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A plain language summary of the PERSEUS study of daratumumab plus bortezomib, lenalidomide, and dexamethasone for treating newly diagnosed multiple myeloma

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Plain Language Summary of Publication

A plain language summary of the PERSEUS study of daratumumab plus bortezomib, lenalidomide, and dexamethasone for treating newly diagnosed multiple myeloma

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Full affiliations can be found at the end of this article

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Where can I find the original article on which this summary is based?

You can find, access for free, and read the original article, titled 'Daratumumab, Bortezomib, Lenalidomide, and Dexamethasone for Multiple Myeloma' that was published in December 2023 in *The New England Journal of Medicine* at https://www.nejm.org/doi/full/10.1056/NEJMoa2312054.

Summary

What is this summary about?

This summary describes the first analysis of the PERSEUS study, which looked at adults with multiple myeloma that had never been treated before, also called newly diagnosed multiple myeloma. Multiple myeloma is a type of cancer in the blood, specifically in plasma cells within the soft, spongy tissue in the center of most bones, called the bone marrow. Researchers wanted to see if adding daratumumab (D) to a standard treatment of three other medicines called **VRd**, which stands for bortezomib (V), lenalidomide (R), and dexamethasone (d), could stop the multiple myeloma from getting worse and help participants live longer without multiple myeloma.

How to say (double click sound icon to play sound)...

- **Hematopoietic:** hee-MA-toh-poy-EH-tik
- **Cytogenetics:** SY-toh-jeh-NEH-tix
- **Chemotherapy:** KEE-moh-THAYR-uh-pee
- **Daratumumab:** DAR-uh-TOOM-oo-mab
- **Bortezomib:** bor-TEH-zow-mib
- **Lenalidomide:** leh-nuh-LI-duh-mide
- **Dexamethasone:** DEK-suh-MEH-thuh-sown
- **Multiple myeloma:** multiple mai-UH-low-muh
- **Autologous stem cell transplant:** aw-TOL-uh-gus stem cell transplant
- **Thrombocytopenia:** THROM-boh-sy-toh-PEE-nee-uh
- **Neutropenia:** noo-troh-PEE-nee-uh

Half of the participants were assigned to the treatment plan with daratumumab; they received **D-VRd** during initial treatment phases (**induction** and **consolidation**), followed by daratumumab as well as lenalidomide (D-R) in the **maintenance** phase. The other half of participants received treatment without daratumumab; they received VRd induction and consolidation followed by lenalidomide alone (R) maintenance. In addition, all participants were able to receive an **autologous stem cell transplant**, a procedure used to further help reduce multiple myeloma.

What were the results?

At the time of this analysis of PERSEUS, about 4 years after participants started the study, participants who received D-VRd treatment followed by D-R maintenance had a better response to treatment

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(as measured by specific **markers** of multiple myeloma) and were more likely to be alive and free from their multiple myeloma getting worse in comparison to participants who received VRd followed by R maintenance. Side effects (unwanted or undesirable effects of treatment) in both treatment groups were in line with the known side effects of daratumumab and VRd.

What do the results mean?

The results of the PERSEUS study showed that including daratumumab in D-VRd induction/consolidation and D-R maintenance was better for treating multiple myeloma than the current standard VRd treatment followed by R maintenance alone in adults with a new diagnosis of multiple myeloma who were also able to receive an autologous stem cell transplant. Of importance, there were no unexpected side effects in either group.

VRd: A combination of treatments including bortezomib (V), lenalidomide (R), and dexamethasone (d), which is the current standard treatment for newly diagnosed multiple myeloma.

D-VRd: A combination of treatments including daratumumab (D) plus bortezomib (V), lenalidomide (R), and dexamethasone (d).

Induction treatment: The first phase of treatment given for multiple myeloma, aimed at reducing the number of cancerous multiple myeloma cells. It typically includes a combination of drugs that are given before proceeding to other treatments, such as autologous stem cell transplant.

Consolidation treatment: Treatment that is given after an autologous stem cell transplant to kill more multiple myeloma cells that may be left in the body. This treatment may be the same combination of treatments given for induction.

Maintenance treatment: Treatment that is given for a longer period of time to help prevent multiple myeloma cells from coming back after they have disappeared following induction/consolidation treatment.

Autologous stem cell transplant: A procedure in which a person's own healthy hematopoietic stem cells (cells that can produce all the blood cell types, including white blood cells, red blood cells, and platelets) are collected from the blood or bone marrow, stored, and then returned to the body after high-dose chemotherapy (drugs used to kill cancer). High-dose chemotherapy helps kill as many leftover multiple myeloma cells as possible but can also damage healthy tissue and blood cells. Giving back the stem cells helps the bone marrow recover from chemotherapy.

Markers: Also referred to as 'signs', are anything found in the blood, urine, or body tissues that can act as an indication that a person has multiple myeloma. These markers are often small substances, usually proteins, produced by multiple myeloma cells or by the body in response to the multiple myeloma. Doctors can use the presence (or absence) of these markers to help diagnose multiple myeloma, to determine if multiple myeloma has come back after treatment, or to monitor whether a treatment is working.

What is the purpose of this plain language summary?

- Daratumumab is used to treat the disease under study that is discussed in this summary, multiple myeloma. However, some countries may not have approved the use of daratumumab, either alone or mixed with other treatments, to treat multiple myeloma yet; please check with your local treating physician for more details.
- The results of this study may differ from those of other studies. Health professionals should make treatment decisions based on all available evidence, not on the results of a single study.

Who is this article for?

This summary is for individuals with multiple myeloma, caregivers, and health care professionals (for example, doctors, physician assistants, nurses, and nurse practitioners) who treat people with multiple myeloma, to help better understand the results of the PERSEUS study.

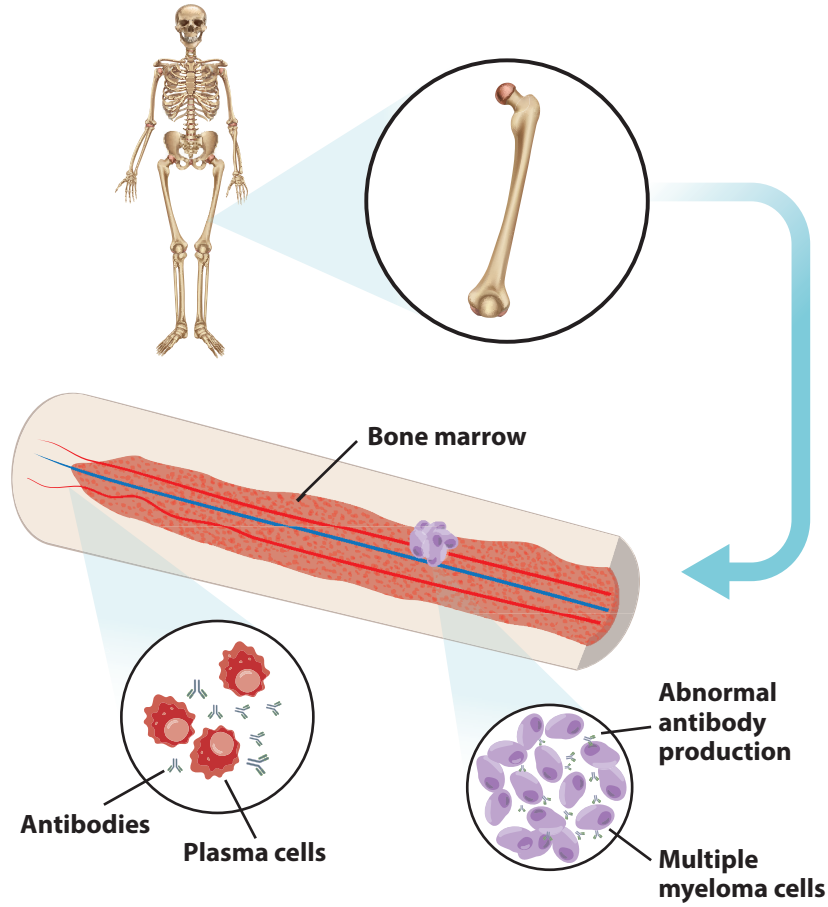
Who sponsored this study?

The PERSEUS study was **sponsored** by the European Myeloma Network in collaboration with Janssen Research & Development, LLC.

Sponsor: A company or organization that oversees and pays for a clinical research study. The sponsor also collects and analyzes the information that was generated during the study.

What is multiple myeloma?

Multiple myeloma is a type of blood cancer that affects a specific type of blood cell, called a plasma cell. Healthy plasma cells make antibodies that normally help fight infections. When a person has multiple myeloma, plasma cells become cancerous, grow uncontrollably, and build up within the bone marrow (the soft tissue found in the center of bones).



Signs or symptoms of multiple myeloma

- Bone pain or bone break (fracture)
- Fatigue, tiredness, and feeling of weakness
- Loss of appetite and weight
- Organ damage (liver, kidney)
- Anemia (low red blood cells)
- Frequent infections

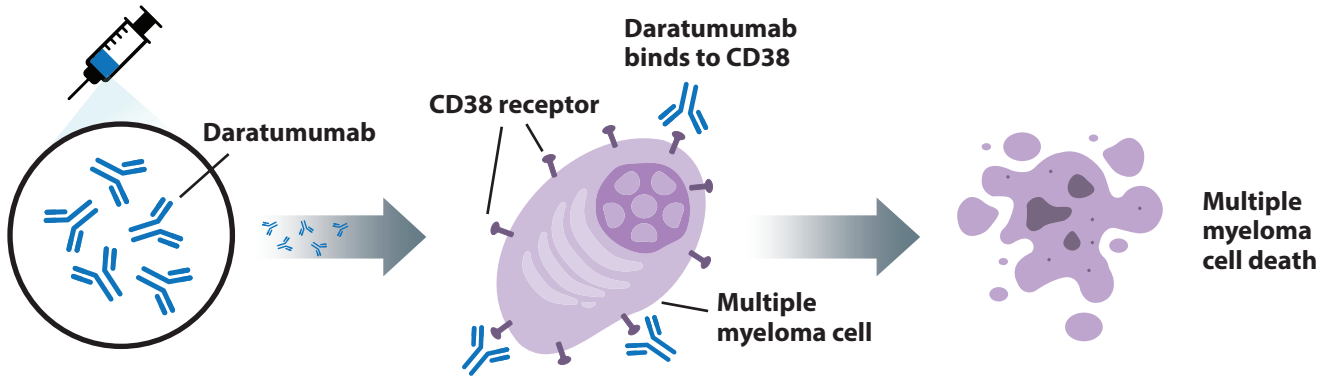
What is daratumumab?

Daratumumab is an anticancer medicine used to treat multiple myeloma. It can be given on its own as monotherapy (meaning with no other drugs), or it can be given as combination therapy (meaning it is given at the same time as several other anticancer drugs to treat multiple myeloma).

Daratumumab is an antibody that has been created in a laboratory to act like the natural antibodies within our body and to recognize a molecule called **CD38**, which is located on the outside surface of multiple myeloma cells.

Daratumumab-based treatments for multiple myeloma are approved for use in many countries.

CD38: This is a type of protein that can be found on the outside surface of some types of blood cells and in high levels on some cancer cells, including multiple myeloma cells.



When daratumumab detects a multiple myeloma cell with CD38, daratumumab binds to the CD38 on the cell surface

Daratumumab works with the body's immune system to kill the multiple myeloma cell and minimize the spread of future multiple myeloma cells

Why did researchers want to do this study?

While treatment options for multiple myeloma have continued to get better, unfortunately multiple myeloma is still not curable, and there is a need for new treatment options to prevent it from coming back (relapse) and attain long-term control of the multiple myeloma.

A similar study, called the GRIFFIN study, also combined daratumumab with VRd induction/consolidation and added daratumumab to R during maintenance. The study also looked at a similar but smaller population of 207 adults with newly diagnosed multiple myeloma who received autologous stem cell transplant. The GRIFFIN study showed that multiple myeloma responded better to D-VRd induction/consolidation followed by D-R maintenance than VRd induction/consolidation followed by only R maintenance. While these results are similar to those of the PERSEUS study, the GRIFFIN study was smaller and only enrolled participants from health care clinics throughout the United States.

The larger PERSEUS study was done in order to evaluate D-VRd and VRd treatment in more participants, as well as in other regions of the world, to confirm the positive results observed in the GRIFFIN study. Additionally, in the PERSEUS study, the researchers' main goal (primary objective of the study) was to measure the period of time before a participant's multiple myeloma got worse, or until the participant died, after getting D-VRd or standard VRd treatment. This main goal was different than that of the GRIFFIN study (which was response).

What was the goal of the PERSEUS study?

The overall goal of the PERSEUS study was to determine if the four-drug combination treatment of D-VRd followed by D-R maintenance was better at delaying the time before participants' multiple myeloma got worse or participants died than the current three-drug standard treatment of VRd followed by R maintenance in participants with newly diagnosed multiple myeloma who were able to receive autologous stem cell transplant.

Who was in the PERSEUS study?

Participants were:

- Between the age of 18–70 years
- Recently diagnosed with multiple myeloma that had never been treated before
- Able to receive autologous stem cell transplant based on their general health status, age, and medical history

PERSEUS enrolled participants from 14 countries across Europe and Australia

709 participants with newly diagnosed multiple myeloma

355 participants received **D-VRd** followed by **D-R maintenance**

354 participants received **VRd** followed by **R maintenance**

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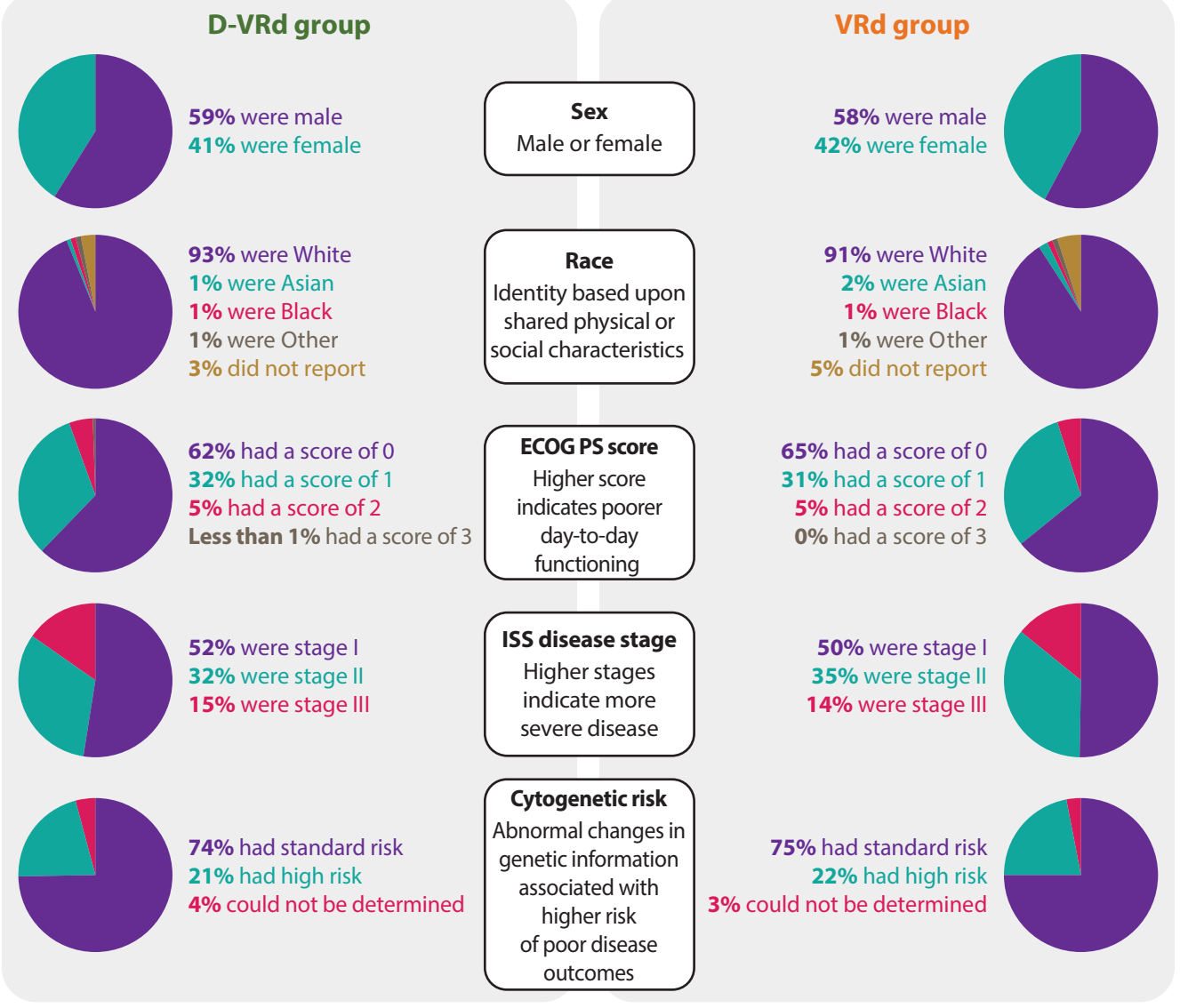
Characteristics of participants who were in the PERSEUS study



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What specific groups of participants did the researchers look more closely at in PERSEUS?

- In PERSEUS, researchers looked at how well D-VRd and VRd worked among all participants who were treated in the study (also called the overall population). In addition, researchers looked at the effect of the treatment in several specific groups of participants who may have been at higher risk for worsening multiple myeloma, for example:
  - ➜ Participants who were 65 years of age or older
  - ➜ Participants with poor functional, day-to-day performance (high **ECOG PS** scores)
  - ➜ Participants with more advanced disease stage (**ISS** stage III disease)
  - ➜ Participants with certain genetic abnormalities that are often associated with worse multiple myeloma (high **cytogenetic risk**)
- In the PERSEUS study, the proportion of Black participants enrolled was small (1% in either treatment group), and race was not captured in 4% of participants as the study was conducted primarily in Europe, in which some countries have restrictions on collecting this information; therefore, researchers did not look at the impact of race in this study. However, the previously conducted GRIFFIN study enrolled a larger proportion of Black participants (15%) and evaluated D-VRd followed by D-R maintenance versus VRd therapy followed by R maintenance among Black and White study participants. More information is provided in the 'Where can I find more information' section near the end of this article.

Eastern Cooperative Oncology Group performance status (ECOG PS): The ECOG PS score describes a participant's level of functioning in terms of their ability to care for themself, daily activity, and physical ability (for example, walking, working, etc). The performance status is graded on a scale from 0 to 4, with a higher score indicating worse functional performance.

International Staging System (ISS): This is a way to rate how advanced the multiple myeloma may be based upon 2 markers within a participant's body. Based upon the levels of each of these specific markers, the multiple myeloma is rated a disease stage. There are three stages: stage I, II, and III. The higher the disease stage, the greater the risk for more severe and aggressive multiple myeloma.

Cytogenetic risk: This describes the possibility of having worse multiple myeloma outcomes and poorer response to treatment based on the presence of specific broken, missing, rearranged, or extra genes/chromosomes in the multiple myeloma cells. A gene holds all the information and instructions for building a specific protein, and a chromosome contains many of these genes. These genetic/chromosome alterations are called cytogenetic abnormalities and impact normal cell functions. With standard-risk multiple myeloma, none of these specific abnormal genes are present, whereas with high-risk multiple myeloma, one or more of these specific abnormal genes are present.

What happened in the study?

How was medicine given in the PERSEUS study?

- This was a randomized study, which means a computer program assigned half of the participants to a group who received D-VRd followed by D-R maintenance and half to a group who received VRd followed by R maintenance.
- Daratumumab (D) and bortezomib (V) were given by subcutaneous injection (under the skin). Lenalidomide (R) and dexamethasone (d) were given by oral administration (pill by mouth).
- This study was open label, which means that both the participant and the doctor knew what treatment the participant was receiving.
- After participants were randomized, they began treatment in the study, which had 4 treatment phases:
  1. D-VRd or VRd induction treatment (4 months)
  2. Autologous stem cell transplant
  3. D-VRd or VRd consolidation treatment (2 months)
  4. D-R or R maintenance treatment, in which participants in each treatment group continued to be treated until the multiple myeloma worsened, they could not tolerate the drugs anymore, or they died
- After 2 years of maintenance treatment, any participant in the D-VRd group who was receiving D-R maintenance, who responded well to treatment, and whose tests showed that they had undetectable multiple myeloma could stop daratumumab maintenance and continue on R maintenance alone. The participant then continued on R maintenance alone until the multiple myeloma worsened, the participant could not tolerate the drugs anymore, or the participant died. Participants restarted daratumumab treatment with R maintenance if their multiple myeloma came back.

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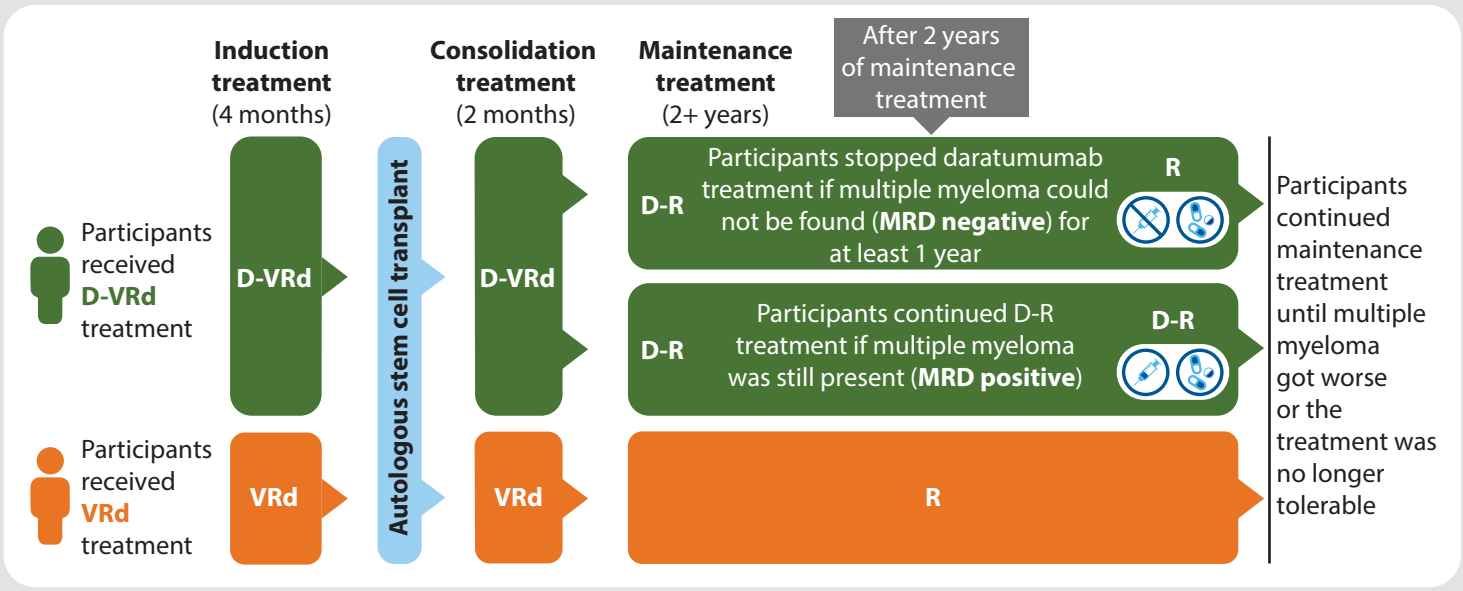


What were the overall results of PERSEUS?

What did the PERSEUS study measure, and how did researchers determine if the treatment worked?

- To find out if the study treatments were reducing the amount of multiple myeloma cells, researchers monitored the participants' overall health and measured several markers using the participant's blood, urine, and/or bone marrow; these 'markers' were a sign that multiple myeloma was present.
- At the time of this first PERSEUS analysis, a median of 47.5 months (almost 4 years) had passed since participants were randomized to a treatment group. This means that at least half of the participants were monitored for at least 47.5 months after they entered the study and received the first dose of their assigned treatment.

Progression-free survival (PFS) results

Progression-free survival (PFS)

The main goal of PERSEUS was to measure the length of time from when a participant was randomized to a treatment to when their multiple myeloma got worse (progressed) or they died

- Researchers called this '**progression-free survival**' or '**PFS**'
- PFS is often reported as a way to determine how well a treatment is working against the multiple myeloma
- Since this was the main goal of the study, it was called the primary endpoint

Primary endpoint

Looking at all participants in the study, did D-VRd followed by D-R maintenance help participants live longer without their multiple myeloma getting worse compared with standard VRd followed by R maintenance?

YES

After almost 4 years, **84% of D-VRd followed by D-R maintenance** participants compared to **68% of VRd followed by R maintenance** participants were alive and without multiple myeloma progression

YES **58%↓**

Participants who received **D-VRd followed by D-R maintenance** were 58% less likely to die or have their multiple myeloma get worse or return compared with those who received standard **VRd followed by R maintenance**

When the researchers looked at specific groups of participants who may be at risk for more severe disease, did **D-VRd followed by D-R maintenance** help participants live longer without their multiple myeloma getting worse compared with standard **VRd followed by R maintenance**?

Age

YES

Among participants **65 years or older**, **D-VRd** slightly reduced the risk of disease progression by **3%** ↓

ISS disease stage

YES

Among participants with **stage III disease**, **D-VRd** reduced the risk of disease progression by **58%** ↓

Cytogenetic risk

YES

Among participants with **high risk**, **D-VRd** reduced the risk of disease progression by **41%** ↓

ECOG PS score

YES

Among participants with an **ECOG PS score of 1 or more**, **D-VRd** reduced the risk of disease progression by **59%** ↓

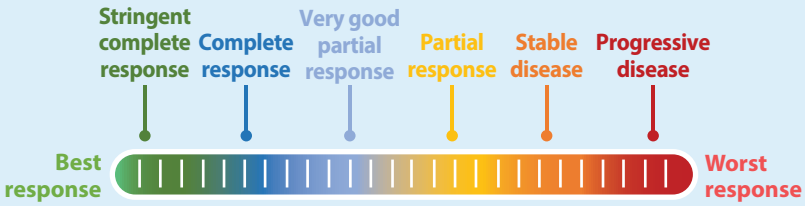
Response results

- In PERSEUS, participants who were treated with D-VRd followed by D-R maintenance had a better response compared with those treated with the current standard treatment of VRd followed by R maintenance.

Response

Another measurement to determine if multiple myeloma treatment is working is called '**response**'

- Doctors determined if a participant's multiple myeloma was responding to treatment by using very specific criteria developed by a group of researchers and doctors called the International Myeloma Working Group (IMWG); these criteria are the standardized way to measure multiple myeloma
- Regular blood and urine tests were performed to check for signs of multiple myeloma, and multiple myeloma cells in the bone marrow were counted to measure the response



Patients with a good response (stringent complete response or complete response) reacted well to treatment, better than those whose multiple myeloma was categorized as partial response or worse

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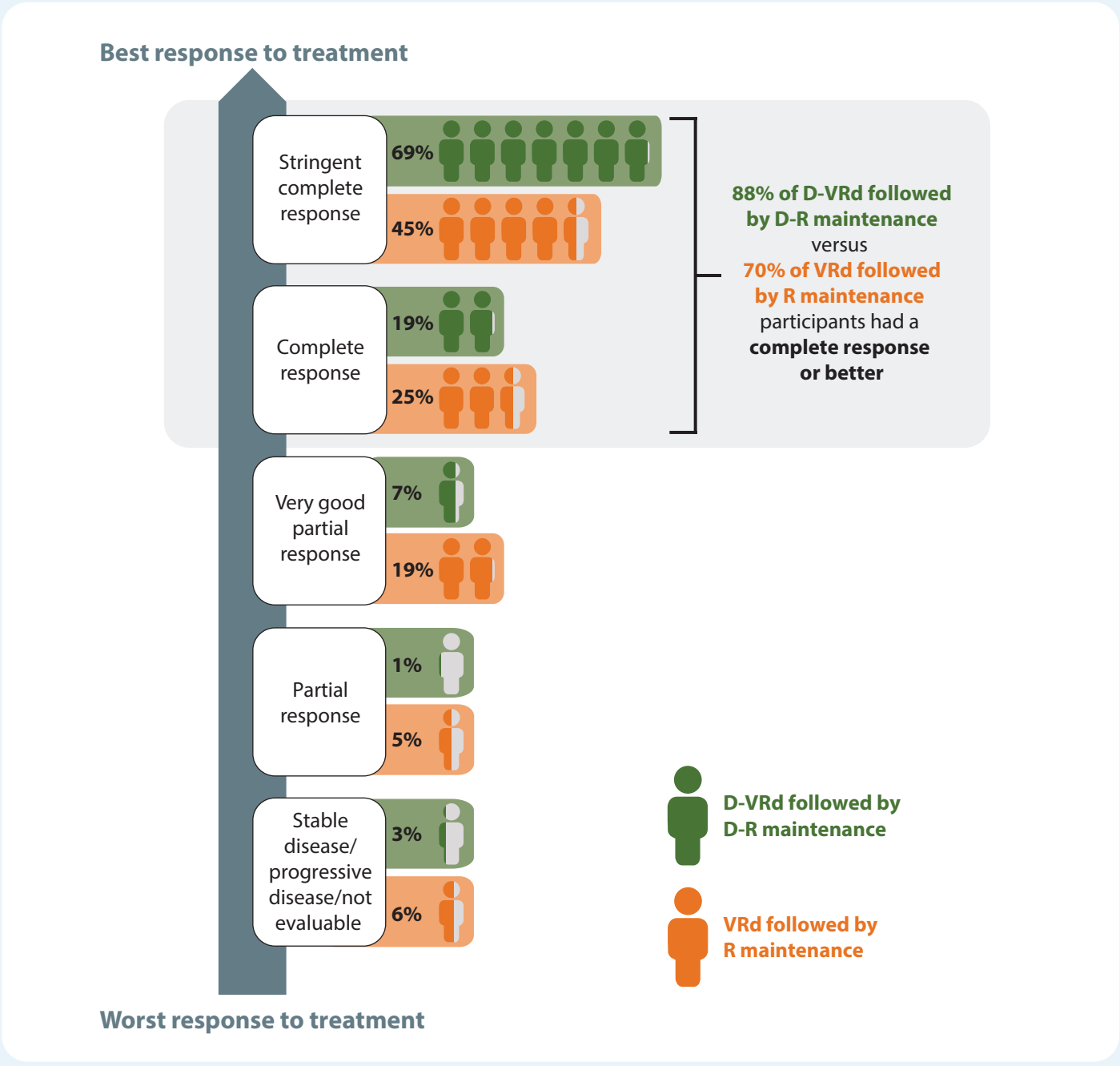
Complete response: A state in which multiple myeloma is undetectable with standard tests. Specifically, no multiple myeloma cells are detected in the blood or urine, and there are few (less than 5%) plasma cells in the bone marrow. However, this does not include additional sensitive testing required for stringent complete response.

Stringent complete response: A deeper response than complete response, following the same criteria as for complete response but also including negative test results for more sensitive testing methods (such as immunofixation and the absence of clonal plasma cells by several measurements). Additionally, an important protein ratio (called the light-chain ratio) is normal.



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Minimal residual disease (MRD) results

Minimal residual disease (MRD)

Another measurement to determine if multiple myeloma treatment is working is called '**minimal residual disease**' or '**MRD**'

- MRD measures if a patient has any remaining (or residual) multiple myeloma cancer cells in the bone marrow during or after treatment
- Participants were MRD negative (meaning they had no sign of multiple myeloma) if no multiple myeloma cells were detected in a sample of 100,000 healthy cells. This is called the 10^{-5} threshold and is the standard threshold used
- A more strict MRD threshold, called 10^{-6}, indicated that no multiple myeloma cells were found in 1,000,000 healthy bone marrow cells
- MRD testing helps doctors understand how well treatments work and whether the multiple myeloma has come back
- Achieving MRD negativity is a goal of many treatments and is often associated with better outcomes
- In PERSEUS, a participant was only considered to be MRD negative if they also had a **complete response or better**

When researchers measured how many multiple myeloma cells were in bone marrow after treatment, did more participants who received D-VRd followed by D-R maintenance have no sign of multiple myeloma?

YES

Participants who received **D-VRd followed by D-R maintenance** were more likely to have no sign of multiple myeloma (**MRD negative**) compared with those who got standard **VRd followed by R maintenance**

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Sustained MRD negativity
This term refers to the long-term absence of multiple myeloma cells in the bone marrow, as measured by MRD testing. More specifically, it can mean that a participant has no sign of multiple myeloma cells at two back-to-back MRD tests, usually 6 or 12 months apart, with no positive MRD result (presence of multiple myeloma) in between

Did more participants who received D-VRd followed by D-R maintenance have sustained MRD negativity (no sign of multiple myeloma for at least 12 months)?

YES

More participants who received **D-VRd followed by D-R maintenance** had sustained MRD negativity (no sign of multiple myeloma) compared with those who received standard **VRd followed by R maintenance**

Participants who were MRD negative (10^{-5}) for at least 12 months

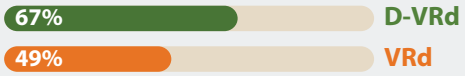
When the researchers looked at specific groups of participants who may be at risk for more severe disease, did D-VRd followed by D-R maintenance help reduce the number of multiple myeloma cells and help participants achieve MRD negativity more than standard VRd followed by R maintenance?

Participants who were **MRD negative at 10^{-5}**

Age

YES

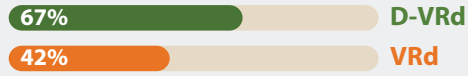
65 years of age or older



ISS disease stage

YES

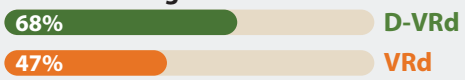
Stage III disease



Cytogenetic risk

YES

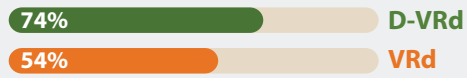
High risk



ECOG PS score

YES

Score of 1 or more



Response-adapted treatment

- In the PERSEUS study, after 2 years of maintenance, participants who received D-VRd followed by D-R maintenance who responded well to treatment (complete response or better) and had no signs of multiple myeloma (i.e., were MRD negative at the 10^{-5} threshold for at least 1 year) could stop daratumumab treatment and continue with R maintenance treatment only.
- Daratumumab was stopped in approximately 2 out of 3 (64%) participants who received D-R maintenance.

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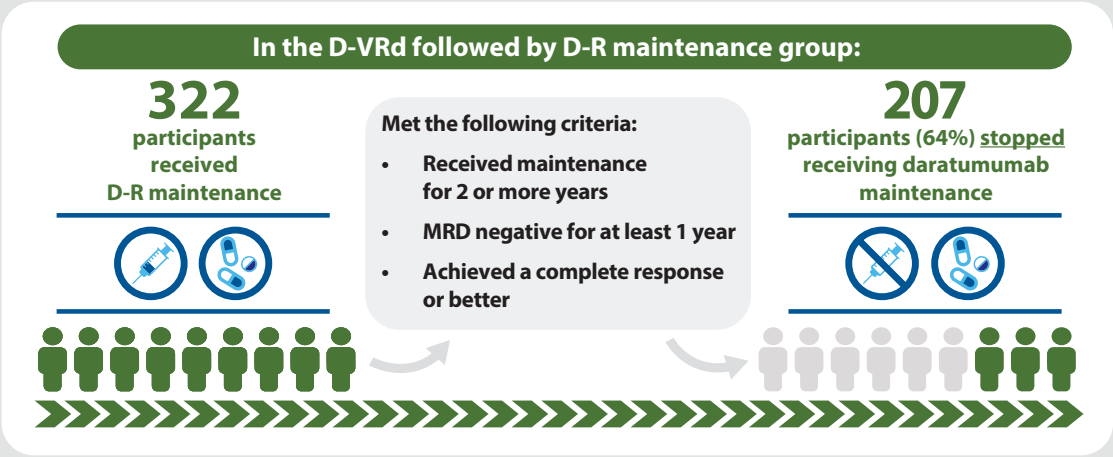
- These results are encouraging as they highlight that many participants who received D-VRd treatment achieved better and long-lasting responses to treatment such that the multiple myeloma was undetectable, and participants were permitted to stop a portion of their treatment during maintenance.

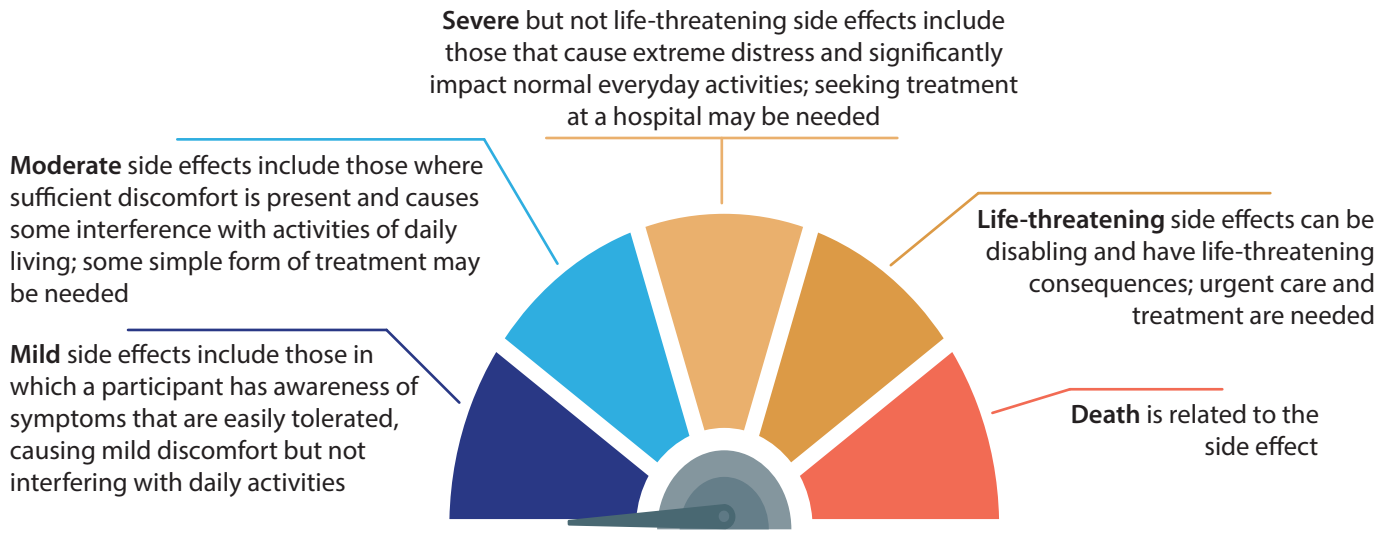


What were the side effects of treatment in the PERSEUS study?

Researchers also wanted to find out if the addition of daratumumab to the current standard VRd treatment would result in more side effects than with VRd alone. Side effects are unwanted or undesirable outcomes of a treatment and can be harmful. To do this, researchers looked at how common and how severe side effects were.

SIDE EFFECTS

Side effects were measured using a grading scale following these descriptions:



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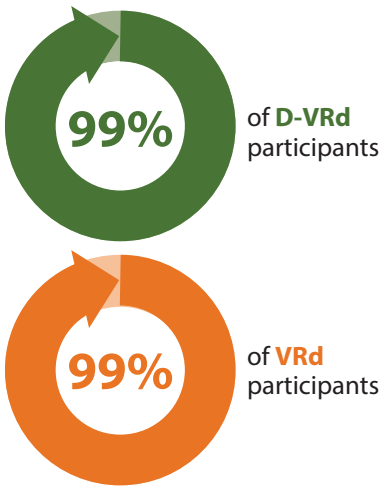
When the researchers looked at the number of side effects overall (of any severity), was there a difference between D-VRd followed by D-R maintenance and VRd followed by R maintenance?

NO

Overall occurrence of side effects was similar between **D-VRd followed by D-R maintenance** and **VRd followed by R maintenance**, with almost all (99%) participants in both groups reporting a side effect of some kind



Most common side effects of any severity reported in PERSEUS

(reported in more than 40% of participants in either treatment group)

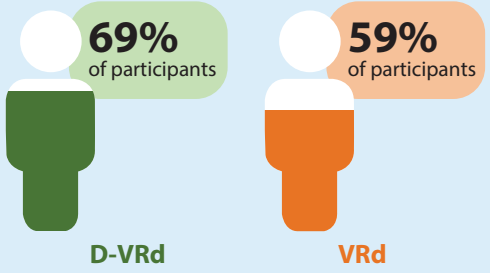
Side effects were reported by participants to the researchers as soon as they occurred

To help manage side effects, participants were treated as needed and appropriately

Side effects may have been brief and were not necessarily present for the length of the study

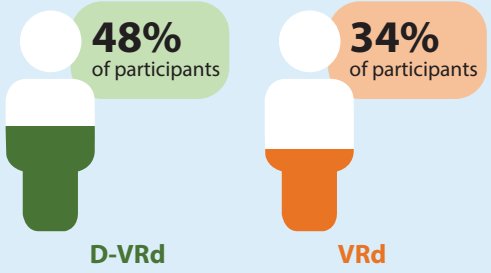
Neutropenia

low number of a specific type of white blood cell, called a neutrophil, that helps fight infections. Low levels of neutrophils make it harder for the body to fight off infection



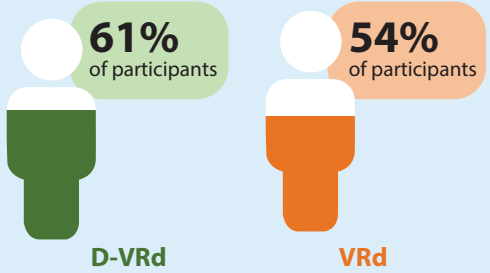
Thrombocytopenia

low number of a specific type of blood cell, called a platelet, that helps in blood clotting. Low levels of platelets mean someone might bleed more easily or it may be harder for bleeding to stop



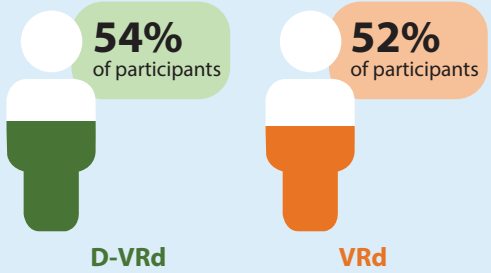
Diarrhea

loose, watery stools with frequent bowel movements (pooping more often)



Peripheral sensory neuropathy

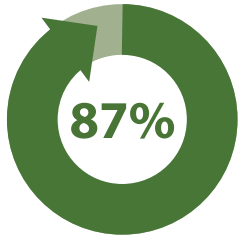
a nerve problem that can cause pain, numbness, tingling, or muscle weakness in the body



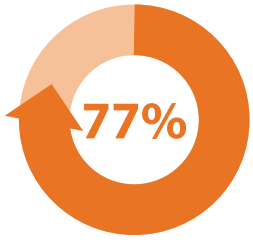
Infections are a common side effect of multiple myeloma treatment.
Did the frequency of infections of any severity differ between those receiving **D-VRd followed by D-R maintenance** and those receiving standard **VRd followed by R maintenance**?

YES

Participants who received **D-VRd followed by D-R maintenance** reported more infections of any severity compared with those who received **VRd followed by R maintenance**. When participants reported an infection, they were treated as needed and appropriately



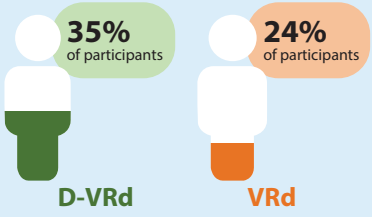
of **D-VRd** participants



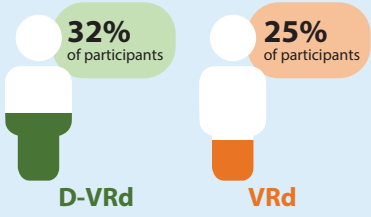
of **VRd** participants

Most common types of infection of any severity in PERSEUS

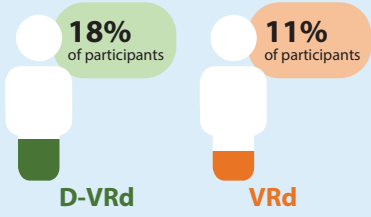
COVID-19
disease caused by the SARS-CoV-2 virus



Upper respiratory tract infection
infection of the throat or sinuses



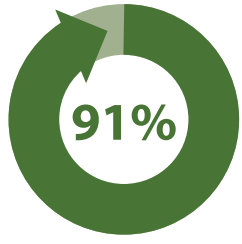
Pneumonia
infection in the lungs



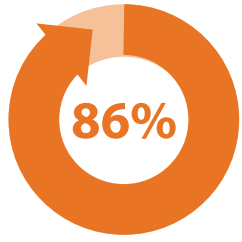
When the researchers looked at the amount of severe or life-threatening side effects, was there a difference between D-VRd followed by D-R maintenance and VRd followed by R maintenance?

YES

Slightly more participants who received **D-VRd followed by D-R maintenance** reported severe or life-threatening side effects compared to those who received standard **VRd followed by R maintenance**



of **D-VRd** participants



of **VRd** participants

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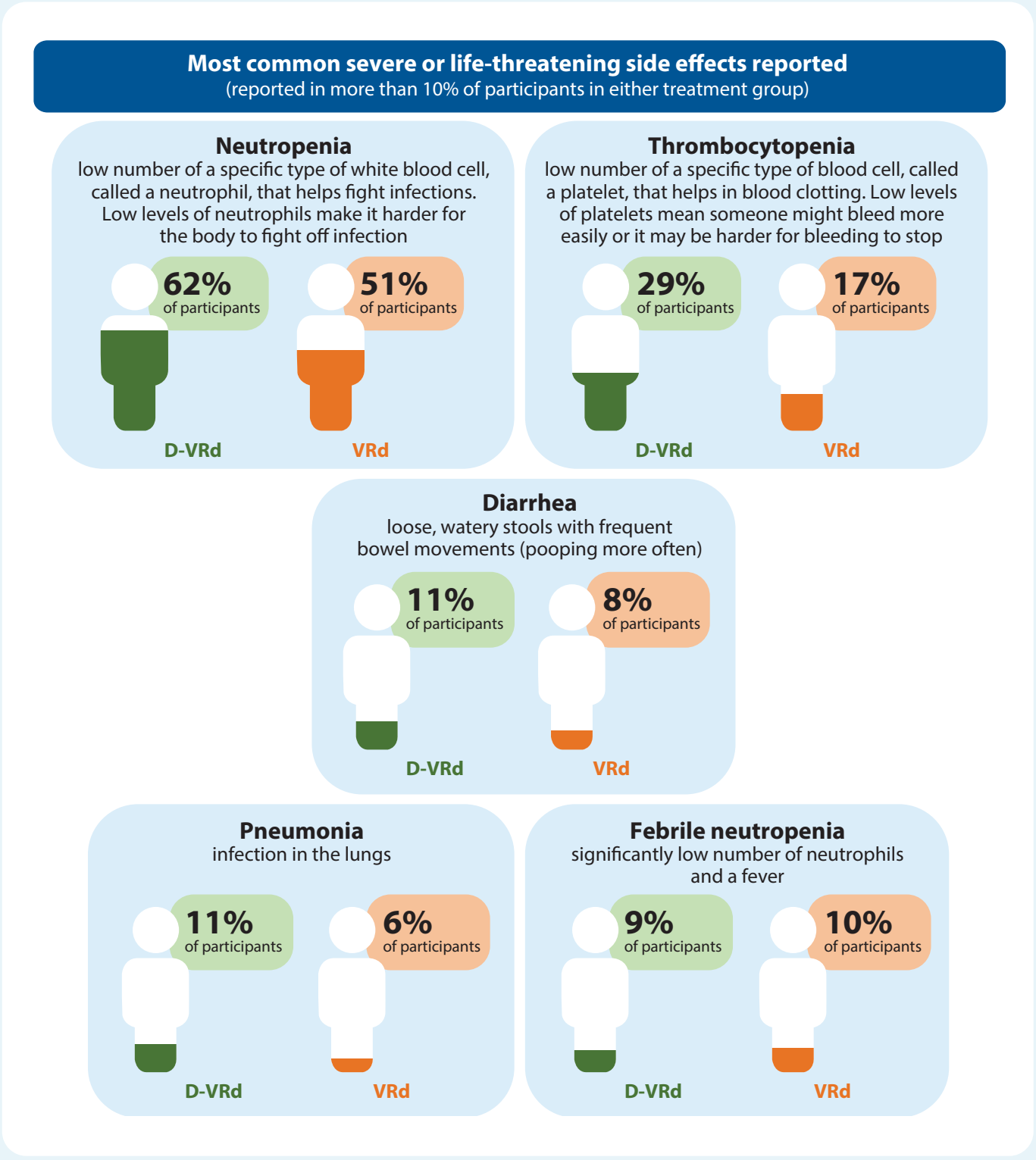

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Some side effects may lead to participants stopping their treatment. Did the number of participants who stopped taking treatment due to any side effect vary between **D-VRd followed by D-R maintenance** and **VRd followed by R maintenance**?

YES

Fewer participants who received **D-VRd followed by D-R maintenance** stopped taking treatment due to any side effect compared with those who received standard **VRd followed by R maintenance**

9% D-VRd

Among those who received study treatment, side effects led 9% of D-VRd and 21% of VRd participants to discontinue treatment

21% VRd

Even though more participants in the VRd group stopped their treatment because of side effects, this does not automatically mean that the D-VRd treatment was easier to handle than the VRd treatment. The differences might be because, in the VRd group, when participants stopped taking lenalidomide during maintenance, it counted as stopping treatment, but in the D-VRd group, participants were still getting daratumumab in maintenance and therefore were not counted as stopping treatment

In **PERSEUS**, how many participants had a life-threatening consequence (death) due to a side effect following D-VRd or VRd treatment?

13 (4%) in the **D-VRd followed by D-R maintenance** group

16 (5%) in the **VRd followed by R maintenance** group

Were other side effects reported among participants who received daratumumab?

- Sometimes, people who receive daratumumab can experience unwanted side effects, also known as injection-related side effects, that occur at the time of treatment administration or shortly afterwards.
- While injection-related side effects are commonly mild, in the PERSEUS study, participants randomized to receive daratumumab also received some specific medications taken before and after injection to help reduce the frequency and severity of injection-related side effects.

In PERSEUS, how many participants who received **D-VRd followed by D-R maintenance** had an injection-related side effect?

6%

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What impact did daratumumab have on autologous stem cell transplants in PERSEUS?

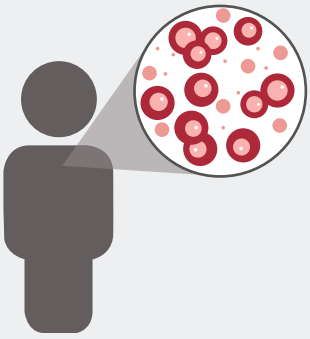
- To perform a successful autologous stem cell transplant, stem cells need to be collected and given back to the participant.
- The collection of over 2 million stem cells per kilogram of a person's body weight is preferred to help repopulate the person's body with healthy blood cells and to help ensure the best transplant possible.

When looking at how many stem cells were collected for autologous stem cell transplant, did participants who received D-VRd treatment have an adequate number of stem cells collected?

YES

D-VRd treatment compared to standard **VRd** treatment did not affect the ability to collect a sufficient amount of stem cells; neither did it impact how well the transplant went

Median number of stem cells collected per treatment group per kilogram of body weight
(meaning that half of the participants had at least this number of stem cells collected)



5.5 million stem cells per kilogram of body weight collected with **D-VRd**

7.4 million stem cells per kilogram of body weight collected with **VRd**

90% of **D-VRd** participants proceeded to transplant

87% of **VRd** participants proceeded to transplant

What do these results mean?

- After almost 4 years, more participants who received D-VRd treatment followed by D-R maintenance:
  - ➔ Were alive without their multiple myeloma getting worse,
  - ➔ Had better treatment responses, and
  - ➔ Had fewer multiple myeloma cells

  compared to those who received the current standard VRd treatment followed by R maintenance.
- Among participants who received daratumumab treatment, 2 out of 3 (64%) participants had undetectable multiple myeloma during maintenance, which allowed them to stop daratumumab treatment and continue maintenance treatment with lenalidomide only.
- In the PERSEUS study, side effects were similar to those seen in other studies with daratumumab or VRd, and no new safety concerns occurred.
- Overall, results from the PERSEUS study show that the combination of daratumumab with the current standard treatment of VRd followed by D-R maintenance represents a potential treatment option for individuals with newly diagnosed multiple myeloma who are able to receive an autologous stem cell transplant.

Where can readers find more information on this study and related publications?

The original article of this study is titled 'Daratumumab, Bortezomib, Lenalidomide, and Dexamethasone for Multiple Myeloma' and was written by Dr. Sonneveld and co-authors and published in *The New England Journal of Medicine* in December 2023 (Sonneveld P, et al. *N Engl J Med.* 2024 Jan 25;390(4):301-313. doi: 10.1056/NEJMoa2312054. Epub 2023 Dec 12. PMID: 38084760). This article can be found and accessed at https://www.nejm.org/doi/full/10.1056/NEJMoa2312054.

An additional correspondence from the authors of the PERSEUS study provided further information and insight into treatment discontinuations in PERSEUS; this was published in *The New England Journal of Medicine* in April 2024 and can be found at https://www.nejm.org/doi/full/10.1056/NEJMc2402133. You can also read more about the PERSEUS study at http://www.clinicaltrials.gov by entering the ClinicalTrials.gov identifier for this study (NCT03710603) into the search field.

Information provided on the GRIFFIN study, mentioned earlier in this summary, was based upon the publication titled 'Addition of daratumumab to lenalidomide, bortezomib, and dexamethasone for transplantation-eligible participants with newly diagnosed multiple myeloma (GRIFFIN): final analysis of an open-label, randomised, phase 2 trial' that was published in *The Lancet Haematology* journal in September 2023. This can be found at https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026(23)00217-X/abstract.

You can also read more about the GRIFFIN study at http://www.clinicaltrials.gov by entering the ClinicalTrials.gov identifier for this study (NCT02874742) into the search field.

To read more about Black participants in the GRIFFIN study, you can find a plain language summary of publication published in *Future Oncology* in December 2022 at https://www.tandfonline.com/doi/10.2217/fon-2022-0775, or you can access the full publication, which is titled 'Post hoc analysis of daratumumab plus lenalidomide, bortezomib and dexamethasone in Black patients from final data of the GRIFFIN study,' that was published in the *British Journal of Haematology* in March 2024 at https://onlinelibrary.wiley.com/doi/epdf/10.1111/bjh.19386.

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This study was sponsored by the European Myeloma Network in collaboration with Janssen Research & Development. PS served on a scientific advisory board for Janssen Pharmaceuticals and Pfizer Pharma GMBH; served as a consultant for SkylineDx; served as an advisory board member for Bristol Myers Squibb; and served as the President of Board for Erasmus Medisch Centrum. MAD served as a consultant for Amgen, BeiGene, Bristol Myers Squibb, Celgene Corporation, GSK, Janssen Global Services, Menarini Silicon Biosystems, Regeneron Pharmaceuticals, Sanofi, and Takeda. M Boccadoro received honoraria (institution) from AbbVie, Amgen, Bristol Myers Squibb, Janssen Pharmaceuticals, Novartis, and Sanofi; received research funding from Amgen, Bristol Myers Squibb, Janssen Pharmaceuticals, Mundipharma, Novartis, and Sanofi; and served on an advisory board for GSK and Janssen Pharmaceuticals. HQ served on a scientific advisory board for AbbVie, Bristol Myers Squibb, and Janssen Pharmaceuticals; and served on an advisory board committee for GSK. M Beksac served on an advisory board for Amgen, Bristol Myers Squibb, Janssen Global Services, Sanofi Pasteur Biologics, and Takeda; and served on a speakers bureau for Janssen Global Services, Sanofi Pasteur Biologics, and Takeda. CH received honoraria from AbbVie Biotherapeutics, Amgen, Bristol Myers Squibb, Celgene, Janssen Global Services, and Pfizer. XL served as a consultant for Janssen Biotech. SM received honoraria and served on advisory boards for Amgen, Bristol Myers Squibb, GSK, Janssen Pharmaceuticals, Sanofi, and Takeda. AP served as a consultant for AbbVie, Amgen, Celgene, Janssen Biotech, Pfizer, Sanofi, and Takeda. MC served as a consultant for AbbVie, Amgen, Bristol Myers Squibb, Celgene, GSK, Janssen Biotech, Karyopharm Therapeutics, Sanofi Pasteur, and Takeda; and is an employee at IRCCS Azienda Ospedaliero-Universitaria di Bologna. A Belotti served on a scientific advisory board for Amgen, GSK, Janssen Cilag EMEA, and Pfizer. A Broijl served on an advisory board for Bristol Myers Squibb, Janssen Pharmaceuticals, and Sanofi; and provided advisory work for Amgen. FG served as a consultant for Amgen, Bristol Myers Squibb, F. Hoffmann-La Roche, Janssen Pharmaceuticals, Pfizer, Sanofi, and Takeda. RM served on an advisory board for Bristol Myers Squibb, GSK, Janssen Cilag EMEA, Janssen Pharmaceuticals, Pfizer, and Takeda; provided speaking services or speaking engagement for AbbVie, Bristol Myers Squibb, Janssen Pharmaceuticals, and Sanofi; provided internal training for Janssen Pharmaceuticals and Amgen; and served as an educational consultant for Janssen Pharmaceuticals. NWCJvdD served on an advisory board for Adaptive Biotechnologies Corporation, Amgen, Bristol Myers Squibb, F. Hoffmann-La Roche, Janssen Biotech, Novartis, Servier Pharmaceuticals, and Takeda; served

as a consultant for Pfizer and AbbVie; and received a grant/contract for clinical studies from Amgen, Bristol Myers Squibb, Janssen Biotech, and Cellectis. EK received clinical trial funding from the European Myeloma Network. FS served on advisory boards for Bristol Myers Squibb, GSK, Janssen Pharmaceuticals, Sanofi, and Takeda; served in speaking engagements for AbbVie, Bristol Myers Squibb, Fondazione Internazionale Menarini, GSK, Janssen Pharmaceuticals, Novartis Pharmaceuticals, Pfizer, Sanofi, and Takeda; and received honoraria for lectures from Amgen. ASB served on an advisory board for Bristol Myers Squibb, Gilead Sciences, Janssen Global Services, Merck Sharp & Dohme Corporation, Novartis Pharma, Sanofi, and Takeda; and served as a consultant for continuous education for Bristol Myers Squibb, Gilead Sciences, Merck Sharp & Dohme Corporation, Novartis Pharma, Sanofi, and Takeda. LR received honoraria for lectures from Amgen, Celgene, GSK, Janssen Biotech, Sanofi, and Takeda. MD served as a consultant for Bristol Myers Squibb; and served on an advisory board for, served as a speaker for, and received research grant funding from Janssen Global Services. WR received travel support from AbbVie; received honoraria (institution) for speaking for Fondation Sanofi Espoir and Janssen Biotech; received honoraria (institution) for serving on an advisory board for Bristol Myers Squibb; and received honoraria (institution) for training from Amgen. HE served as a consultant for Amgen, Bristol Myers Squibb, GSK, Janssen Global Services, Sanofi Pasteur, and Takeda. AS served as an advisory board member for Janssen Global Services. RH served as a consultant for AbbVie, Amgen, Celgene, Janssen Cilag EMEA, Novartis, and Takeda; received grants or contracts from Amgen, Bristol Myers Squibb, Celgene, Janssen Cilag EMEA, Novartis, and Takeda; and received travel support from Amgen, Bristol Myers Squibb, Celgene, Janssen Cilag EMEA, Novartis, and Takeda. TA is an employee of and holds stock or stock options in Genmab. JW and DV are employees of Johnson & Johnson. EMJvB is an employee of Janssen. VV and AS-A are employees of and hold stock or stock options in Janssen. CJdB and RC are employees of Janssen and hold stock in Johnson & Johnson. PR-O served on speakers bureaus for AbbVie, Bristol Myers Squibb, Janssen Global Services, and Regeneron Pharmaceuticals; served on advisory boards for Bristol Myers Squibb, F. Hoffmann-La Roche, GSK, Janssen Global Services, Laboratorios Pfizer, and Sanofi Pasteur; served as a steering committee member for Bristol Myers Squibb, Janssen Pharmaceuticals, and Regeneron Pharmaceuticals; served as a consultant for AbbVie and F. Hoffmann-La Roche; and received honoraria for lectures from Sanofi Pasteur. JB served as a consultant for Amgen, Celgene, Janssen Pharmaceuticals, and Sanofi-Aventis. PM served on an advisory board for AbbVie, Amgen, Celgene, GSK, Janssen Biotech, and Sanofi. PJH, EA, TS, AV, AJ, SL, and YL have no financial interests to declare. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

Competing interests disclosure

HQ served as a lead investigator for GSK. PJH served on a scientific advisory board (in which honoraria was not accepted) for Antengene, Gilead Sciences, iTeos Therapeutics, Janssen Biotech, and Pfizer. The authors have no other competing interests or relevant affiliations with any organization or entity with the subject matter or materials discussed in the manuscript apart from those disclosed.

Writing disclosure

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