Swiss Summary of the Risk Management Plan (RMP)

for

YESCARTA®

(axicabtagene ciloleucel)

Version 1.0 (June 2019)

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1. SUMMARY OF RISK MANAGEMENT PLAN FOR YESCARTA (AXICABTAGENE CILOLEUCEL)]

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine.

The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimize them.

The RMP summary of Yescarta (axicabtagene ciloleucel) is a concise document and does not claim to be exhaustive. As the RMP is an international document, the summary might differ from the "Arzneimittelinformation" approved and published in Switzerland, e.g. by mentioning risks occurring in populations or indications not included in the Swiss authorization. Please note that the reference document which is valid and relevant for the effective and safe use of Yescarta in Switzerland is the "Arzneimittelinformation" (see www.swissmedicinfo.ch) approved and authorized by Swissmedic.

Kite Pharma EU B.V. is fully responsible for the accuracy and correctness of the content of the published summary RMP of Yescarta.

1.1. The Medicine and What it is Used For

Yescarta is authorized for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) and primary mediastinal large B-cell lymphoma (PMBCL), after two or more lines of systemic therapy (see SmPC for the full indication). It contains axicabtagene ciloleucel as the active substance and it is a single infusion product for autologous and intravenous use only.

Further information about the evaluation of Yescarta's benefits can be found in Yescarta's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage*:*

http://www.ema.europa.eu/ema/index.jsp?curl=/pages/medicines/human/medicines/human_med_002292.jsp&mid=WC0b01ac058001d124.

1.2. Risks Associated with the Medicine and Activities to Minimize or Further Characterize the Risks

Important risks of Yescarta, together with measures to minimize such risks and the proposed studies for learning more about Yescarta's risks, are outlined below.

Measures to minimize the risks identified for medicinal products can be:

- Specific Information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;

- Important advice on the medicine's packaging;

- The authorized pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;

- The medicine's legal status — the way a medicine is supplied to the public (e.g. with or without prescription) can help to minimizes its risks.

Together, these measures constitute routine risk minimization measures.

In the case of Yescarta, these measures are supplemented with additional risk minimization measures mentioned under relevant important risks, below.

In addition to these measures, information about adverse reactions is collected continuously and regularly analyzed (eg, via the periodic safety update report [PSUR]) so that immediate action can be taken as necessary. These measures constitute routine pharmacovigilance activities.

If important information that may affect the safe use of Yescarta is not yet available, it is listed under 'missing information' below.

1.2.1. List of Important Risks and Missing Information

Important risks of Yescarta are risks that need special risk management activities to further investigate or minimize the risk, so that the medicinal product can be safely administered. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Yescarta. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine);

Table 1-1. List of Important Risks and Missing Information

Important Identified Risks	Serious neurologic adverse reactions including cerebral oedema
	Cytokine release syndrome (CRS)
	Cytopenias including aplastic anaemia
	Infections
	Hypogammaglobulinaemia
Important Potential Risks	Secondary malignancy
	Immunogenicity
	Replication-competent retrovirus (RCR)

	Tumor lysis syndrome (TLS)
	Aggravation of graft vs host disease (GvHD)
	Transmission of infectious agents via product
	Decrease in viability of the product due to inappropriate preparation of infusion
Missing Information	Use in pregnancy and lactation
	Use in non-Caucasian patient populations
	New occurrence or exacerbation of an autoimmune disorder
	Long term safety

1.2.2. Summary of Important Risks

Table 1-2. Summary of Important Identified Risks

Important Identified Risk	**Serious Neurologic Adverse Reactions including Cerebral Oedema**
Evidence for linking the risk to the medicine	Although neurologic toxicity is associated with axicabtagene ciloleucel, the mechanisms underlying the neurologic events remain unclear. Results of ZUMA-1 showed that 64% of the patients experienced neurologic events, 25% of the patients experienced serious neurologic events, and 28% of the patients experienced grade 3 or higher neurologic events.
Risk factors and risk groups	*Patient factors* Multiple groups have found anti-CD19 CAR T cells in the cerebrospinal fluid (CSF) of patients, and elevated IL-6 levels in the CSF have been observed in patients experiencing neurotoxicity (Brudno and Kochenderfer 2016). AUC at 1 month and peak levels of anti-CD19 CAR T cells as well as the peak and AUC of IL-15 and IL-6, along with several other cytokines, were associated with neurologic events. Compared with subjects ≥65 years of age, subjects <65 years of age had a lower incidence of neurologic events (61% vs 75%). Compared with males, females had a higher incidence of serious neurologic events (33% vs 21%). *Dose-related* Subjects who received product with total anti-CD19 CAR T-cell number greater than the population median had higher incidences of neurologic events (70.0% vs 58.8%). Subjects dosed with product potency (defined as interferon gamma [IFN-γ] production) greater than the population median had higher neurologic events (66.0% vs 62.7%); and neurologic SAEs (30.0% vs 19.6%).
Risk Minimization Measure(s)	Routine risk minimization measures: SmPC sections 4.2, 4.4 and 4.8 PL sections: 2, 4 Other routine risk minimization measures beyond the Product Information: Use restricted to physicians experienced in the treatment of hematological cancers Additional risk minimization measures: HCP educational material PAC

	Controlled distribution program
Additional Pharmacovigilance activities	Registry, prescriber survey, and studies ZUMA-1 – ZUMA-6 See Part VI Section 1.2.3 of this summary for an overview of the post-authorization development plan.
Important Identified Risk	**Cytokine Release Syndrome (CRS)**
Evidence for linking the risk to the medicine	CRS is induced by activated anti-CD19 CAR T cells upon engagement with the CD19 target and may involve a generalized and reversible inflammatory process. In ZUMA-1, 93% of the patients experienced CRS; 13% had severe CRS. CRS is considered an important identified risk due to its frequency and seriousness and the potential for severe outcomes if left untreated.
Risk factors and risk groups	*Patient factors* In some reports, the severity of CRS and elevation of serum cytokines have been related to disease burden, with higher disease burden predicting more toxicity presumably because this leads to higher levels of T-cell activation (Almasbak et al, 2016; Brudno and Kochenderfer 2016). Maude et al. reported that the baseline disease burden (the percentage of blast cells in bone marrow before infusion) correlated with the severity of the CRS; a higher disease burden was significantly associated with severe CRS (P = 0.002) (Maude et al, 2014). CRS associated with adoptive T-cell therapies has been consistently associated with elevated IFN-γ, IL-6, and tumor necrosis factor alpha (TNFα) levels, and increases in IL-2, granulocyte macrophage–colony-stimulating factor (GM-CSF), IL-10, IL-8, IL-5, and fractalkine (Kalos et al, 2011; Kochenderfer et al, 2012; Grupp et al, 2013; Davila et al, 2014). In ZUMA-1 no significant difference in incidence of CRS were observed in subjects based on their performance status (i.e., ECOG), age, or gender. CRS has been known to be associated with end organ dysfunction (e.g., hepatic, renal, cardiac, pulmonary). In addition, worsening of underlying organ pathologies can occur in the setting of CRS. *Dose-related* Subjects who received product with total T-cells number greater than the population median had a higher incidence of Grade 3 or higher CRS (17.6% vs 8.0%). Subjects dosed with product potency (defined as IFN-γ production) > the population median had higher Grade 3 or higher CRS (20.0% vs 5.9%).
Risk Minimization Measure(s)	Routine risk minimization measures: SmPC sections 4.2, 4.4 and 4.8 PL sections: 2, 4 Other routine risk minimization measures beyond the Product Information: Use restricted to physicians experienced in the treatment of hematological cancers Additional risk minimization measures: HCP educational material PAC Controlled distribution program
Additional Pharmacovigilance activities	Registry, prescriber survey, and studies ZUMA-1 –ZUMA-6 See Part VI Section 1.2.3 of this summary for an overview of the post-authorization development plan.

Important Identified Risk	**Cytopenias including Aplastic Anaemia**
Evidence for linking the risk to the medicine	Cytopenias are consistent with the known toxicities of the conditioning regimen of chemotherapy. In addition axicabtagene ciloleucel may cause myelosuppression by a cytokine mediated mechanism. In ZUMA-1, Phase 2, 84%, 66%, and 58% of the patients had neutropenia, anaemia and thrombocytopenia, respectively; 78%, 43% and 38% of these cases were Grade 3 or higher, respectively. There were no reported AEs of aplastic anaemia, and one reported AE of bone marrow failure considered not related to Yescarta. Cytopenias are considered important identified risk due to their frequency, seriousness and severity which could lead to important clinical manifestations such as infection or bleeding.
Risk factors and risk groups	A systematic review of cancer patients receiving chemotherapy showed that older age, poor performance status, female gender, comorbidities, and low BMI are risks factors for the development of febrile neutropenia (Lyman et al, 2014). The risk of febrile neutropenia increases in direct proportion to the severity and duration of neutropenia (Lyman and Rolston 2010). Bone marrow involvement was found to be a risk factor for chemotherapy induced neutropenia and fever (Kitay-Cohen et al, 1996).
Risk Minimization Measure(s)	Routine risk minimization measures: SmPC sections 4.4 and 4.8 PL sections: 2, 4 Other routine risk minimization measures beyond the Product Information: Use restricted to physicians experienced in the treatment of hematological cancers Additional risk minimization measures: None
Additional Pharmacovigilance activities	Registry, and studies ZUMA-1 –ZUMA-6 See Part VI Section 1.2.3 of this summary for an overview of the post-authorization development plan
Important Identified Risk	**Infections**
Evidence for linking the risk to the medicine	Infections, especially serious infections, are consistent with the known toxicities of the conditioning regimen of chemotherapy. In addition axicabtagene ciloleucel can cause depletion of B-cells. In ZUMA-1 Phase 2, 38% of the patients had any infection. Infections are considered important identified risk due to their frequency, seriousness and severity if left untreated. Thus, further evaluation of frequency, severity, seriousness and outcome of this risk in the post-marketing period is warranted.
Risk factors and risk groups	Factors that predispose to infection are divided into those that are host associated and those that are treatment associated. *Patient factors* Host-associated factors include underlying immune deficiencies, medical comorbidities, past infections, poor nutritional status, and psychological stress. The type of malignancy and status of the malignancy (i.e., active or in remission) are important factors in determining infection risk. Patients with acute lymphoma who are neutropenic, either due to their underlying disease or due to cytotoxic chemotherapy, are at risk for a different set of infections than those who are not neutropenic (Zembower 2014). *Additive or synergistic factors* Treatment-associated factors include surgery, radiation, immunosuppressant therapies, antimicrobial use, and invasive procedures are important factors in the risk of infections (Zembower 2014).

Risk Minimization Measure(s)	Routine risk minimization measures: SmPC sections 4.4 and 4.8 PL sections: 2, 4 Other routine risk minimization measures beyond the Product Information: Use restricted to physicians experienced in the treatment of hematological cancers Additional risk minimization measures: None
Additional Pharmacovigilance activities	Registry, and studies ZUMA-1 –ZUMA-6 See Part VI Section 1.2.3 of this summary for an overview of the post-authorization development plan
Important Identified Risk	**Hypogammaglobulinaemia**
Evidence for linking the risk to the medicine	Hypogammaglobinemia is caused by B-cell aplasia. In ZUMA-1, 11% of the patients experienced hypogammaglobinemia. Hypogammaglobinemia is considered an important identified risk due to the risk of infections if left untreated.
Risk factors and risk groups	Prior treatment with rituximab and concomitant use of other drugs (e.g. steroids) that can induce Hypogammaglobulinemia.
Risk Minimization Measure(s)	Routine risk minimization measures: SmPC sections 4.4 and 4.8 PL section: 4 Other routine risk minimization measures beyond the Product Information: Use restricted to physicians experienced in the treatment of hematological cancers Additional risk minimization measures: None
Additional Pharmacovigilance activities	Registry, and studies ZUMA-1 –ZUMA-6 See Part VI Section 1.2.3 of this summary for an overview of the post-authorization development plan

Table 1-3. Summary of Important Potential Risks

Important Potential Risk	**Secondary Malignancy**
Evidence for linking the risk to the medicine	Secondary malignancy is consistent with the known outcomes of immunosuppression and/or genotoxicity resulting from chemotherapy. Patients with NHL are known to be at risk for developing secondary malignancies (Tward et al, 2006; Smeland et al, 2016). Secondary malignancy is serious, potentially life-threatening and would require medical intervention and hence it is an important potential risk.
Risk factors and risk groups	*Patient factors* Age is a risk factor for secondary malignancy (Andre et al, 2004; Moser et al, 2006). A meta-analysis showed that NHL patients experience a higher risk for secondary malignant neoplasms than the general population (pooled relative risk of 1.88 overall and 1.32 for solid tumors) (Pirani et al, 2011). *Additive or synergistic factors* Use of any type of chemotherapy alone was associated with higher risk for secondary malignant neoplasms. A similar result was observed in the sub-analysis on patients treated only with alkylating agents, while the pooled relative risk of secondary malignant neoplasms for patients who underwent treatment with CHOP or CHOP-like or radiotherapy alone was raised but not statistically significant. A combined modality of treatment was significantly associated with the risk for overall secondary malignant neoplasms but not for solid tumors (Pirani et al, 2011).
Risk Minimization Measure(s)	Routine risk minimization measures: SmPC sections 4.4 Other routine risk minimization measures beyond the Product Information: Use restricted to physicians experienced in the treatment of hematological cancers Additional risk minimization measures: None
Additional Pharmacovigilance activities	Registry, and studies ZUMA-1 –ZUMA-6 See Part VI Section 1.2.3 of this summary for an overview of the post-authorization development plan
Important Potential Risk	**Immunogenicity**
Evidence for linking the risk to the medicine	Immunogenicity, defined as the development of antibodies to either 1) the murine monoclonal antibody FMC63, the parent antibody from which the scFv utilized in the axicabtagene ciloleucel product was derived, or 2) bovine serum albumin, a trace contaminant in the product, was assessed in ZUMA-1. Immunogenicity was investigated in ZUMA-1 and does not indicate a significant development of antibodies. Furthermore, those patients in whom antibodies existed did not show any evidence of immunological allergic reactions. Antibodies can reduce efficacy and can cause safety issues like anaphylaxis, CRS, infusion reactions etc. that may require medical intervention and hence it is an important potential risk.
Risk factors and risk groups	Not known.

Risk Minimization Measure(s)	Routine risk minimization measures: SmPC section 4.8 Other routine risk minimization measures beyond the Product Information: Use restricted to physicians experienced in the treatment of hematological cancers Additional risk minimization measures: None
Additional Pharmacovigilance activities	Registry, and studies ZUMA-1 –ZUMA6 See Part VI Section 1.2.3 of this summary for an overview of the post-authorization development plan
Important Potential Risk	**Replication-Competent Retrovirus (RCR)**
Evidence for linking the risk to the medicine	As a retroviral vector is used in the production of axicabtagene ciloleucel, a potential risks exists for the presence of RCR. No subjects tested positive for presence of RCR, however RCR is considered important potential risk due to the risk of genotoxicity that may lead to secondary malignancy. Thus further evaluation of frequency of this risk in the post-marketing period is warranted.
Risk factors and risk groups	Not applicable
Risk Minimization Measure(s)	Routine risk minimization measures: Other routine risk minimization measures beyond the Product Information: Use restricted to physicians experienced in the treatment of hematological cancers Additional risk minimization measures: None
Additional Pharmacovigilance activities	Registry, and studies ZUMA-1 –ZUMA-6 See Part VI Section 1.2.3 of this summary for an overview of the post-authorization development plan
Important Potential Risk	**Tumor lysis syndrome (TLS)**
Evidence for linking the risk to the medicine	TLS occurs as a result of massive tumor cell death and thus it is consistent with the potential effects of conditioning chemotherapy and axicabtagene ciloleucel treatment. In ZUMA-1 there were two cases of TLS of which one occurred with conditioning chemotherapy before axicabtagene ciloleucel treatment. TLS is considered an important potential risk due to the seriousness of the condition.
Risk factors and risk groups	Patients with bulky disease, baseline elevated uric acid and renal impairment
Risk Minimization Measure(s)	Routine risk minimization measures: SmPC sections 4.4 Other routine risk minimization measures beyond the Product Information: Use restricted to physicians experienced in the treatment of hematological cancers Additional risk minimization measures: None
Additional Pharmacovigilance activities	Registry, and studies ZUMA-1 –ZUMA-6 See Part VI Section 1.2.3 of this summary for an overview of the post-authorization development plan

Important Potential Risk	**Aggravation of Graft vs Host Disease (GvHD)**
Evidence for linking the risk to the medicine	The evidence of GvHD or aggravation of GvHD after administration of engineered CAR T cells in patients with a previous allo-HSCT is limited. As noted previously, Kochenderfer et al reported results from a study using donor derived leukocytes (from prior allo-HSCT donor) expressing a CD19 CAR to patients with persistent B-cell malignancies following allo-HSCT (Kochenderfer et al, 2013); updated data presented by(Brudno et al, 2016) and demonstrated that of 20 patients with either B-ALL, CLL or non-Hodgkin lymphoma (NHL), no patients developed acute GvHD and 2 patients developed chronic GvHD after CAR T-cell infusion. In another clinical study, however, 2 patients with relapsed or refractory B-ALL who received allogeneic CD19 CAR T cells developed GvHD 3 to 4 weeks after CAR T-cell infusion. One patient presented with grade 2 liver GvHD, whereas the other developed grade 2 skin and liver GvHD. One of these patients died of relapse 8 weeks after T-cell infusion, whereas the other developed a hematologic CR as well as partial regression of extramedullary leukemic disease (Dai et al, 2015). Maude et al (Maude et al, 2014), Lee et al (Lee et al, 2015), and Park et al (Park et al, 2018) reported on the administration of recipient-derived CAR T cells for patients with relapsed or refractory ALL or NHL and observed no GvHD following CD 19 CAR T infusion(Smith et al, 2018). It is important to note that patients with a history of allogeneic stem cell transplantation were excluded from the ZUMA-1 study. As GvHD can be life threatening or cause chronic comorbidities, it is considered an important potential risk.
Risk factors and risk groups	Patients who had undergone a prior allo-HSCT and then received donor derived CAR T cells (from prior allo-HSCT donor) appear to be at an increased risk of developing aggravation of GvHD or GvHD.
Risk Minimization Measure(s)	Routine risk minimization measures: SmPC section 4.8 PL section 2 Other routine risk minimization measures beyond the Product Information: Use restricted to physicians experienced in the treatment of hematological cancers Additional risk minimization measures: None
Additional Pharmacovigilance activities	Registry See Part VI Section 1.2.3 of this summary for an overview of the post-authorization development plan
Important Potential Risk	**Transmission of Infectious Agents via Product**
Evidence for linking the risk to the medicine	Needle stick injuries may occur among health care providers, although they have been reduced by minimizing handling of body fluids and needles. No health care providers experienced exposure to axicabtagene ciloleucel during the ZUMA-1 study. Administration of axicabtagene ciloleucel is not associated with a risk of splash or spill and disposal of used and exposed materials should follow local biosafety guidelines.
Risk factors and risk groups	Needle stick or other means of exposure to axicabtagene ciloleucel (e.g. through broken skin) are the main risk factors. Risk groups are the manufacturing personnel and health care providers handling patient cells.

Risk Minimization Measure(s)	Routine risk minimization measures: SmPC Sections 4.2 PL Section 3 Additional risk minimization measures: None
Additional Pharmacovigilance activities	None
Important Potential Risk	**Decrease in Viability of the Product due to Inappropriate Preparation of Infusion**
Evidence for linking the risk to the medicine	The axicabtagene ciloleucel product bag must be inspected for breaches of container integrity before thawing. Axicabtagene ciloleucel should be thawed at approximately 37°C using either a water bath or dry thaw method until there is no visible ice in the infusion bag. The contents of the bag should be gently mixed to disperse clumps of cellular material. If visible cell clumps remain, the contents of the bag should be continued to be gently mixed. Thawing should take approximately 3 to 5 minutes. After thawing the cells per specifications, axicabtagene ciloleucel is stable at room temperature for up to 3 hours, however the infusion should begin within 30 minutes of the thaw completion time. Axicabtagene ciloleucel must be prepared and administered per specifications or there is a potential risk of decrease in viability of the product.
Risk factors and risk groups	The main risk factor is lack of adherence to the specifications for preparation of infusion. Risk groups are the patients receiving the cell infusion.
Risk Minimization Measure(s)	Routine risk minimization measures: SmPC section 4.2 Additional risk minimization measures: Guide to handling and method of administration
Additional Pharmacovigilance activities	Prescriber survey

Table 1-4. Summary of Missing Information

Missing information	**Use in pregnancy and lactation**
Risk Minimization Measure(s)	Routine risk minimization measures: SmPC section 4.6 PL section: 2 Other routine risk minimization measures beyond the Product Information: Use restricted to physicians experienced in the treatment of hematological cancers Additional risk minimization measures: None
Additional Pharmacovigilance activities	Registry See Part VI Section 1.2.3 of this summary for an overview of the post-authorization development plan

Missing information	**Use in Non-Caucasian Patient Populations**
Risk Minimization Measure(s)	Routine risk minimization measures: Other routine risk minimization measures beyond the Product Information: Use restricted to physicians experienced in the treatment of hematological cancers Additional risk minimization measures: None
Additional Pharmacovigilance activities	Registry, and studies ZUMA-1 –ZUMA-6 See Part VI Section 1.2.3 of this summary for an overview of the post-authorization development plan
Missing information	**New Occurrence or Exacerbation of an Autoimmune Disorder**
Risk Minimization Measure(s)	Routine risk minimization measures: SmPC section 5.1 Other routine risk minimization measures beyond the Product Information: Use restricted to physicians experienced in the treatment of hematological cancers Additional risk minimization measures: None
Additional Pharmacovigilance activities	Registry See Part VI Section 1.2.3 of this summary for an overview of the post-authorization development plan
Missing information	**Long Term Safety**
Risk Minimization Measure(s)	Routine risk minimization measures: Other routine risk minimization measures beyond the Product Information: Use restricted to physicians experienced in the treatment of hematological cancers Additional risk minimization measures: None
Additional Pharmacovigilance activities	Registry, and studies ZUMA-1 –ZUMA-6 See Part VI Section 1.2.3 of this summary for an overview of the post-authorization development plan

1.2.3. Post-authorization Development Plan

1.2.3.1. Studies which are Conditions of the Marketing Authorization

Table 1-5. Studies as Condition of the Marketing Authorization

Short Study Name	**Purpose of the Study**
Planned Prospective, long-term, non-interventional cohort study of recipients of axicabtagene ciloleucel for treatment of relapsed/refractory large B cell lymphomas	Additional characterization of the identified risks, further evaluation of potential risks and missing information.

1.2.3.2. Other Studies in Post-Authorization Development Plan

Table 1-6. Other Studies in Post-Authorization Development Plan

Short Study Name	Purpose of the Study
Planned Prescriber survey (study name to be determined)	Evaluating the effectiveness of risk minimization activity: HCP educational material, Guide to handling and method of administration, and Patient Alert Card
ZUMA-1 - Phase 1/2 study to assess safety and efficacy of axicabtagene ciloleucel in refractory aggressive NHL.	Ongoing clinical trial, additional characterization of the risks of serious neurologic adverse reactions including cerebral oedema, CRS, cytopenias including aplastic anaemia, infections, hypogammaglobulinemia, secondary malignancy, immunogenicity, RCR, TLS, use in non-Caucasian patient population, long term safety.
ZUMA-2 - Phase 2 study to assess efficacy and safety of KTE-C19 in subjects with relapsed/refractory in MCL.	Ongoing clinical trial, additional characterization of the risks serious neurologic adverse reactions including cerebral oedema, CRS, cytopenias including aplastic anaemia, infections, hypogammaglobulinemia, secondary malignancy, immunogenicity, RCR, TLS, use in non-Caucasian patient population, long term safety.
ZUMA-3 - Phase 1/2 study to assess efficacy and safety of KTE-C19 in relapsed/refractory Adult ALL patients	Ongoing clinical trial, additional characterization of the risks of serious neurologic adverse reactions including cerebral oedema, CRS, cytopenias including aplastic anaemia, infections, hypogammaglobulinemia, secondary malignancy, immunogenicity, RCR, TLS, use in non-Caucasian patient population, long term safety.
ZUMA-4 - Phase 1/2 study to assess efficacy and safety of KTE-C19 in relapsed/refractory pediatric ALL patients.	Ongoing clinical trial, additional characterization of the risks of serious neurologic adverse reactions including cerebral oedema, CRS, cytopenias including aplastic anaemia, infections, hypogammaglobulinemia, secondary malignancy, immunogenicity, RCR, TLS, use in non-Caucasian patient population, long term safety.
ZUMA-5 - Phase 1/2 study to assess efficacy and safety of axicabtagene ciloleucel in relapsed/refractory indolent NHL patients.	Ongoing clinical trial, additional characterization of the risks of serious neurologic adverse reactions including cerebral oedema, CRS, cytopenias including aplastic anaemia, infections, hypogammaglobulinemia, secondary malignancy, immunogenicity, RCR, TLS, use in non-Caucasian patient population, long term safety.
ZUMA-6 - Phase 1/2 supportive study to assess efficacy and safety of axicabtagene ciloleucel in combination with atezolizumab in refractory DLBCL patients.	Ongoing clinical trial, additional characterization of the risks of serious neurologic adverse reactions including cerebral oedema, CRS, cytopenias including aplastic anaemia, infections, hypogammaglobulinemia, secondary malignancy, immunogenicity, RCR, TLS, use in non-Caucasian patient population, long term safety.

This summary was last updated in June 2019.