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Clinical Trials Summary for out of hours Important Reference

Study Title	PASenger Study
Study Summary	A Phase 3 Randomized, Open-label Study of JNJ-78278343, a T Cell-redirecting agent targeting Human Kallikrein 2, with Docetaxel Versus Docetaxel for Metastatic Castration-Resistant Prostate Cancer
Principal Investigator	Professor Omi Parikh
Research Team responsible for the Study	Sub Investigator Natalie Charnley Lead Nurse Catherine Walmsley
Drug therapy	**ARM A Pasritamig (JNJ-78278343) with docetaxel** **ARM B Docetaxel**

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Differentiating between CR, IRR and ICANS

	IRR	CRS	ICANS
Key symptoms	• Allergic/hypersensitivity (e.g., chills, flushing, fatigue, itching, cough, urticaria) • Bronchospasm • Gastrointestinal issues like nausea and vomiting can also occur	• Fever (≥38°C) • Hypotension • Hypoxia	• Neurological (e.g., confusion, aphasia, altered levels of consciousness, headache) • Seizures
Onset	During or immediately after infusion (within 2 hours after infusion completed)	Hours to days after infusion (usually develops later than IRR)	Typically, after CRS symptoms
Fever	Absent or mild	Present (≥38°C)	Can be present, but less specific than for CRS
Main drug interventions	• IV fluids • Paracetamol • H1/H2 receptor antagonist • Glucocorticoids • Bronchodilators • Adrenaline (recommended for Grade 3 or higher) • Methylprednisolone (recommended for Grade 3 or higher)	• Supplemental O2 • IV fluids • Tocilizumab (recommended for Grade 2 or higher) • Corticosteroids (recommended for Grade 3 or higher) • Vasopressors (Grade 3 or higher)	• Manage CRS if present • Dexamethasone (recommended for Grade 2 or higher)
Tocilizumab Response	Not responsive	Typically responsive	Not typically responsive
Pasritamig Phase 1 Reported AE at RP2D (Related TEAE)	~20% (all are Grade 1 and Grade 2)	<10% (all are Grade 1) Median time of CRS onset is 1 day. Relative to most recent dose.	None

Guidelines for grading and management of IRR

Graded according to CTCAE 5.0	Treatment/Drug
Grade 2 Mild or moderate reaction: requires therapy or interruption of administration but responds promptly to symptomatic treatment.	**Interrupt administration (if still receiving infusion)** • IV fluids • Diphenhydramine 50 mg IV (or equivalent), acetaminophen/ paracetamol 500 mg to 1,000 mg or both • Consider glucocorticoids and bronchodilator therapy • Monitor participant until recovery from symptoms **Complete administration (if applicable**) • Following recovery from symptoms, administration may be restarted at a slower rate **If symptoms recur**: • Stop study treatment administration • Diphenhydramine 50 mg IV • Consider glucocorticoids and bronchodilator therapy • Monitor participant until recovery from symptoms • Treatment rechallenge at next scheduled dose per PI discretion
Grade 3 or Grade 4 **Grade 3**: prolonged (e.g., not rapidly responsive to symptomatic medication or brief interruption of administration); recurrence of symptoms following initial improvement; hospitalisation indicated for clinical sequelae (e.g., renal impairment, pulmonary infiltrates). **Grade 4**: life-threatening; urgent intervention indicated (e.g., vasopressor or ventilator support indicated).	**Stop administration (if applicable)** • Start IV saline infusion • Bronchodilators • Adrenaline 0.2 to 1 mg of a 1:1,000 solution for SC administration or 0.1 to 0.25 mg of a 1:10,000 solution injected slowly for IV administration • Diphenhydramine 50 mg IV • Methylprednisolone 100 mg IV (or equivalent) • Follow institutional guidelines for the treatment of anaphylaxis • Monitor until medically stable

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Guidelines for grading and management of Cytokine release syndrome (CRS)

Tocilizumab can be located in main hospital pharmacy or Ribblesdale ward during cycle 1 day 1, cycle 1 day 8 and cycle 1 day 15

CRS Grade per ASTEC guidelines	Presenting symptoms	Tocilizumab*	Corticosteroids
Grade 1	Temperature ≥38˚C	May be considered.+	N/A
Grade 2	Temperature ≥38˚C with either: • Hypotension responsive to fluids and not requiring vasopressors. Or, • Oxygen requirement of low-flow nasal canula or blow-by.	Administer tocilizumab	• Manage per guidance below if no improvement within 24 hours of starting tocilizumab
Grade 3	Temperature ≥38˚C with either: • Hypotension requiring 1 vasopressor with or without vasopressin. Or, • Oxygen requirement of high-flow nasal cannula, facemask, non-rebreather mask or Venturi mask.	Administer tocilizumab	• If no improvement, administer methylprednisolone 1 mg/kg IV twice daily or equivalent dexamethasone (e.g., 10 mg IV every 6 hours). • Continue corticosteroids until the event is Grade ≤1, then taper over 3 days.
Grade 4	Temperature ≥38˚C with either: • Hypotension requiring multiple vasopressors (excluding vasopressin). Or, • Oxygen requirement of positive pressure (e.g., CPAP, BiPAP, intubation, and mechanical ventilation).	Administer tocilizumab	• As above or administer methylprednisolone 1,000 mg IV per day for 3 days per investigator discretion. • If no improvement or if condition worsens, consider alternate immunosuppressants.

*Administer tocilizumab 8 mg/kg IV over 1 hour (not to exceed 800 mg). Repeat tocilizumab every 8 hours as needed if not responsive to IV fluids or increasing supplemental oxygen. Limit to a maximum of 3 doses in a 24-hour period; maximum total of 4 doses.

+Tocilizumab may be considered in participants who are at high risk of progressing or clinically progressing towards a higher-grade CRS or participants who have high-grade fever >24 hours not responding to supportive measures.

Guidelines for grading and management of ICANS

ICANS Grade per ASTCT Guidelines	Presenting Symptoms	Concurrent CRS	No Concurrent CRS
Grade 1	ICE score: 7-9 or depressed level of consciousness: awakens spontaneously.	• Management of CRS as appropriate. • Monitor neurologic symptoms and consider neurology consultation.	• Monitor neurologic symptoms and consider neurology consultation. • Consider dexamethasone
		• Consider non-sedating antiseizure medicines (e.g., levetiracetam) for seizure prophylaxis.	
Grade 2	ICE score 3-6 or depressed level of consciousness: awakens to voice	• Administer tocilizumab for management of CRS. • If no improvement after starting tocilizumab, administer dexamethasone 10 mg IV every 6 hours. Continue dexamethasone until the event is Grade ≤1, then taper.	• Administer dexamethasone 10 mg IV every 6 hours. Continue dexamethasone until the event is Grade ≤1, then taper.
		• Consider non-sedating antiseizure medicines (e.g., levetiracetam) for seizure prophylaxis. • Consider neurology consultation and other specialists (i.e., intensivists) for further evaluation, as needed.	

Guidelines for Grading and management of ICANS (cont)

Grade 3	ICE score 0-2 or depressed level of consciousness: awakens only to tactile stimulus or seizures, either: • any clinical seizure, focal or generalised, that resolves rapidly, or • non-convulsive seizures on EEG that resolve with intervention, or increased ICP: focal/local oedema on neuroimaging	• Administer tocilizumab for management of CRS. • In addition, administer dexamethasone 10 mg IV with the first dose of tocilizumab and repeat dose every 6 hours. Continue dexamethasone until the event is Grade ≤1, then taper.	• Administer dexamethasone 10 mg IV every 6 hours. Continue dexamethasone until the event is Grade ≤1, then taper.
		• Consider non-sedating antiseizure medicines (e.g., levetiracetam) for seizure prophylaxis. • Consider neurology consultation and other specialists (i.e., intensivists) for further evaluation, as needed.	
Grade 4	ICE score 0 or depressed level of consciousness either: • participant is unarousable or requires vigorous or repetitive tactile stimuli to arouse, or • stupor or coma, or seizures, either: • life-threatening prolonged seizure (>5 minutes), or • repetitive clinical or electrical seizures without return to baseline in between,	• Administer tocilizumab for management of CRS. • Consider administration of methylprednisolone 1,000 mg IV per day with first dose of tocilizumab and continue methylprednisolone 1,000 mg IV per day for 2 or more days, per investigator discretion.	• Consider administration of methylprednisolone 1,000 mg IV per day for 3 days; if improves, then manage as above.

Grade 4 (cont)	or motor findings: • deep focal motor weakness such as hemiparesis or paraparesis, or increased ICP/cerebral oedema, with signs/symptoms such as: • diffuse cerebral oedema on neuroimaging, or • decerebrate or decorticate posturing, or • cranial nerve VI palsy, or • papilledema, or • Cushing's triad.	• Consider non-sedating antiseizure medicines (e.g., levetiracetam) for seizure prophylaxis. • Consider neurology consultation and other specialists (i.e., intensivists) for further evaluation, as needed.