108
1	Time horizon 10 Years	\$40,757
2	Time horizon 20 Years	\$30,064
3	Discount rate 5%	\$19,394
4	Discount rate 0%	\$26,552
6	Long-term remission patients, excess mortality SMR=4.00 ⁷	\$30,381
7	Long-term remission patients, excess mortality SMR=9.05 ⁸	\$38,167
8	Long-term remission patients, excess mortality SMR=1.09 ⁹	\$24,355
9	CRS utility decrement, alternative literature-based source	\$24,777
10	Long-term remission patients' utility, alternative source	\$26,629
11	KTE-X19 AEs disutility from ZUMA-3	\$23,816

LIMITATIONS

- Survival data for comparators are sourced directly from clinical trials; differences in trial patient populations may account for difference in survival outcomes projected in this analysis.
- KTE-X19 EFS/OS extrapolations using the mITT phase 2 data set are based on a small sample size with less than 2 year follow up data, long-term extrapolations are associated with high-uncertainty.

CONCLUSIONS

- KTE-X19 is a cost-effective treatment compared to commonly used treatment options for R/R aALL in the US.
- Therefore, KTE-X19 is an economically and clinically effective option to add to the current treatment landscape.

DISCLOSURE

CF, GC, and BK are employees of Kite Pharma, A Gilead Company. NS and AR received consulting fees from Kite Pharmaceuticals.

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Figure 1b. KTE-X19 pre-infusion decision tree

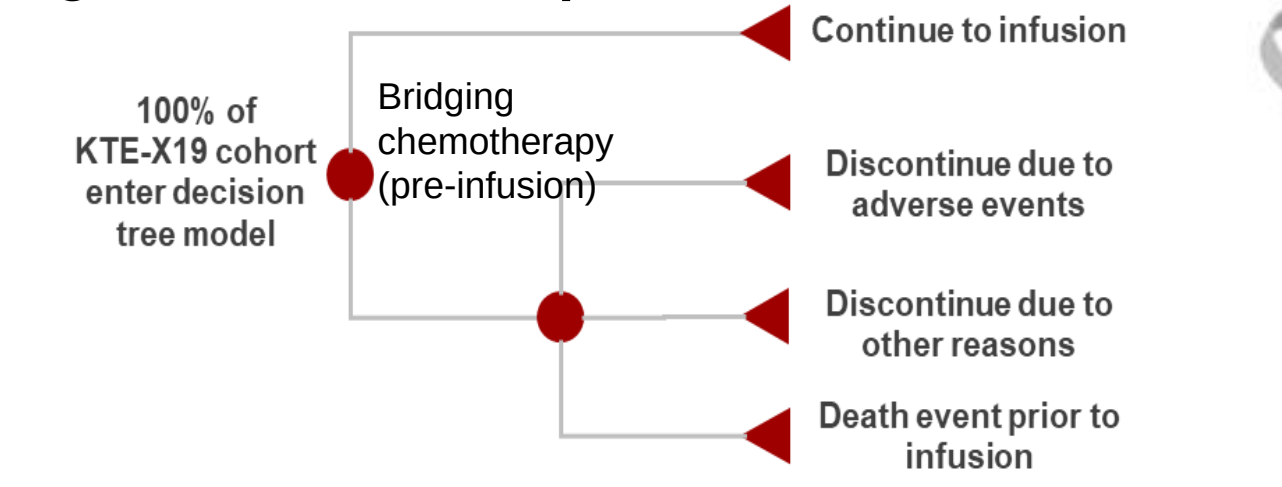


Figure 1a. Model Structure

