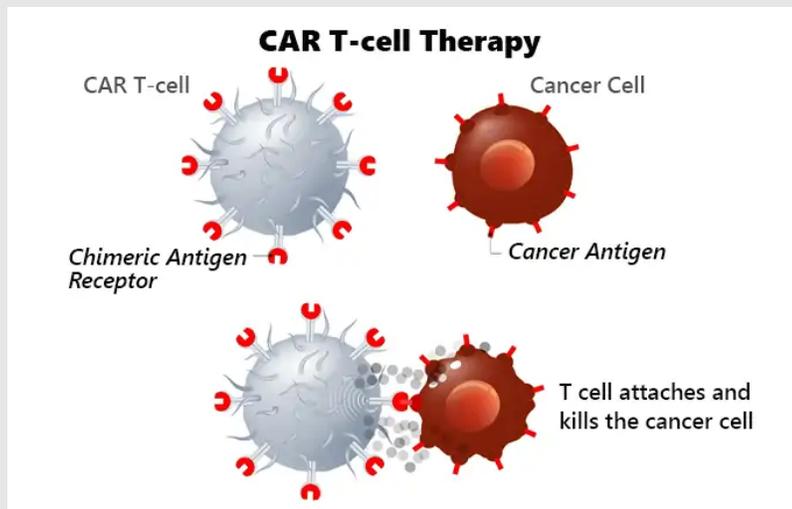


## Using Modeling to Demonstrate the Kinetics of Liso-Cel Transgene

Bristol Myers Squibb (BMS) sought to develop lisocabtagene maraleucel, a CAR-T cell therapy, to treat patients with relapsed/refractory large B-cell lymphoma. Historically, large between-subject variability has been noted with CAR T-cell therapies. The client needed to understand how patient characteristics might contribute to CAR T-cell expansion variability. Certara developed a population cellular kinetic model to characterize the kinetics of the liso-cel transgene, via quantitative polymerase chain reaction assessment after intravenous infusion of liso-cel, and to understand covariates that might influence liso-cel kinetics in individual patients.

Certara pharmacometricians employed nonlinear mixed-effects modeling to develop a population cellular kinetic model for liso-cel. Covariates for the analysis included baseline intrinsic factors such as age, baseline disease characteristics, and liso-cel and coadministration factor.

Liso-cel cellular kinetics were well described by our model that featured lag, exponential growth, and biexponential decay phases. The magnitude of effect on liso-cel expansion metrics demonstrated that the covariate associations were smaller than the residual between-subject variability in the population. The covariates tested were not considered to have a meaningful impact on liso-cel kinetics. Thus, dose adjustments are not needed for specific populations.



***CAR T-cell therapy is a form of immunotherapy that alters a patient's T cells. A patient's T cells are taken from their body, and a chimeric antigen receptor (CAR) is added to the cells in a lab. The engineered CAR T cells are then reintroduced into the patient to fight their cancer.***

Bristol Myers Squibb is an American multinational pharmaceutical company, headquartered in New York City. The client is one of the world's largest pharmaceutical companies and is consistently ranked on the Fortune 500 list of the largest U.S. corporations. The client manufactures prescription pharmaceuticals and biologics in several therapeutic areas, including cancer, HIV/AIDS, cardiovascular disease, diabetes, hepatitis, rheumatoid arthritis, and psychiatric disorders.



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