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CANCER CENTER

# Tackling MonumenTAL Toxicities of Talquetamab

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# Disclosures

- I will be discussing "off-label" uses of the following medications:
  - Tocilizumab

# Objectives

- Discuss mechanism of action of talquetamab-tgvs in multiple myeloma
- Review dosing and administration of talquetamab-tgvs
- Summarize the management of common toxicities associated with talquetamab-tgvs

# Introduction

- Despite recent advances, multiple myeloma is still considered incurable
- Chimeric Antigen Receptor T-cell (CAR-T) therapy and bi-specific T-cell engagers (BiTEs) are additional treatment options
- Talquetamab-tgvs (Talvey™) is one of three bi-specific antibodies approved in multiple myeloma
  - Approved following four or more lines of therapy



# Mechanism of Action

- Binds to CD3 on T-cells and G protein-coupled receptor class C group 5 member D (GPRC5D) on plasma cells
- Results in T-cell activation and destruction of tumor cells
- T-cell activation induces the release of proinflammatory cytokines
- Recruits bystander immune and non-immune cells which results in further release of proinflammatory cytokines and cytokine storm

# Dosing

Dosing Schedule	Day	Dose	
<b>Weekly Dosing</b>			
Step-up dosing schedule	Day 1	Step-up dose 1	0.01 mg/kg SQ
	Day 4*	Step-up dose 2	0.06 mg/kg SQ
	Day 7*	First treatment dose	0.4 mg/kg SQ
Weekly Dosing Schedule	One week after first treatment dose	Subsequent treatment doses	0.4 mg/kg SQ
<b>Biweekly Dosing</b>			
Step-up dosing schedule	Day 1	Step-up dose 1	0.01 mg/kg SQ
	Day 4*	Step-up dose 2	0.06 mg/kg SQ
	Day 7*	Step-up dose 3	0.4 mg/kg SQ
	Day 10**	First treatment dose	0.8 mg/kg SQ
Biweekly Dosing Schedule	Two week after first treatment dose	Subsequent treatment doses	0.8 mg/kg SQ

SQ: Subcutaneously; \*Dose may be given 2 to 4 days after previous dose \*\*Dose may be given 2 to 7 days after previous dose  
1/17/2024

# Administration and Pre-medications

- Requires hospitalization for 48 hours following all step-up doses and first treatment dose
- Pre-medications should be administered 1 to 3 hours prior to each step-up dose and first treatment dose
- Recommended pre-medications:
  - Corticosteroid
  - Histamine-1 (H1) receptor antagonist
  - Antipyretic

# Common Toxicities

	Any grade (%)	Grade 3-4 (%)
Pyrexia	83	4.7
Cytokine release syndrome (CRS)	76	1.5
Dysgeusia	70	0
Nail disorder	50	0
Musculoskeletal pain	43	3.2
Skin disorder	41	0.3
Rash	38	3.5
Fatigue	37	3.5
Weight decreased	35	1.5
Dry Mouth	34	0
ICANS	9	NR

ICANS: Immune effector cell-associated neurotoxicity syndrome; NR: Not reported

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Talvey [Package Insert]. Horsham, PA: Janssen Biotech. 2023.

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# Cytokine Release Syndrome Presentation

- Fever ( $> 100.4^{\circ}\text{F}$ )
  - Respiratory distress
  - Hypotension
  - Rigors
  - Dizziness
  - Tachycardia
  - Elevated transaminases
  - Myalgia/arthralgia
  - Nausea/vomiting
  - Diarrhea
- CRS is most likely to occur following:
    - Step-up doses
    - First treatment dose
  - Average time to CRS onset: 27 hours (range: 0.1-167 hours)

# Management of Cytokine Release Syndrome

Grade	General Management	Talquetamab Management
Grade 1	<ul style="list-style-type: none"> <li>• Symptomatic management of constitutional symptoms</li> <li>• Consider tocilizumab for persistent fever, may repeat every 8 hours for 3 doses/24 hours</li> </ul>	<ul style="list-style-type: none"> <li>• Withhold dose until resolution</li> <li>• Administer pre-medications prior to next dose</li> </ul>
Grade 2	<ul style="list-style-type: none"> <li>• Intravenous fluid bolus, repeat as needed</li> <li>• Supplemental oxygen as needed to keep O2 saturations &gt; 90%</li> <li>• Administer tocilizumab, may repeat every 8 hours for 3 doses/24 hours</li> <li>• Consider initiation of steroids if no improvement in within 24 hours</li> </ul>	<ul style="list-style-type: none"> <li>• Withhold dose until resolution</li> <li>• Administer pre-medications prior to next dose</li> <li>• 48-hr hospitalization following next dose</li> </ul>
Grade 3	<ul style="list-style-type: none"> <li>• Supportive care management as per grade 2</li> <li>• Administer tocilizumab as per grade 2</li> <li>• Initiate steroids until grade 1 or less, then taper</li> <li>• Consider alternative agent if rapid deterioration or no improvement following tocilizumab</li> </ul>	<ul style="list-style-type: none"> <li>• Management as per grade 2</li> <li>• Permanently discontinue for recurrent Grade 3 CRS or CRS that lasts &gt; 48 hours</li> </ul>
Grade 4	<ul style="list-style-type: none"> <li>• Use vasopressors and mechanical ventilation if needed</li> <li>• Administer tocilizumab and steroids as per previous criteria</li> <li>• Consider alternative agent if no improvement</li> </ul>	<ul style="list-style-type: none"> <li>• Permanently discontinue</li> </ul>



# Neurotoxicity Presentation

- Aphasia
- Tremor
- Encephalopathy
- Lethargy
- Obtundation
- Stupor
- Seizures
- Coma
- May occur with or without cytokine release syndrome
- Average time to neurotoxicity onset: 2.5 days (range: 1-16 days)
- Median duration: 2 days (range: 1-22 days)

# Management of ICANS

Grade	General Management	Talquetamab Management
Grade 1	<ul style="list-style-type: none"> <li>Utilization of lorazepam or haloperidol for agitated patients</li> <li>Consider tocilizumab if associated with concurrent grade 2 or greater CRS</li> <li>Consider seizure prophylaxis</li> </ul>	<ul style="list-style-type: none"> <li>Withhold dose until resolution</li> </ul>
Grade 2	<ul style="list-style-type: none"> <li>Manage as per grade 1</li> <li>Consider tocilizumab if associated with concurrent grade 2 or greater CRS</li> <li>Administer corticosteroids until resolution to grade 1 or less</li> </ul>	<ul style="list-style-type: none"> <li>Withhold dose until resolution</li> <li>48-hr hospitalization following next dose</li> </ul>
Grade 3	<ul style="list-style-type: none"> <li>Manage as per grade 1</li> <li>Consider tocilizumab if associated with concurrent grade 2 or greater CRS</li> <li>Administer corticosteroids until resolution to grade 1 or less</li> <li>Consider repeat CT or MRI every 2-3 days if persistent neurotoxicity <math>\geq</math> grade 3</li> </ul>	<ul style="list-style-type: none"> <li>Management as per grade 2</li> <li>Permanently discontinue for recurrent Grade 3 ICANS</li> </ul>
Grade 4	<ul style="list-style-type: none"> <li>Manage as per grade 3</li> <li>Consider tocilizumab if associated with concurrent grade 2 or greater CRS</li> <li>If rapid deterioration or persistent grade 4, consider alternative therapies</li> </ul>	<ul style="list-style-type: none"> <li>Permanently discontinue</li> </ul>

# Dermatologic Toxicity Presentation

- Palmar/Plantar Desquamation
  - Dry Skin
  - Rash
  - Nail Loss
  - Pruritis
  - Hyperpigmentation
  - Eczema
  - Skin Exfoliation
- 
- Median time to onset of skin toxicities: 24 days (range: 3-384 days)
  - Median duration: 39 days (range: 1-154 days)
  - Median time to onset of nail toxicities: 50.5 days (range: 6-316 days)

# Management of Dermatologic Toxicities

- Withhold dose for grade 3 or 4 skin toxicity
  - May resume once resolves to grade 1 or better
- Can consider combination of ammonium lactate, triamcinolone cream, and Vaseline
- Systemic corticosteroids can be considered for generalized rash



# Oral Toxicity Presentation

- Dysgeusia
- Dry Mouth
- Ageusia
- Dysphagia
- Stomatitis
- Oral toxicities occurred in 80% of patients
  - Can result in significant weight loss
  - 65% of patients did not have resolution of symptoms
- Median time to onset: 15 days (range: 1-634 days)

# Management of Oral Toxicities

Grade	Talquetamab Management
Grade 1-2	<ul style="list-style-type: none"><li>• Provide supportive care</li><li>• Consider withholding dose if not responsive to supportive care</li></ul>
Grade 3	<ul style="list-style-type: none"><li>• Management as per grade 1-2</li><li>• Withhold dose until resolution to grade 1 or better</li></ul>
Grade 4	<ul style="list-style-type: none"><li>• Permanently discontinue</li></ul>

- Supportive care measures:
  - Saliva substitute sprays/rinses
  - Sugar-free hard candies or gum
  - Utilize plastic utensils
  - Eat soft or moist foods
  - Oral hydration
  - Dietary counseling

Talvey [Package Insert]. Horsham, PA: Janssen Biotech. 2023.

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Mancia S, et al. *Blood*. 138 (2021):1658-59.

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# Talquetamab Risk Evaluation and Mitigation Strategy (REMS)

- Requirements include:
  - Completion of prescriber training and knowledge assessment
  - Completion of prescriber enrollment form
  - Enrollment by the pharmacy/healthcare setting
  - Provide patient with education regarding CRS and ICANS symptoms
    - Patient wallet card should be provided prior to first dose of talquetamab

# Summary

- Bi-specific antibodies cause T-cell activation which activates proinflammatory cytokines resulting in CRS and neurotoxicity
- Common adverse events with Talquetamab include CRS, dysgeusia, weight loss, and skin toxicity
- Talquetamab may need to be held depending on the severity of adverse events

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# Alternative Therapies for CRS/ICANS

- Anakinra
- Siltuximab
- Etanercept
- Infliximab
- Ruxolitinib
- Intrathecal chemotherapy