Administration of Teclistamab

Centers for Medicare & Medicaid Services
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Unmet Need for Heavily Treated Multiple Myeloma Patients

- Despite recent advances in treatment, nearly all myeloma patients will relapse[1]
- Many will receive multiple lines of therapy throughout their disease course, increasing the likelihood of retreatment with similar classes of therapies[1, 2]
- Subsequently, efficacy outcomes decrease with each line of therapy as ~79% of patients become refractory to the three main myeloma drug classes (PIs, IMiDs, and anti-CD38 antibodies)[1]

1. Ghandi et al, 2019. 2. Madduri et al, 2020.

Outcomes are Poor for Patients Refractory to the Three Main Classes of Myeloma Therapies

- Outcomes for triple-class refractory (1 PI, 1 IMiD, 1 anti-CD38) and penta-refractory (2 PIs, 2 IMiDs, 1 anti-CD38) patients are poor, with a median overall survival (OS) of 9.2 and 5.6 months, respectively[1]

- Current treatment options for patients with triple-class refractory disease are limited by toxicities and accessibility

1. Ghandi et al, 2019

Teclistamab Product Overview

- Teclistamab is a full-sized bispecific antibody that redirects a patient's own T cells to target myeloma cells by binding to CD3 and B Cell Maturation Antigen (BCMA)

- Teclistamab is currently under investigation for adult patients with relapsed or refractory multiple myeloma who have received at least three prior therapies, including a proteasome inhibitor (PI), an immunomodulatory agent (IMiD) and an anti-CD38 monoclonal antibody
  - On June 1, 2021, teclistamab was granted Breakthrough Therapy Designation by the Food and Drug Administration (FDA).[1]
  - Johnson & Johnson Healthcare Systems Inc., on behalf of Janssen Pharmaceuticals, submitted a New Technology Add-on Payment Application seeking qualification for add-on payments under the hospital Inpatient Prospective Payment System for Federal Fiscal Year 2023.

- This product is not yet approved

- Teclistamab (JNJ-957) will have a trade name upon approval and has no other identifiers

1. Janssen announces U.S. FDA Breakthrough Therapy Designation granted for teclistamab for the treatment of relapsed or refractory multiple myeloma. Jun 1, 2021. https://www.jnj.com/janssen-announces-u-s-fda-breakthrough-therapy-designation-granted-for-teclistamab-for-the-treatment-of-relapsed-or-refractory-multiple-myeloma Accessed November 16, 2021.

DuoBody Platform: Novel T-cell Redirectors for the Treatment of Multiple Myeloma

DuoBodys provide a novel and improved clinical option for T-cell redirecting therapy:

- Off-the-shelf; no delay for manufacturing or product preparation
- Uses the patient's own immune cells (endogenous) to target myeloma cells; no genetic programming required
- Full-sized IgG structure allows for intermittent vs. continuous subcutaneous dosing
- Targets are selected based on lineage selective expression and demonstration of specificity in cell killing

Teclistamab is anticipated to be the first FDA-approved bispecific antibody therapy for patients with multiple myeloma.

BCMA, B-cell maturation antigen

GPRC5D, G-protein coupled receptor family C group 5 member D.

NOTE: Teclistamab has been built by Janssen R&D using Genmab DuoBody® technology.

Teclistamab: Overall Safety Profile from MajesTEC-1 Trial

Safety Analysis Set N=165		
AEs ≥20%, n (%)	Any Grade	Grade 3/4
Neutropenia	108 (65.5)	94 (57.0)
Anemia	82 (49.7)	57 (34.5)
Thrombocytopenia	63 (38.2)	35 (21.2)
Lymphopenia	56 (33.9)	53 (32.1)
CRS	118 (71.5)	1 (0.6)
Injection site erythema	42 (25.5)	0 (0)
Fatigue	41 (24.8)	3 (1.8)
Nausea	40 (24.2)	1 (0.6)
Headache	36 (21.8)	1 (0.6)
Diarrhea	34 (20.6)	4 (2.4)

Teclistamab was well tolerated; no patients required dose reduction

- Only 1 patient discontinued due to an AE (adenoviral pneumonia)
- Serious AEs occurred in 88 patients (53.3%)
  - Teclistamab-related serious AEs[a] occurred in 33 patients
- Injection-site reactions occurred in 58 patients (35.2%; all grade 1/2)
- Infections occurred in 104 (63%) patients (grade 3/4: 35.2%)
  - 9 (5.5%) patients had opportunistic infections[b]
- 119 patients (72.1%) had evidence of hypogammaglobulinemia[c]
  - 41 of these patients received IVIG at any time during the study (at physician discretion)
- There were 9 deaths due to AEs; none were related to teclistamab
  - COVID-19 (n=7)
  - Pneumonia (n=1)
  - Hemoperitoneum (n=1)

[a]Considered to be related by the investigator; [b]Included adenovirus infection, adenovirus reactivation, cytomegalovirus viremia, cytomegalovirus reactivation, hepatitis B virus reactivation, BK virus infection, *Pneumocystis jirovecii* pneumonia, and aspergillus; [c]Assessed by AE or lab values (postbaseline IgG level below 500 mg/dL).

AE, adverse event; CRS, cytokine release syndrome; Ig, immunoglobulin; IVIG, intravenous immunoglobulin; TEAE, treatment-emergent adverse event

Moreau et al. ASH 2021. Oral Abstract 653.

Teclistamab: Cytokine Release Syndrome in MajesTEC-1 Trial

Parameter	Safety Analysis Set N=165
Patients with CRS, n (%)	118 (71.5)
Patients with ≥2 CRS events	54 (32.7)
Time to onset (days), median (range)	2 (1–6)
Duration (days), median (range)	2 (1–9)
Patients who received supportive measures[a], n (%)	109 (66.1)
Tocilizumab	60 (36.4)
Low-flow oxygen by nasal cannula[b]	21 (12.7)
Steroids	13 (7.9)
Single vasopressor	1 (0.6)

- All grade CRS rate (maximum) was 71.5%
  - Grade 1: 82 (49.7%)
  - Grade 2: 35 (21.2%)
  - Grade 3: 1 (0.6%)
- All CRS events were grade 1/2, except for 1 transient-grade 3 CRS event that fully resolved, and 97% of events were confined to step-up and cycle 1
- All CRS events resolved, with no treatment discontinuations due to CRS
- Over the course of their treatment, 2.4% of patients received >1 dose of tocilizumab for a single CRS event

[a]A patient could receive >1 supportive therapy; [b]≤6 L/min; [c]CRS was graded using Lee et al *Blood* 2014 in the phase 1 portion of the study and ASTCT in phase 2; in this combined analysis, Lee et al *Blood* 2014 criteria were mapped to ASTCT criteria for patients in the phase 1 portion.
ASTCT, American Society for Transplantation and Cellular Therapy; CRS, cytokine release syndrome

Moreau et al. ASH 2021. Oral Abstract 653.

Teclistamab: Neurotoxicity from MajesTEC-1 trial

Parameter	Safety Analysis Set N=165
Patients with neurotoxicity, n (%)	21 (12.7)
Headache	14 (8.5)
ICANS[a]	5 (3.0)
Encephalopathy	2 (1.2)
Tremor	2 (1.2)
Patients with grade ≥3 events	0
Time to onset, median (range) days	2.5 (1–7)
Duration, median (range) days	3.0 (1–37)
Patients requiring supportive measures for neurotoxicity, n (%)	12 (7.3)
Tocilizumab	3 (1.8)
Dexamethasone	3 (1.8)
Levetiracetam	1 (0.6)

- **The overall incidence of neurotoxicity was low**
- **The most commonly reported neurotoxicity event was headache (14 patients [8.5%])**
- **All events were grade 1/2**
- **There were no treatment discontinuations or dose reductions due to neurotoxicity[b]**
- 12 patients (7.3%) required supportive measures for neurotoxicity
- There were 5 patients with ICANS events at the RP2D
  - All were grade 1/2
  - Most (7/9) ICANS events were concurrent with CRS; all resolved

[a]1 of the events of confusional state reported in a patient treated at RP2D in phase 1 was considered by the sponsor to be consistent with ICANS and presented as such in summaries of ICANS events; [b]TEAEs under the "nervous system disorder" or "psychiatric disorder" SOC that were judged by the investigator to be related to study drug; including ICANS events.

CRS, cytokine release syndrome; ICANS, immune effector cell–associated neurotoxicity syndrome; RP2D, recommended phase 2 dose; SOC, system organ class

Moreau et al. ASH 2021. Oral Abstract 653.

Preparation and Administration

- Teclistamab should be administered via subcutaneous injection only.
- Teclistamab should be administered by a healthcare provider with adequate medical equipment and personnel to manage severe reactions, including cytokine release syndrome.
- Teclistamab solution for injection is colorless to light yellow.
- Teclistamab 10 mg/mL vial and teclistamab 90 mg/mL vial are supplied as ready-to-use solution for injection that do not need dilution prior to administration.
- Teclistamab vials of different concentrations should not be combined to achieve treatment dose.
- Aseptic technique should be used to prepare and administer teclistamab.

Preparation and Administration cont.

- Teclistamab is a drug that is administered subcutaneously.
- Patients receiving teclistamab receive two priming doses: .06 mg/kg for the first priming dose, and .3 mg/kg for the second priming dose.
- For the third dose onward, patients receive 1.5 mg/kg doses once weekly until disease progression or unacceptable toxicity.
- Teclistamab step-up dosing was administered in the inpatient setting in clinical trials. A patient may be admitted for inpatient administration of the first two step-up doses and first full dose or providers may administer all teclistamab doses in the outpatient setting with proper safety precautions.
- Subsequent doses will typically be administered in the outpatient setting, but inpatient administration may be appropriate for some patients.

Documentation of Administration

- Teclistamab administration should be documented consistent with the documentation associated with other subcutaneous injections.
- Documentation of administration within the medical record would most commonly be found in the Medication Administration Record (MAR), physician orders, and progress notes.

Summary

- Outcomes are poor for patients who progress after treatment with the three main myeloma drug classes (PIs, IMiDs, and CD38 monoclonal antibodies).
- Existing therapies have limitations including efficacy, safety, and/or access.
- There is no standard of care for patients with triple or penta-class refractory multiple myeloma.
- Teclistamab has been designated as a breakthrough therapy by the FDA in adult patients with relapsed or refractory multiple myeloma.
- Teclistamab has a unique mechanism of action and is anticipated to be the first FDA-approved bispecific antibody therapy for multiple myeloma that redirects T cells via CD3 to BCMA-expressing multiple myeloma cells.
- Currently, there is no ICD-10-PCS code for the use of teclistamab.

1. Janssen announces U.S. FDA Breakthrough Therapy Designation granted for teclistamab for the treatment of relapsed or refractory multiple myeloma. Jun 1, 2021. https://www.jnj.com/janssen-announces-u-s-fda-breakthrough-therapy-designation-granted-for-teclistamab-for-the-treatment-of-relapsed-or-refractory-multiple-myeloma Accessed November 16, 2021.