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COST-EFFECTIVENESS OF KTE-X19 IN PATIENTS WITH RELAPSED/REFRACTORY MANTLE CELL LYMPHOMA

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Disclosures

- Gilead srl (Consultancy)

Background and aims

- Mantle cell lymphoma (MCL) patients failing chemoimmunotherapy and ibrutinib face a poor prognosis
- KTE-X19 is a chimeric antigen receptor (CAR) T-cell therapy adopting transduced anti-CD19 CD3+ autologous lymphocytes
- ZUMA-2 trial after a median follow-up of 17.5mo reported an overall response rate (ORR) for 92%, with a Complete Response (CR) rate of 67% in relapsed/refractory (R/R) MCL patients previously treated with ibrutinib[1]
- The present study aimed at comparing the clinical and economic outcomes of R/R MCL patients treated with KTE-X-19 versus the standard of care (SOC) in the Italian Healthcare System

1- Wang M, et al. Blood. 2020;136(suppl 1):20-22.

Methods

- A partitioned-survival model was used to extrapolate progression-free survival (PFS), overall survival (OS) and healthcare costs of R/R MCL patients over a lifetime horizon, using the assumption that patients whose disease had not progressed after 5 years experienced long-term remission[1]
- Rituximab, bendamustine, cytarabine (R-BAC) was the baseline standard-of-care (SOC)[2]
- The source of safety and survival data for KTE-X19 was ZUMA-2 trial (17.5mo median follow-up data)[3]
- PFS utility from ZUMA-2 trial = 0.824 (-0.10 for progressing pts)
- Costs and health outcomes were discounted at 3% per year.

1- Bansal et al MDM 2019; 2- McCullogh et al BJH 2020; 3- Wang M, et al. Blood. 2020;136(suppl 1):20-22.

Therapies	Code or dose	Unit cost
Fludarabine	50 mg	€76.74
Ciclofosphamide	1,000 mg 2,000 mg	€11.88 €23.76
Apheresis	99.72	€402.85
Crioconservazione	90.60.3	€361,50
KTE-X19		€360,000
Rituximab	100 mg 500 mg	€444.15 €1,110.17
Bendamustine	25 mg 100 mg	€46.41 €185.64
Cytarabine	500 mg 1,000 mg	€7.64 €15.29
Tocilizumab	400 mg	€708.93
Intravenous immunoglobulins	10 gr	€831.00
Parenteral drug administration (outpt)	DRG410	€47

Value data input

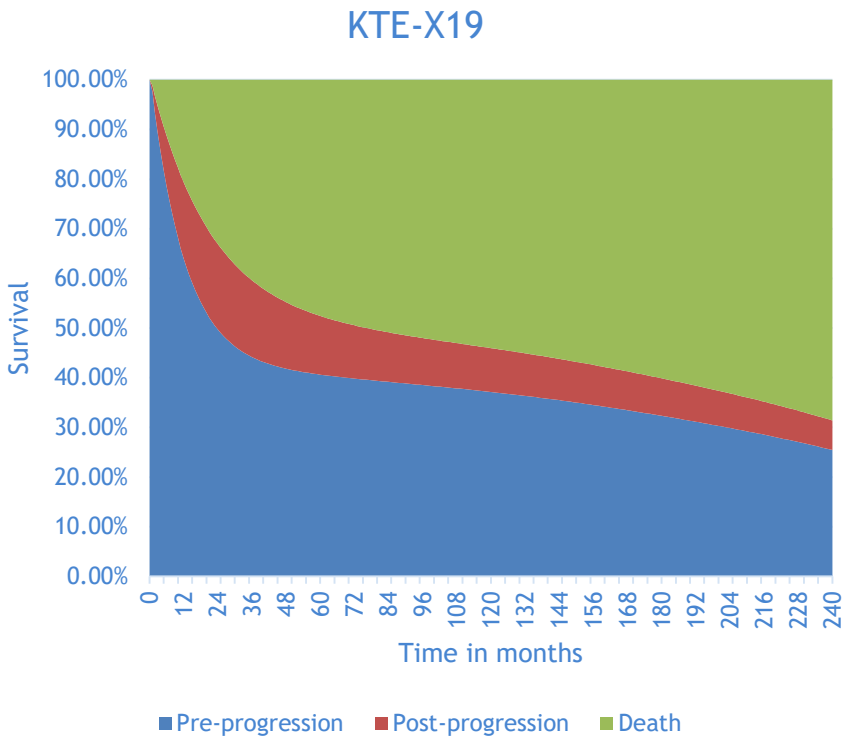
Inpatient stay	Unit	Unit cost	Consumption
ICU stay	day	€1,383	21.2 * 23%
Non-ICU stay	day	€405	21.2 * 77%
Allogeneic SCT	whole stay	€179,418	0.31 (R-BAC)

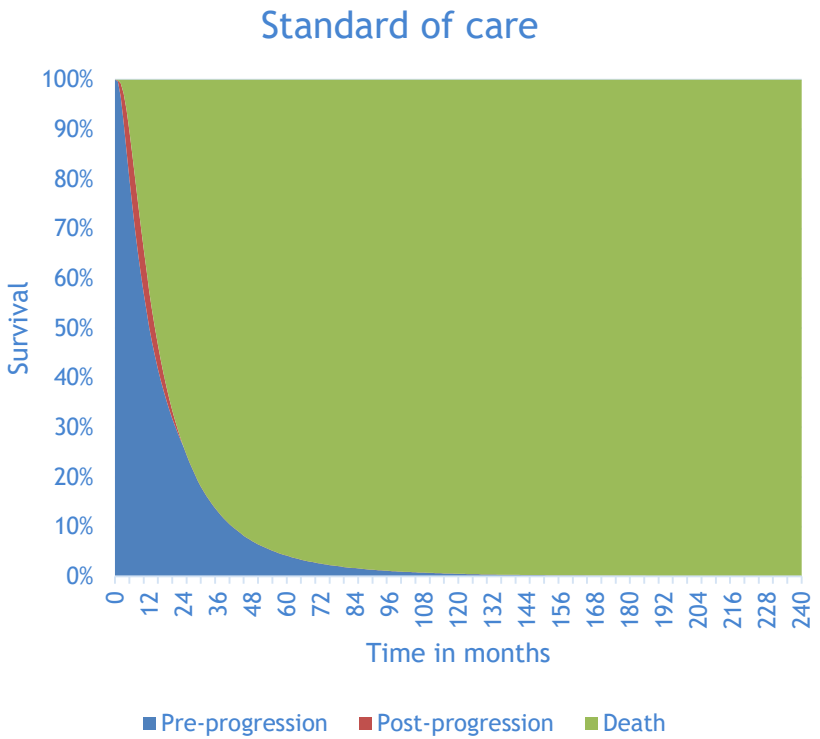
1-Tan 2012, 2-Maziarz 2018

ADVERSE EVENTS	Utility (days)	Costs	Frequency KTE-X19
CRS grade 2-4	-0.760 (12)	€5,671	62%
Encephalopathy	-0.15 (12)	€3,433	12%
Pneumonia or respiratory failure	-0.15 (7)	€2,102	19%
Sepsis	-0.15 (23)	€3,433	6%
Acute renal failure	-0.15 (7)	€2,417	7%
Hypogammaglobulinemia	0	€44,903	20%

3-Campione 2014, 4-Wehler 2017, NICE Z1 submission

Time spent in health states





Baseline analysis vs R-BAC

	KTE-X19	R-BAC	Incremental difference
Total life years	8.85	1.56	7.28
Progression-free	7.09	1.46	5.63
Post-progression	1.76	0.10	1.66
Total quality-adjusted life years	6.40	1.20	5.20
Progression-free	5.33	1.13	4.19
Post-progression	1.16	0.07	1.06
Adverse events	-0.05	0.00	-0.05
Total costs	€411,403	€74,415	€336,988
Treatment-related	€376,884	€49,639	
Disease-management	€9,464	€1,641	€7,824
End-of-life	€6,858	€4,965	€1,107
Management of adverse events	€21,197	€0	€21,197
Cost per life years	-	-	**€46,264**
Cost per QALY	-	-	**€64,798**

Results using alternative comparators

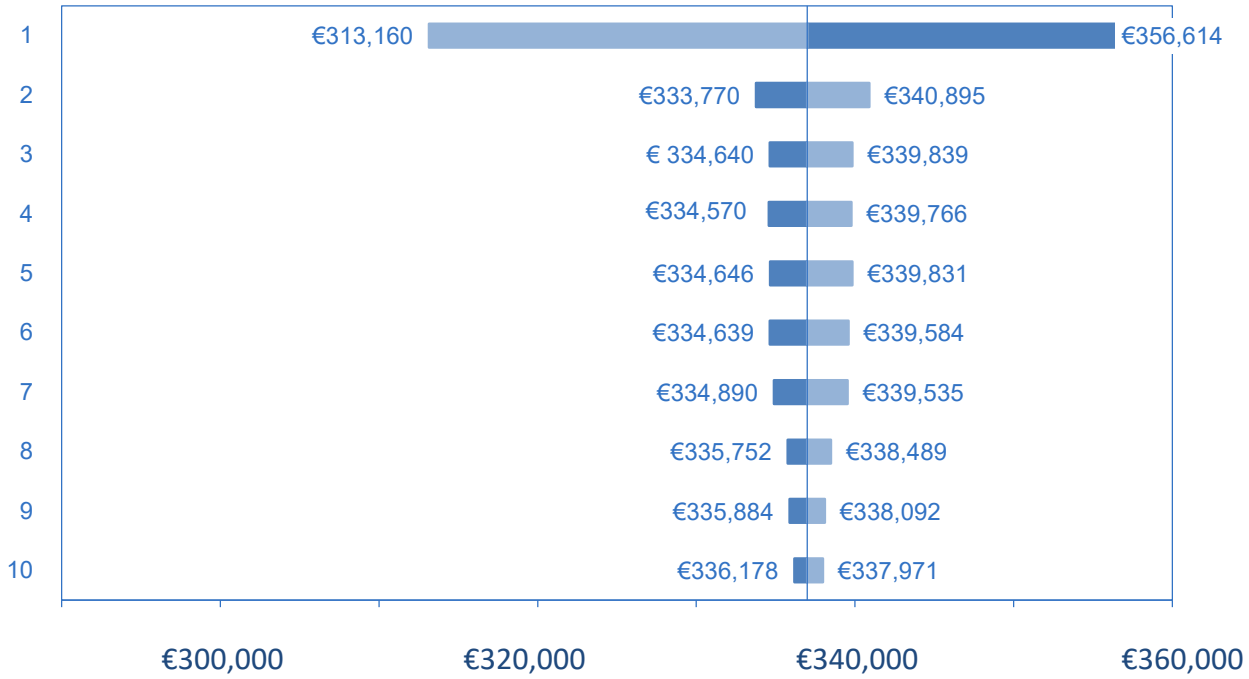
- OS from meta-analysis of 4 studies devoted to R/R post-ibrutinib MCL patients, treated with BAC, acalabrutinib,venetoclax, lenalidomide [1,4]. Gompertz shape for long-term extrapolations
- PFS from meta-analysis of 2 studies. Lognormal shape for long-term extrapolation. The meta-analysis estimated PFS/OS ratio to be 0.76
- SCHOLAR-2 is a real-world retrospective study including patient-level OS data from 59 R/R MCL propensity-matched to ZUMA-2 patients[5]. Weibull distribution per long-term extrapolations. PFS estimated as 0.76*OS.

	KTE-X19	SCHOLAR-2	Incremental difference	Meta-analysis	Incremental difference
Total life years	8.85	2.30	6.55	1.65	7.20
Total quality-adjusted life years	6.40	1.69	4.72	1.22	5.18
Total costs	€411,403	€138,269	€273,134	€121,270	€290,133
Treatment-related	376,884	€129,036	€247,848	€113,339	€263,545
Cost per life years	-	-	€41,716	-	€40,319
Cost per QALY	-	-	€57,915	-	€56,010

1-Martin P, Blood 2016: 1559.. 2-McCullogh R, Br J Haematol 2020:684. 3-Eyre TA, Haematologica 2019:e68. 4-Jain P, Br J Haematol 2018:578, 5-Simons CL, J Med Econ 2021:421.

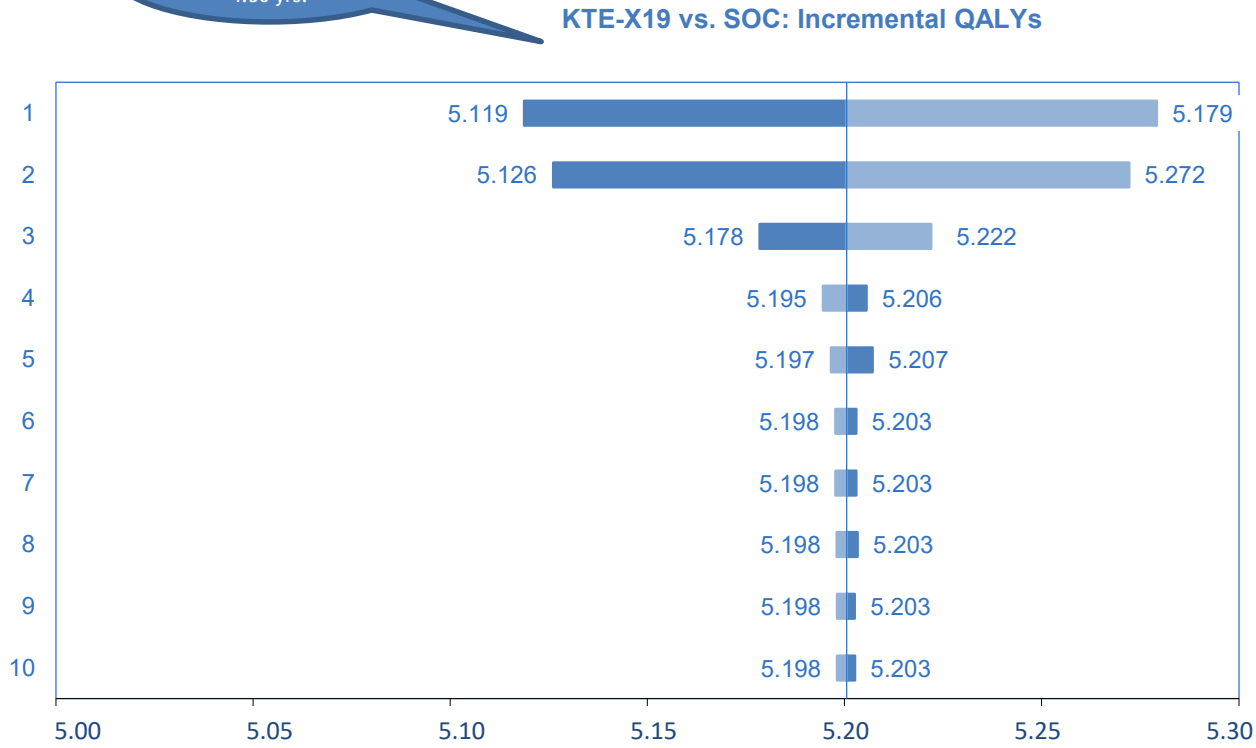
Sensitivity analysis

ICUR 84,564 at age 70 yrs

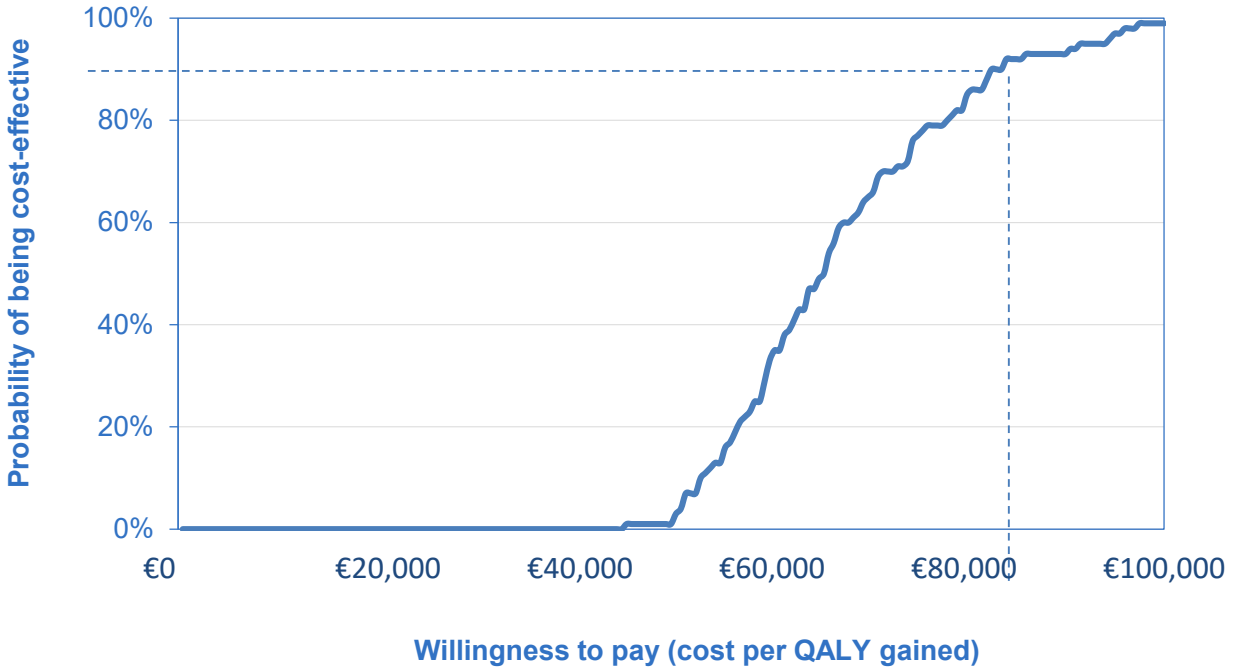


Sensitivity analysis

Age + 5 yrs reduces incremental QALE to 4.30 yrs.



Second-order sensitivity analysis



At a WTP threshold of €87,330 per QALY (Martone N 2014) the probability of KTE-X19 being cost-effective was ~90%.

Conclusions

- In refractory/relapsed MCL patients after chemoimmunotherapy and ibrutinib, KTE-X19 is an effective therapy as compared with R-BAC and other SOC treatments.
- In the Italian healthcare system KTE-X19 is expected to generate 5.20 discounted QALYs at a cost of €64,798 per QALY saved.
- The ICER is similar to CAR-T therapies for R/R DLBCL in the same healthcare setting
- The most influential model parameters were patients' age, KTE-X19 acquisition cost and time-horizon for the analysis.
- The results were also impacted by utility scores attributed to patients in the post progression and long-remission health states