SUPPLEMENTAL DATA

Supplemental Table 1. JULIET CRS Management Algorithm
Pretreatment
Acetaminophen/paracetamol and diphenhydramine/H1 antihistamine Prophylaxis for complications of TLS as appropriate
Tisagenlecleucel infusion **Prodromal syndrome:** low-grade fevers, fatigue, anorexia (hours to days)
Observation, rule out infection (surveillance cultures) Antibiotics per local guidelines (febrile neutropenia) Symptomatic support
Symptom progression: High fevers, hypoxia, mild hypotension **1st-Line Management:** Oxygen, fluids, low-dose vasopressor support, antipyretics Monitor/manage complications of TLS
Further symptom progression: • Hemodynamic instability despite IV fluids and moderate- to high-dose vasopressor support **OR** • Worsening respiratory distress, including pulmonary infiltrates increasing oxygen requirement including high-flow O_2 and/or need for mechanical ventilation **OR** • Rapid clinical deterioration **2nd-Line Management:**
Tocilizumab: IV infusion over 1 hour • Patient weight <30 kg: 12 mg/kg IV • Patient weight ≥30 kg: 8 mg/kg IV (max dose 800 mg) Hemodynamic and respiratory support
Lack of clinical improvement while awaiting tocilizumab response **3rd-Line Management:**
Consider other diagnosis causing clinical deterioration (ie, sepsis, adrenal insufficiency) If no improvement within 1st dose of tocilizumab within 12 to 18 hours, consider steroids (plan rapid taper after hemodynamic normalization): 2 mg/kg methylprednisolone as an initial dose, then 2 mg/kg per day. As steroids are tapered quickly, monitor for adrenal insufficiency and need for hydrocortisone replacement If no response to steroids within 24 hours, consider 2nd dose of tocilizumab (dosed as above) Hemodynamic and respiratory support
Lack of clinical improvement while awaiting response to 3rd-line management **4th-Line Management:**
Consider other diagnosis causing clinical deterioration (ie, sepsis, adrenal insufficiency) If no response to steroids and 2nd dose of tocilizumab within 24 hours or further clinical deterioration, consider siltuximab 11 mg/kg IV over 1 hour (if available in country). Hemodynamic and respiratory support
Lack of clinical improvement while awaiting response to 4th-line management **5th-Line Management:**
Consider other diagnosis causing clinical deterioration (ie, sepsis, adrenal insufficiency) In ongoing CRS despite prior therapy, consider anti-T cell therapies such as cyclophosphamide, anti-thymocyte globulin, or alemtuzumab Hemodynamic and respiratory support

CRS, cytokine release syndrome; IV, intravenous; TLS, tumor lysis syndrome.
Novartis data on file.

Supplemental Table 2. ZUMA-1 CRS Management Algorithm		
CRS Grading Assessment	**Extensive Comorbidities or Older Age? No/Yes**	**Treatment**
Grade 1: • Fever (defined as ≥38.3°C) • Constitutional symptoms	N/A	• Vigilant supportive care • Assess for infection • Treat fever and neutropenia if present, monitor fluid balance, antipyretics, and analgesics as needed
Grade 2: • Hypotension: responds to fluids or one low-dose vasopressor • Hypoxia: responds to <40% O_2 • Organ toxicity: grade 2	No	• As above for grade 1 • Monitor organ function closely • Monitor with continuous cardiac telemetry and pulse oximetry
Grade 2: • Hypotension: responds to fluids or one low-dose vasopressor • Hypoxia: responds to <40% O_2 • Organ toxicity: grade 2	Yes	• Consider tocilizumab (8 mg/kg IV over 1 hour, not to exceed 800 mg) ± corticosteroids (eg, methylprednisolone 1 mg/kg BID or dexamethasone 10 mg every 6 hours)
Grade 3: • Hypotension: requires multiple vasopressors or high-dose vasopressors • Hypoxia: requires ≥40% O_2 • Organ toxicity: grade 3 **or** grade 4 transaminitis	N/A	
Grade 4 • Mechanical ventilation • Organ toxicity: grade 4 excluding transaminitis	N/A	• As above for grade 2/3 • Corticosteroids (eg, methylprednisolone 1 g/day × 3, followed by a rapid taper consisting of 250 mg BID × 2 days, 125 mg BID × 2 days, and then 60 mg BID × 2 days)

BID, twice daily; CRS, cytokine release syndrome; IV, intravenous; N/A, not applicable.