

Plain language summary of the MajesTEC-1 study of teclistamab for the treatment of people with relapsed or refractory multiple myeloma

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First draft submitted: 31 March 2023; Accepted for publication: 13 April 2023; Published online: 3 May 2023

Summary

What is this summary about?

This is a summary of a phase 1–2 clinical trial called MajesTEC-1. This trial tested the cancer drug teclistamab in people with relapsed or refractory multiple myeloma, a cancer that forms in a certain type of white blood cells known as plasma cells. Most participants who took part in the study had at least 3 prior treatments for multiple myeloma before their cancer came back.

How to say...

• **Teclistamab:** tek-LIS-tuh-mab

How was the study in this summary conducted?

A total of 165 participants from 9 countries were included in this study. All participants were given teclistamab once per week and monitored for side effects. Once participants started taking teclistamab, they were checked regularly to monitor if their cancer had no change, improved (responded to treatment), or worsened or spread (known as disease progression).

What were the results of the study?

After approximately 14.1 months of follow-up (from 2020 to 2021), 63% of participants who were given teclistamab had a decrease in myeloma burden, meaning that they responded to treatment with teclistamab. Participants who responded to teclistamab lived without their myeloma coming back for approximately 18.4 months. The most common side effects were infections, cytokine release syndrome, abnormally low white and red blood cell counts (neutropenia, lymphopenia, and anemia), and low platelet cell counts (thrombocytopenia). Approximately 65% of participants experienced serious side effects.

What do the results of this study mean?

Overall, more than half of the participants (63%) in the MajesTEC-1 study responded to treatment with teclistamab despite previous myeloma treatment failures.

Who should read this article?

The authors of the original research article wrote the current summary to help patients, caregivers, and healthcare professionals understand the results of the MajesTEC-1 study.

Who sponsored this study?

The MajesTEC-1 study was sponsored by Janssen Research and Development.

What is relapsed or refractory multiple myeloma?

Multiple myeloma is a type of blood cancer that forms in plasma cells, a specific kind of white blood cell. Although there are many different therapies available to treat multiple myeloma, almost all patients will relapse or become refractory to treatment. People with relapsed or refractory multiple myeloma have fewer available treatment options and are less likely to respond to treatment than people with newly diagnosed multiple myeloma.

RRMM

R

Relapsed

When cancer improves with treatment at first but then comes back, it is considered to have relapsed

R

Refractory

When cancer does not respond to treatment, it is considered refractory

MM

Multiple myeloma

Multiple myeloma is a type of blood cancer that forms in plasma cells, a specific kind of white blood cell

What is teclistamab?

Teclistamab is an anti-cancer medication known as a **therapeutic bispecific antibody**, which is a type of immunotherapy. Bispecific antibodies are considered an “off-the-shelf” immunotherapy treatment because they can be directly given to a patient without the need to collect the individual patient’s immune cells, unlike another treatment called chimeric antigen receptor-T cells (CAR-T). Teclistamab brings immune cells in contact with cancer cells by binding to 2 proteins called CD3 and B-cell maturation antigen, also known as BCMA. CD3 is a protein found on a specific type of immune cell known as a T cell, and BCMA is a protein found in large numbers on the surface of multiple myeloma cells.

Therapeutic bispecific antibody:

A therapeutic bispecific antibody (like teclistamab) is used to treat cancer and is designed to recognize 2 different proteins, 1 on cancer cells and another on an immune cell. Bispecific antibodies bring these 2 cells together, allowing immune cells to recognize and kill cancer cells.



Teclistamab mechanism of action

- Teclistamab binds to a protein on cancer cells and a protein on T cells, which are a type of immune cell
- Bringing T cells and cancer cells into contact with one another results in T-cell activation and cancer cell death

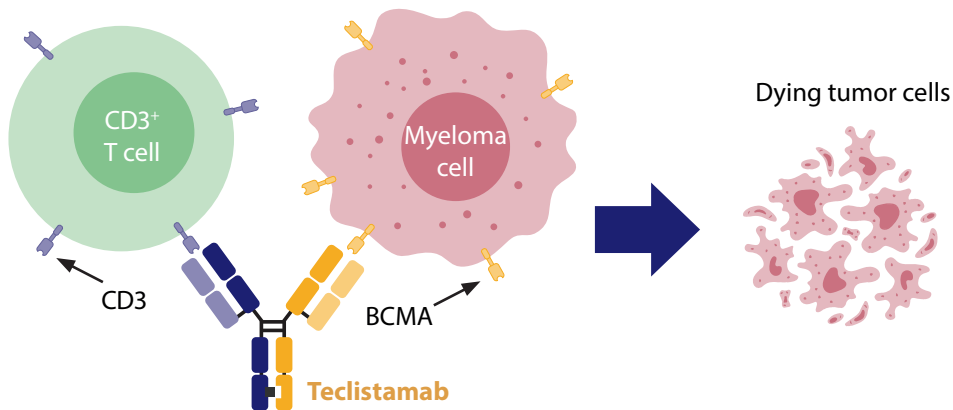


Figure adapted from Singh A, Dees S, Grewal IS. Overcoming the challenges associated with CD3⁺ T-cell redirection in cancer. *Br. J. Cancer* 124, 1037–1048 (2021). <http://creativecommons.org/licenses/by/4.0>.

What did the MajesTEC-1 study look at?

Researchers wanted to know whether teclistamab would reduce the amount of myeloma in participants who had relapsed or were refractory to previous treatments. They looked at the following for each participant:

- The proportion of participants who showed at least a 50% decrease in indicators of myeloma in blood and at least a 90% decrease in indicators of myeloma in urine (known as overall response rate)
- The total amount of time after first response to treatment that participants who responded to teclistamab lived without their myeloma coming back (known as duration of response)
- The total amount of time after receiving the first dose of teclistamab that all participants remained alive before their myeloma got worse (known as **progression-free survival**)
- The total amount of time after receiving the first dose of teclistamab that each participant remained alive, with or without their myeloma getting worse (known as overall survival)



Disease progression: When laboratory tests show that indicators of multiple myeloma are increasing, it is a sign that the cancer is getting worse, known as disease progression.

Who participated in the MajesTEC-1 study?

A total of 165 participants took part in the MajesTEC-1 study. Participants had multiple myeloma and previously received at least 3 anti-cancer treatments including:

- A drug that kills cancer cells by activating or suppressing the immune system (known as an immunomodulatory drug)
- A drug that prevents the breakdown of proteins in cancer cells (known as a proteasome inhibitor)
- A therapeutic antibody that recognizes CD38, a protein found on plasma cells (including myeloma cells)



Participants had been diagnosed with multiple myeloma for a median of 6 years. Although participants were required to have received at least 3 prior anti-cancer treatments, many participants had received more, so the overall group had received a **median** of 5 prior anti-cancer treatments before being treated with teclistamab. All participants showed signs of multiple myeloma in their blood or urine at levels that met specific criteria when measured with laboratory tests.

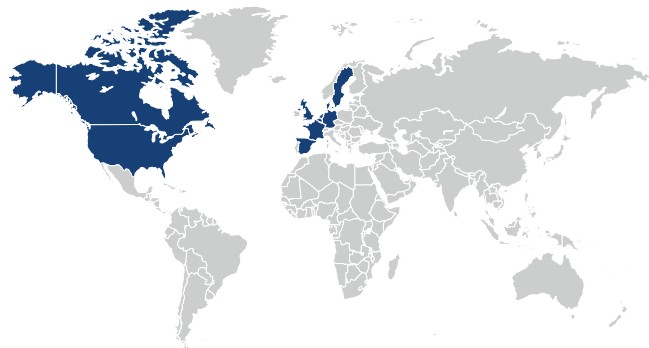
Median: The median is the middle value when all values are listed in order from smallest to largest.

Who took part in the study?

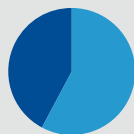
- MajesTEC-1 was a global study
- This analysis included participants from 9 countries

Countries included:

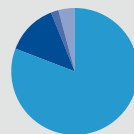
United States	Germany	Sweden
Canada	The Netherlands	United Kingdom
France	Spain	Belgium



Of the participants who took part:



58% were male
42% were female



81% were White
13% were Black
2% were Asian
4% were another race



15% were 75 years old or older



78% had stopped responding to 3 or more different types of anti-multiple myeloma therapies

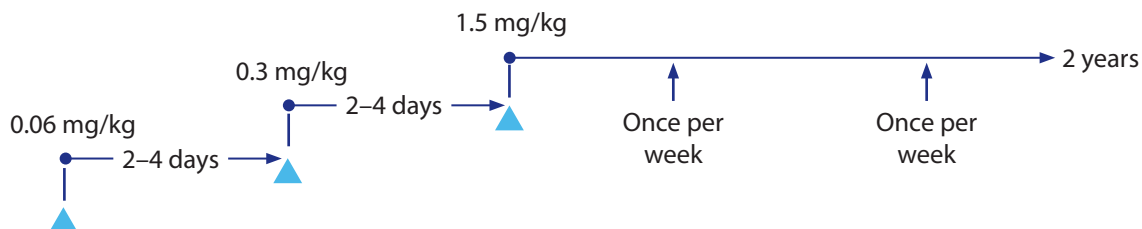
What happened in the MajesTEC-1 study?

Participants included in this analysis joined the MajesTEC-1 study between **March 2020** and **August 2021** and received the recommended dose of teclistamab. First, participants in the study received 2 injections of lower doses of teclistamab (known as step-up doses) to reduce the risk of side effects. Then participants started once-weekly injections of the full dose of teclistamab. Participants were hospitalized and treated with dexamethasone (a steroid to reduce inflammation), acetaminophen (a pain killer and fever reducer), and diphenhydramine (to reduce the risk of allergic reactions) before the initial low-dose injections and the first full-dose injection.

Participants continued to receive teclistamab once per week until the end of the study or until their cancer worsened (disease progression), they died, or they withdrew from the study for reasons such as unfavorable side effects. Researchers regularly checked for signs of multiple myeloma in the participants' blood and urine and also measured the amount of cancer cells in participants' bone marrow.

Teclistamab



- "Step-up" doses of teclistamab prior to first full dose
- Injections of 1.5 mg/kg of teclistamab once per week



Teclistamab

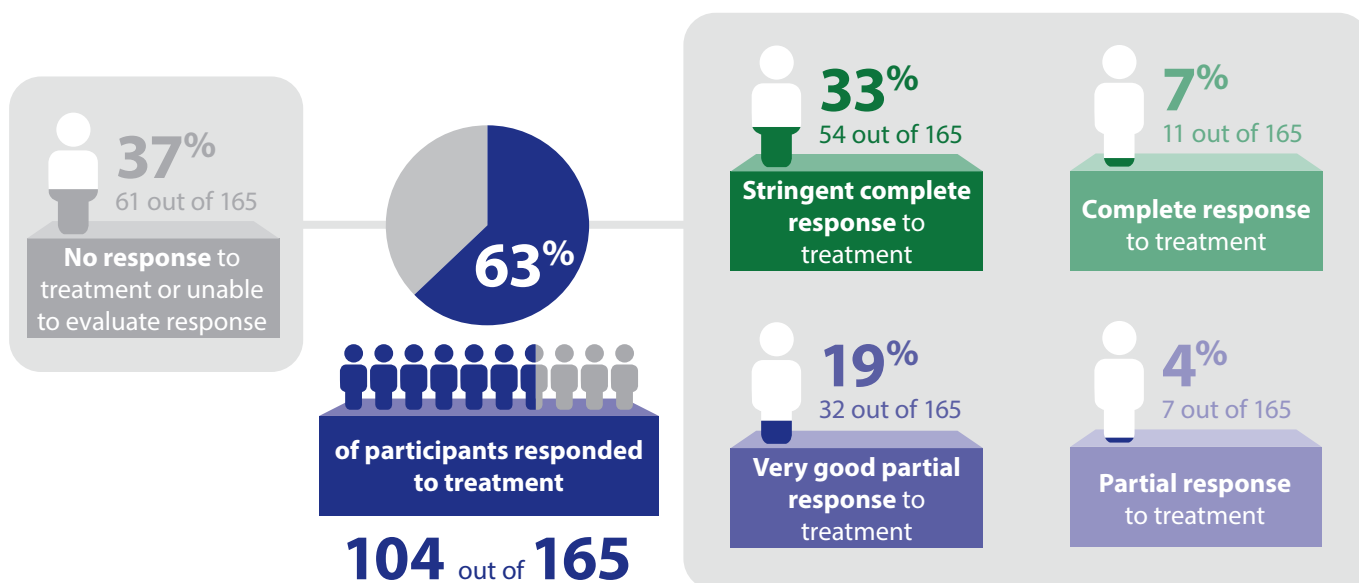
Dexamethasone
Acetaminophen
Diphenhydramine

Participants continued to receive teclistamab until the end of the study unless their cancer worsened or they withdrew from the trial

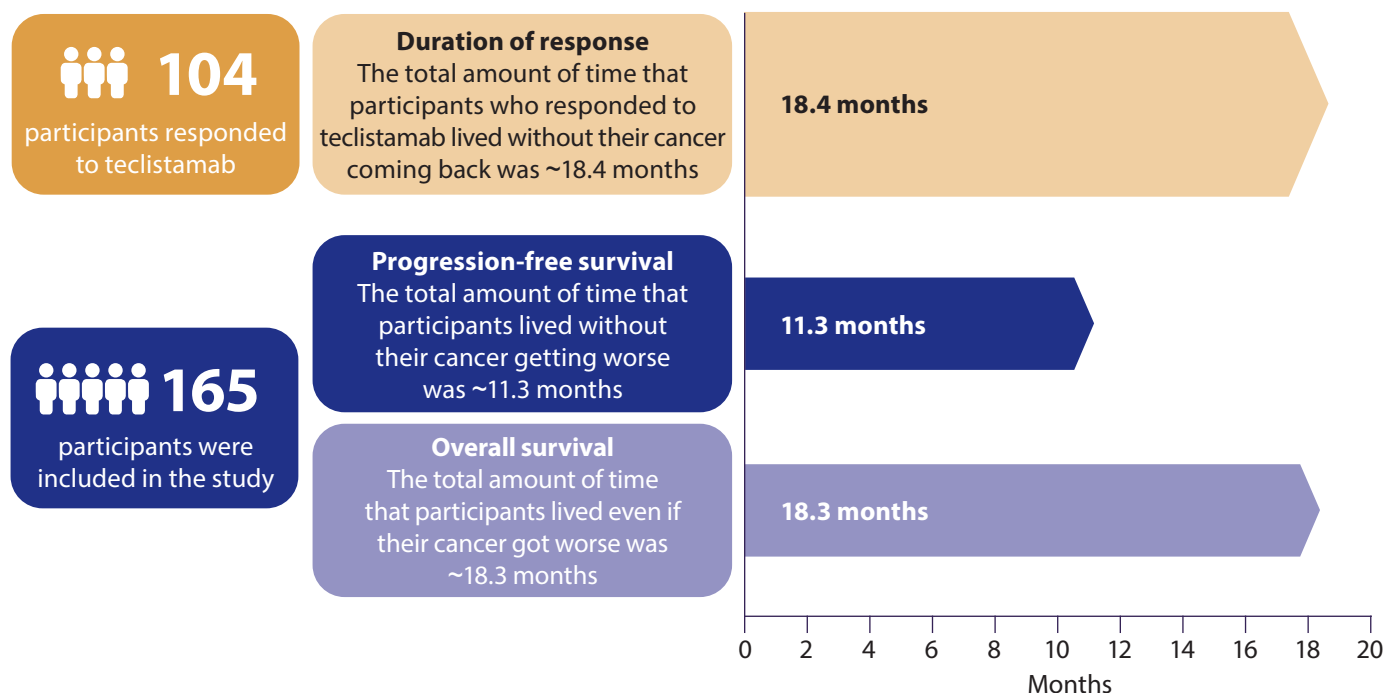
Treatment response	Signs of myeloma in blood and urine tests 	Signs of myeloma in bone marrow 
Stringent complete response	Complete response plus normal amounts of proteins called "light chains" that may be found in urine	No cancer cells in bone marrow
Complete response	No signs of myeloma in blood or urine	Less than 5% cancer cells in bone marrow
Very good partial response	Decrease of signs of myeloma in blood of 90% or more Less than 100 mg of signs of myeloma in urine	No change required
Partial response	Decrease of signs of myeloma in blood of 50% or more Decrease of signs of myeloma in urine of 90% or more	No change required

What were the main findings from the MajesTEC-1 study?

104 of 165 participants (63%) in the MajesTEC-1 study responded to teclistamab, meaning that they had less cancer than when they started treatment, including 65 participants who had no detectable cancer cells at any time during the study. Participants started responding to treatment approximately 1.2 months after they began taking teclistamab. Participants who responded to teclistamab lived without their myeloma coming back for a median of 18.4 months.



Participants in the MajesTEC-1 study lived without their myeloma getting worse for a median (calculated as the middle value when listed from shortest to longest time) of 11.3 months. Overall, participants lived for a median of 18.3 months regardless of whether they responded to treatment. These numbers may change in the future as more data are collected.



How many participants had side effects in the MajesTEC-1 study?

Researchers monitored for side effects of teclistamab in all 165 participants who took at least 1 full dose of teclistamab. The most common side effects were infections, cytokine release syndrome, and side effects related to blood cell counts, including low numbers of white or red blood cells (known as neutropenia, anemia, and lymphopenia) and low numbers of platelet cells (known as thrombocytopenia).

Side effects from drugs tested in clinical trials are considered to be serious if they result in hospitalization, cause permanent damage to a person's health, lead to death, increase the likelihood that the person will die, or if the researcher considers it to be a significant event.

Teclistamab

Serious side effects

65%

107 out of 165



- 65% of participants who took teclistamab had serious side effects
- The most common were COVID-19, pneumonia, and cytokine release syndrome
- 5 participants who took teclistamab died because of side effects that researchers thought were related to treatment, including COVID-19, viral infection impacting the brain, liver failure, and pneumonia

Patients who had abnormally low white blood cell counts could be treated with a drug that stimulates the body to make more blood cells, called granulocyte colony stimulating factor.

Some participants also had abnormally low levels of immunoglobulins (a type of antibody), a condition known as hypogammaglobulinemia, during treatment with teclistamab, which could be treated by supplementing immunoglobulins if needed. Because abnormally low levels of white blood cells and immunoglobulins can make it harder for a person's immune system to fight off infections, 74 participants (45%) in the MajesTEC-1 study developed infections that researchers considered to be severe or life-threatening. Of participants in the MajesTEC-1 study who developed hypogammaglobulinemia, 65 received intravenous immunoglobulins to help fight infection.

Cytokine release syndrome occurred in 119 study participants (72.1%). It usually lasted for ~2 days and most often occurred early in treatment, after the "step-up" doses or the first full dose of teclistamab. Cytokine release syndrome was mild or moderate in all but 1 of the participants. This means that participants had a fever and some may have also had decreased blood pressure or low blood oxygen levels. Researchers in the MajesTEC-1 study were able to treat cytokine release syndrome using:

- A drug called tocilizumab, which reduces cytokine activity
- Steroids to reduce inflammation
- A drug known as a vasopressor to increase blood pressure
- Supportive oxygen when needed

Why are infections common?

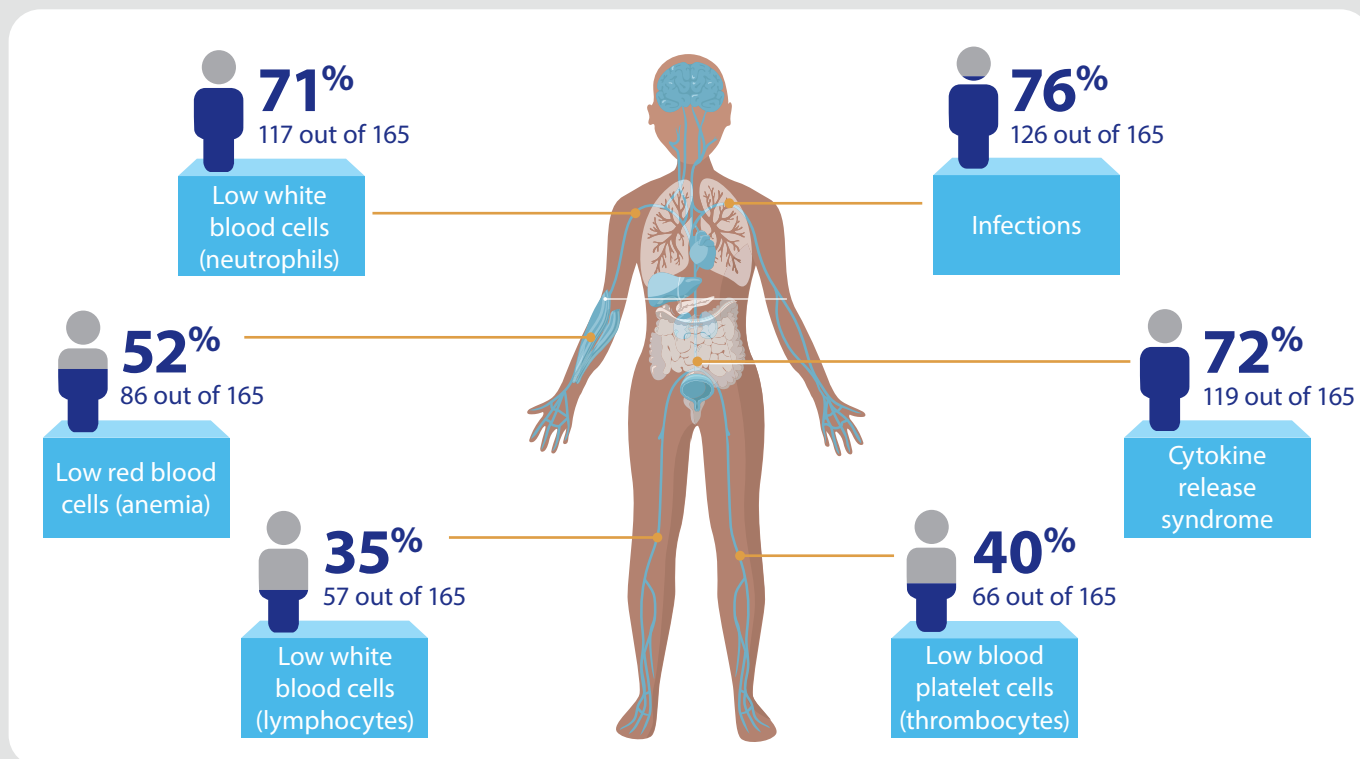
People with multiple myeloma are already more likely to develop infections, and drugs like teclistamab that cause reduced white blood cell counts and low levels of antibodies can further increase risk of infection.

Cytokine release syndrome:

Therapies like teclistamab that activate the immune system cause the release of immune signaling chemicals called cytokines. Higher than normal levels of cytokines can cause side effects like fever, low blood pressure, and low blood oxygen levels.

How many participants in the MajesTEC-1 study had serious side effects?

What were the most common side effects in the MajesTEC-1 study?



How many participants stopped treatment because of side effects in the MajesTEC-1 study?

Skipped a dose of teclistamab



63%

104 out of 165

- 63% of participants who took teclistamab **skipped a dose** because of side effects

Stopped taking teclistamab



1%

2 out of 165

- Only 1% of participants **stopped taking teclistamab** because of pneumonia caused by a virus or side effects impacting the brain

What do the results of the MajesTEC-1 study mean?

- The results of the MajesTEC-1 study were encouraging because 63% of participants with relapsed or refractory multiple myeloma who had received at least 3 prior treatments responded to teclistamab treatment, even though they were resistant to many of the currently available treatment options
- Side effects of teclistamab were mostly not severe and went away with clinical management
- Participants who responded to teclistamab lived without their myeloma coming back for ~18.4 months
- These results suggest that teclistamab could be used for patients with relapsed or refractory multiple myeloma who have limited treatment options

Where to find more information

Original research article

The original research article, "Teclistamab in relapsed or refractory multiple myeloma," was published in the *New England Journal of Medicine* (Moreau *et al.* *N. Engl. J. Med.* 387(6), 495–505 [2022]). You can read the full article at: https://www.nejm.org/doi/10.1056/NEJMoa2203478?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed

Trial registration site

You can read more about the phase 1-2 MajesTEC-1 study at the following trial registration websites:

- <https://clinicaltrials.gov/ct2/show/NCT03145181>
- <https://clinicaltrials.gov/ct2/show/NCT04557098>

Acknowledgments

The authors acknowledge the patients and investigators who participated in this study, in addition to the staff members at the study sites, the Data Review and Safety Monitoring Committees, Alliance Foundation Trials (AFT; <https://acknowledgments.alliancefound.org>), and the Janssen Team. This work was funded by Janssen Oncology. The MajesTEC-1 study was sponsored by Janssen Oncology and designed in partnership with AFT. Editorial and medical writing support were provided by Carolyn Farnsworth, Katie Yoest, PhD, and Katie Veleta, PhD, of MedThink SciCom and were funded by Janssen Global Services, LLC.

Financial & competing interests disclosure

The authors' full disclosure information can be found in the original research article. Writing support for this summary was provided under the direction of the author(s) by Katie Yoest, PhD, and Katie Veleta, PhD, of MedThink SciCom and was funded by Janssen Research and Development.