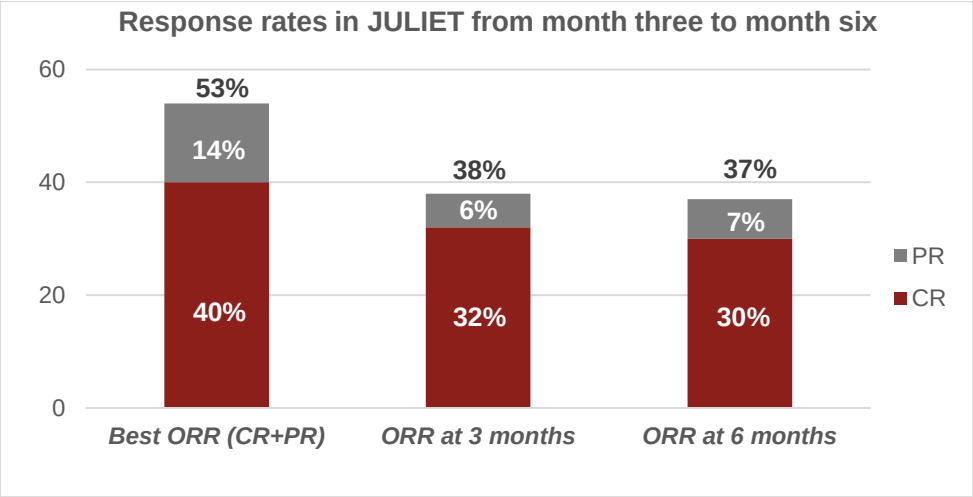
The JULIET Clinical Trial
Fact Sheet

- The JULIET clinical trial is a global, multi-center Phase II registration trial investigating CTL019* (tisagenlecleucel) for use in diffuse large B-cell lymphoma (DLBCL), the most common form of non-Hodgkin lymphoma (NHL)[1].
- The Novartis-sponsored JULIET trial was conducted in collaboration with the University of Pennsylvania to evaluate the safety and efficacy of CTL019 in adult patients with relapsed or refractory (r/r) DLBCL. Relapsed/refractory DLBCL is an aggressive (fast-growing), complex and difficult-to-treat disease, and patients with DLBCL often have worse prognosis than other forms of NHL[2,3].

Trial	JULIET Trial (NCT02445248)[4,5]
Overview	Novartis-sponsored global, multi-center, Phase II study evaluating the safety and efficacy of CTL019, for investigational use in adult patients with r/r DLBCL
Trial Design	• Single-arm, open-label trial of 147 enrolled patients (18 years or older), of which 99 were infused • Patients had r/r DLBCL and had progressed after receiving ≥2 lines of chemotherapy, and were ineligible for or failed autologous stem cell transplant (ASCT) • Fifty percent of patients had three or more lines of chemotherapy and 47% had a prior ASCT  **Enrolled patients from 27 study centers in 10 countries across the US, Canada, Europe, Australia and Japan**
Primary & Secondary Endpoints	• The primary endpoint was best overall response (ORR) (complete response [CR] + partial response [PR]) determined by a central review conducted by an independent review committee • The secondary endpoints included duration of response (DOR) and overall survival (OS)
Trial Results	• The study met its primary objective of ORR • At the time of primary analysis, the best ORR was **53%** (**95% CI, 42%-64%**; p<0.0001;), with **40%** of patients achieving a CR and **14%** of patients achieving a PR among 81 infused patients with at least three months follow-up or who discontinued earlier for any reason • Twenty-six patients (26%) were infused in the outpatient setting; of those, 20 patients (77%) remained outpatient for ≥ 3 days after infusion • Forty-three patients discontinued before infusion and the majority (n=34) did so due to rapid progression of their disease or deterioration in their clinical status. This reflects the acute and progressive nature of the disease of the patients • Only 9 of 147 (6.1%) enrolled patients could not be infused due to inability to manufacture an adequate dose of CAR-T cells. Over the course of JULIET, with continuous process improvements, manufacturing success rate improved to 97% for the last 30 patients

Trial Results



- At month three, the CR rate was **32%** and the PR rate was **6%**, which remained consistent to month six (**30% CR, 7% PR**)
- The median duration of response was not reached. The relapse-free probability at six months was **74% (95% CI, 52%-87%)**
- The median overall survival was not reached. The median time from infusion to data cutoff was 5.6 months

Safety

- Cytokine release syndrome (CRS)ǂ occurred in 58% of all infused patients, and 23% experienced grade 3/4 CRS (15% grade 3; 8% grade 4)
- Neurologic events occurred in 21% of patients (n=21), and 12% experienced grade 3/4 neurologic events
- There were no deaths attributed to CTL019, CRS, or neurologic events. No cerebral edema events were reported
- Grade 3/4 cytopenias lasting more than 28 days, grade 3/4 infections and grade 3/4 febrile neutropenia occurred in 27%, 20% and 13% of patients, respectively

ǂ CRS is a known AE of the investigational therapy that may occur when the genetically engineered cells become activated in the patient's body.

Next steps

Based on these data, Novartis submitted an application to the FDA in October 2017 for CTL019 in adult patients with r/r DLBCL who are ineligible for or relapse after ASCT. Novartis also submitted an application to the European Medicines Agency (EMA) in November 2017 for CTL019 for the treatment of adult patients with r/r DLBCL who are ineligible for ASCT, and for children and young adults, age 3 to 35 years, with r/r B-cell acute lymphoblastic leukemia.

** CTL019 is investigational for the treatment of adult patients with relapsed/refractory DLBCL.*

References:

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2. American Society of Clinical Oncology. Lymphoma – Non-Hodgkin. http://www.cancer.net/cancer-types/lymphoma-non-hodgkin. Accessed December 2017.
3. Lymphoma Research Foundation. Diffuse Large B-Cell Lymphoma (DLBCL). http://www.lymphoma.org/site/pp.asp?c=bkLTKaOQLmK8E&b=6300153. Accessed December 2017.
4. Awasthi, R., et al. "Clinical Pharmacology of CTL019 in Patients with Relapsed/Refractory (r/r) Diffuse Large B-Cell Lymphoma (DLBCL)" 59th American Society of Hematology (ASH) Annual Meeting, December 2017.
5. Schuster, S.J., et al. "Primary Analysis of Juliet: A Global, Pivotal, Phase 2 Trial of CTL019 in Adult Patients with Relapsed or Refractory Diffuse Large B-Cell Lymphoma." Abstract #577. 59th American Society of Hematology (ASH) Annual Meeting, December 2017.
6. Kymriah (tisagenlecleucel) Prescribing information. East Hanover, New Jersey, USA: Novartis Pharmaceuticals Corporation. Accessed December 2017.

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