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A plain language summary of the final analysis of the GRIFFIN study of daratumumab plus lenalidomide, bortezomib, and dexamethasone for people with newly diagnosed multiple myeloma

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Full author affiliations can be found at the end of this article.

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

You can find and access for a fee the original article, titled 'Addition of daratumumab to lenalidomide, bortezomib, and dexamethasone for transplantation-eligible patients with newly diagnosed multiple myeloma (GRIFFIN): final analysis of an open-label, randomised, phase 2 trial', published in *The Lancet Haematology* journal at: [https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026\(23\)00217-X/abstract](https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026(23)00217-X/abstract).

The GRIFFIN article, titled 'Daratumumab in transplant-eligible patients with newly diagnosed multiple myeloma: final analysis of clinically relevant subgroups in GRIFFIN', focusing on specific groups of participants with certain multiple myeloma characteristics or other factors that could lead to worse outcomes (based on specific disease or participant characteristics) is free to read and published in *The Blood Cancer Journal* at: <https://www.nature.com/articles/s41408-024-01088-6>.

The GRIFFIN article, titled 'Health-related quality of life in transplant-eligible patients with newly diagnosed multiple myeloma treated with daratumumab, lenalidomide, bortezomib, and dexamethasone: Patient-reported outcomes from GRIFFIN', focusing on how treatment impacted the participants' quality of life, is free to read and published in *The American Journal of Hematology* at: <https://onlinelibrary.wiley.com/doi/10.1002/ajh.27326>.

How to say (download PDF and double click sound icon to play sound)...

- **Multiple myeloma:** multiple mai-UH-low-muh
- **Daratumumab:** DAR-uh-TOOM-oo-mab
- **Lenalidomide:** leh-nuh-LI-duh-mide
- **Bortezomib:** bor-TEH-zo-mib
- **Dexamethasone:** DEK-suh-MEH-thuh-sown
- **Autologous stem cell transplant:** aw-TOL-uh-gus stem cell transplant
- **Cytogenetic:** sigh-tow-juh-NET-ik
- **Neutropenia:** noo-TRUH-pee-nee-uh
- **Lymphopenia:** lim-FOW-pee-nee-uh
- **Leukopenia:** loo-KOW-pee-nee-uh
- **Thrombocytopenia:** throm-BOH-sahy-tuh-pee-nee-uh
- **Pneumonia:** nyoo-MOH-nee-uh
- **Hypophosphatemia:** hai-POW-faa-sfuh-tee-mee-uh

Summary

What is this summary about?

This summary describes the final analysis of the GRIFFIN study. In this study, participants were newly diagnosed with a type of blood and bone marrow cancer called multiple myeloma, had never received any treatment, and were able to undergo an **autologous stem cell transplant**. The GRIFFIN study looked at adding the drug **daratumumab** (D) to a combination of standard treatments called **RvD** (lenalidomide [R], bortezomib [V], and dexamethasone [d]) during the treatment phases **induction** and **consolidation**, followed by daratumumab and lenalidomide (D-R) **maintenance**. Participants also received an autologous stem cell transplant to further help reduce multiple myeloma. The GRIFFIN study looked at



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whether **D-RVd** followed by D-R maintenance was better at killing multiple myeloma cells compared with RVd on its own followed by R maintenance on its own, and if treatments were safe. This summary also describes results from 2 other GRIFFIN publications: one that looked at participants with certain multiple myeloma characteristics or demographic factors that are associated with worse outcomes, and another that looked at how treatments impacted the participants' quality of life.

What were the results?

At the time of the final analysis of GRIFFIN, participants who were treated with D-RVd followed by D-R maintenance had very low (undetectable) levels of multiple myeloma cells and multiple myeloma markers (biological signs) and were more likely to be alive without the multiple myeloma getting worse or coming back compared with participants who received standard RVd treatment followed by R maintenance. There was also a pattern of similar benefits achieved by participants who were at risk for worse outcomes. Additionally, participants who received D-RVd treatment followed by D-R maintenance reported less pain, less fatigue (extreme tiredness), and greater improvements in their ability to conduct daily physical activities. While some side effects (unwanted or unexpected effects of treatment) were higher with D-RVd, side effects in both groups were as expected, and adding daratumumab did not reduce a participant's ability to handle treatment.

What do the results of the study mean?

Results of the GRIFFIN study showed that D-RVd treatment followed by D-R maintenance was better at treating multiple myeloma than the standard treatment of RVd followed by R maintenance in adults with a new diagnosis of multiple myeloma who were able to receive an autologous stem cell transplant, with no unexpected side effects of treatment.

Autologous stem cell transplant: This is a standard procedure for patients with multiple myeloma who are able to undergo this procedure (as determined by their age, medical history, and overall health). In this process, a high dose of chemotherapy, an anti-cancer drug, is given to kill cancer cells but may also hurt normal bone marrow cells. Therefore, the patient's bone marrow cells are replaced with healthy **stem cells** that have been collected from the patient and frozen beforehand in a process called stem cell mobilization.

Stem cells: Special cells that are found in the bone marrow and are important because they can develop into many different types of blood cells, including different types of normal white blood cells (e.g., plasma cells) as well as red blood cells and platelets (small particles in the blood that help stop bleeding).

Daratumumab: An immunotherapy used for treating multiple myeloma. Immunotherapies boost a patient's own ability to detect and kill cancer cells, including multiple myeloma cells. When daratumumab is included in a treatment plan, it is often abbreviated (D).

RVd: Combination treatment including lenalidomide (R), bortezomib (V), and dexamethasone (d) that is the current standard-of-care treatment for newly diagnosed multiple myeloma.

Induction treatment: The first treatment received for multiple myeloma, which can last around 4 months. The aim of this treatment phase is to reduce the amount of cancer cells. Induction treatment commonly includes a combination of drugs given before moving on to other treatment phases, such as autologous stem cell transplant.

Consolidation treatment: This treatment is given after autologous stem cell transplant (if received) and may be similar to the treatment plan given for induction therapy. It can last around 2 months. This treatment phase aims to kill any remaining cancer cells that may be left in the body after the transplant.

Maintenance treatment: This treatment is given once all other phases (induction/transplant/consolidation) are complete to help destroy any remaining myeloma cells and prevent the cancer from coming back. This treatment phase often lasts a longer period of time and may help to keep the benefits of treatment around for longer.

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

What is the purpose of this plain language summary?

The purpose of this plain language summary is to help you to understand the findings from recent research.

Daratumumab is used to treat the disease under study that is discussed in this summary, multiple myeloma. However, some countries may not have yet approved the use of daratumumab to treat multiple myeloma either alone or mixed with other treatments; please check with your local treating physician for more details.

Results of these studies may differ from those of other studies; therefore, 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 may help individuals with multiple myeloma, caregivers, and health care professionals (such as doctors, physician assistants, nurses, and nurse practitioners) who treat people with multiple myeloma to better understand the results of the GRIFFIN study.

Who sponsored this study?

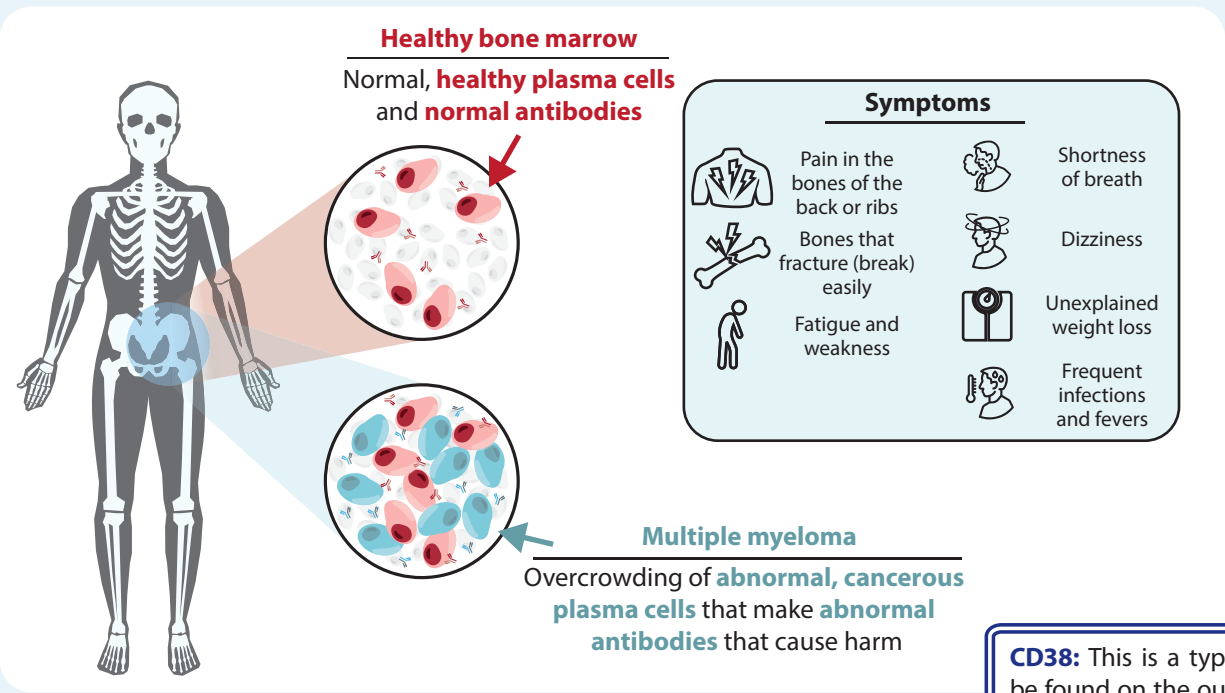
The **sponsor** of the GRIFFIN study was Janssen Oncology, which provided funding for this study. Janssen also designed and conducted this study in partnership with Alliance Foundation Trials and the Alliance Multiple Myeloma Committee.

Sponsor: A company or organization that oversees and conducts 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 form of blood and bone marrow cancer that develops in a type of white blood cell known as a plasma cell, which is found in the bone marrow (the soft, spongy tissue at the center of bones).
- Healthy plasma cells help protect the body from infection by making **antibodies**, which are a part of the body's natural defense system called the immune system.
- When a person has multiple myeloma, plasma cells are transformed into cancerous cells that grow uncontrollably and fail to produce normal, protective antibodies.
- This rapid production of cancerous cells overcrowds the bone marrow, preventing normal plasma cells from working properly and causing problems, such as bone and organ damage throughout the body, as well as an increased risk of infection (due to low numbers of white blood cells, which help to prevent infection), low numbers of red blood cells and platelets, fatigue (extreme tiredness, due to low number of red blood cells or anemia), and kidney damage (due to abnormal proteins in the body).

Antibodies: Special proteins that are normally made by the body to protect against harmful things like viruses and bacteria, which can cause infections. Antibodies can recognize, mark, and help destroy cancer cells or foreign invaders, such as bacteria and viruses. Artificial antibodies can be made in a laboratory by drug companies to fight diseases, including cancer, by targeting specific proteins on cancer cells and allowing them to destroy the cancer cells.



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.

What is daratumumab?



Daratumumab can be given by itself as a **monotherapy** or in combination with other drugs as part of a **combination treatment**, and can be infused (injected) into the vein or given as an injection under the skin

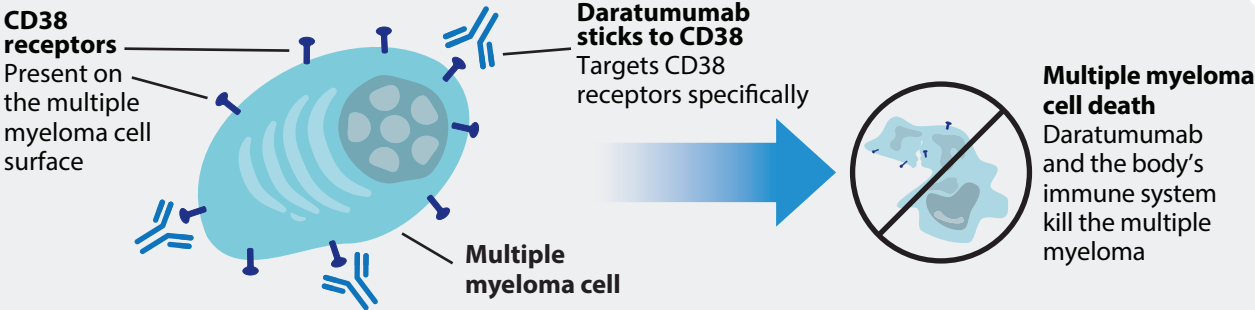


Daratumumab is an **immunotherapy** because it uses the patient's own immune system to help kill multiple myeloma cells



Daratumumab has gained **regulatory approval** for use in multiple countries **globally**

How does daratumumab work?



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

Why did researchers want to do this study?

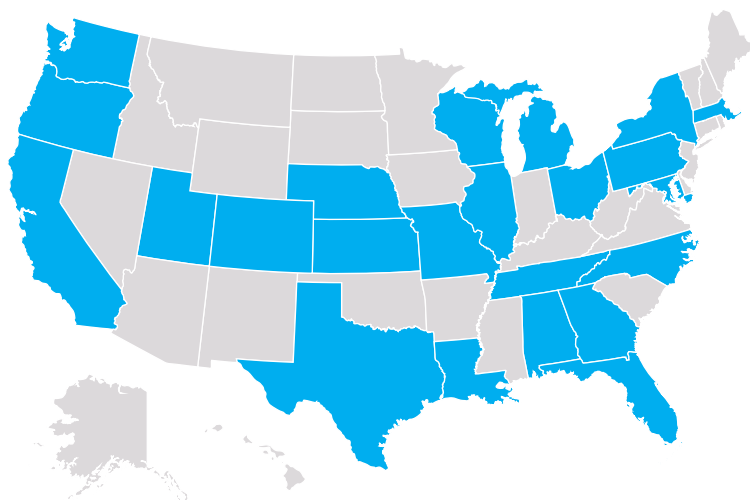
- Among patients with newly diagnosed multiple myeloma, the current standard of care is the RVd treatment plan and autologous stem cell transplant followed by R maintenance therapy. However, multiple myeloma is a difficult disease to cure, and eventually the disease will worsen, even in patients who have a good initial response to therapy.
- The GRIFFIN study enrolled participants between 20 December 2016 and 10 April 2018 from the United States who could receive an autologous stem cell transplant. The GRIFFIN study explored whether the inclusion of daratumumab in D-RVd treatment followed by D-R maintenance was better at treating newly diagnosed multiple myeloma than the current standard treatment of RVd followed by R maintenance. The researchers' main goal was to measure how well study participants' multiple myeloma responded to treatment and to assess whether deeper (or better) responses were achieved with D-RVd followed by D-R maintenance compared with RVd followed by R maintenance.
- Another study, called the PERSEUS study, was initiated upon the positive findings of the GRIFFIN study in order to obtain regulatory approval for this specific treatment plan. PERSEUS, which was larger and conducted among participants from Europe and Australia, compared the same treatment combinations (D-RVd followed by D-R maintenance versus RVd followed by R maintenance). The main goal of the PERSEUS study (primary objective of the clinical study) was to measure the period of time before a participant's multiple myeloma got worse or until the participant died after receiving D-RVd or standard RVd treatment. This was also measured in the GRIFFIN study; however, the PERSEUS study included more participants and was set up from the start to look at this outcome in a more rigorous way. The first analysis of the larger phase 3 PERSEUS study was recently reported and showed very similar results to those of the GRIFFIN study. Based on the results of the PERSEUS study, on 30 July 2024, the United States Food and Drug Administration (FDA) approved D-RVd for induction and consolidation treatment in patients who are eligible for autologous stem cell transplant with newly diagnosed multiple myeloma.

What was the goal of the GRIFFIN study?

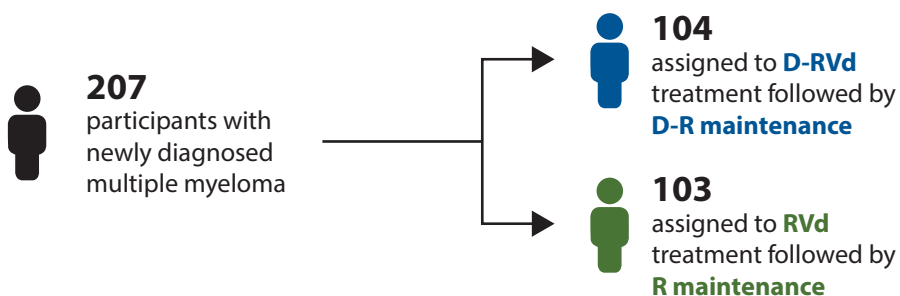
- The overall goal of the GRIFFIN study was to determine if the combination treatment of D-RVd followed by D-R maintenance worked better than treatment with RVd followed by R maintenance in participants with newly diagnosed multiple myeloma who were able to receive an autologous stem cell transplant.
- This summary provides an overview of the data from the final analysis of the GRIFFIN study, after all patients completed the study, died, or withdrew from the study.
- Previous publications have reported results from GRIFFIN at earlier times during the study period, including the main goal of the study (primary endpoint), which was to measure response to treatment after participants completed autologous stem cell transplant and consolidation treatment.
- Article references (and links) for earlier GRIFFIN publications can be found in the section at the end of this summary, which provides additional information to readers.

1. Between the age of 18–70 years
2. Recently or newly diagnosed with multiple myeloma and had not received any prior cancer treatment
3. Able to receive autologous stem cell transplant based on their general health status, age, and medical history

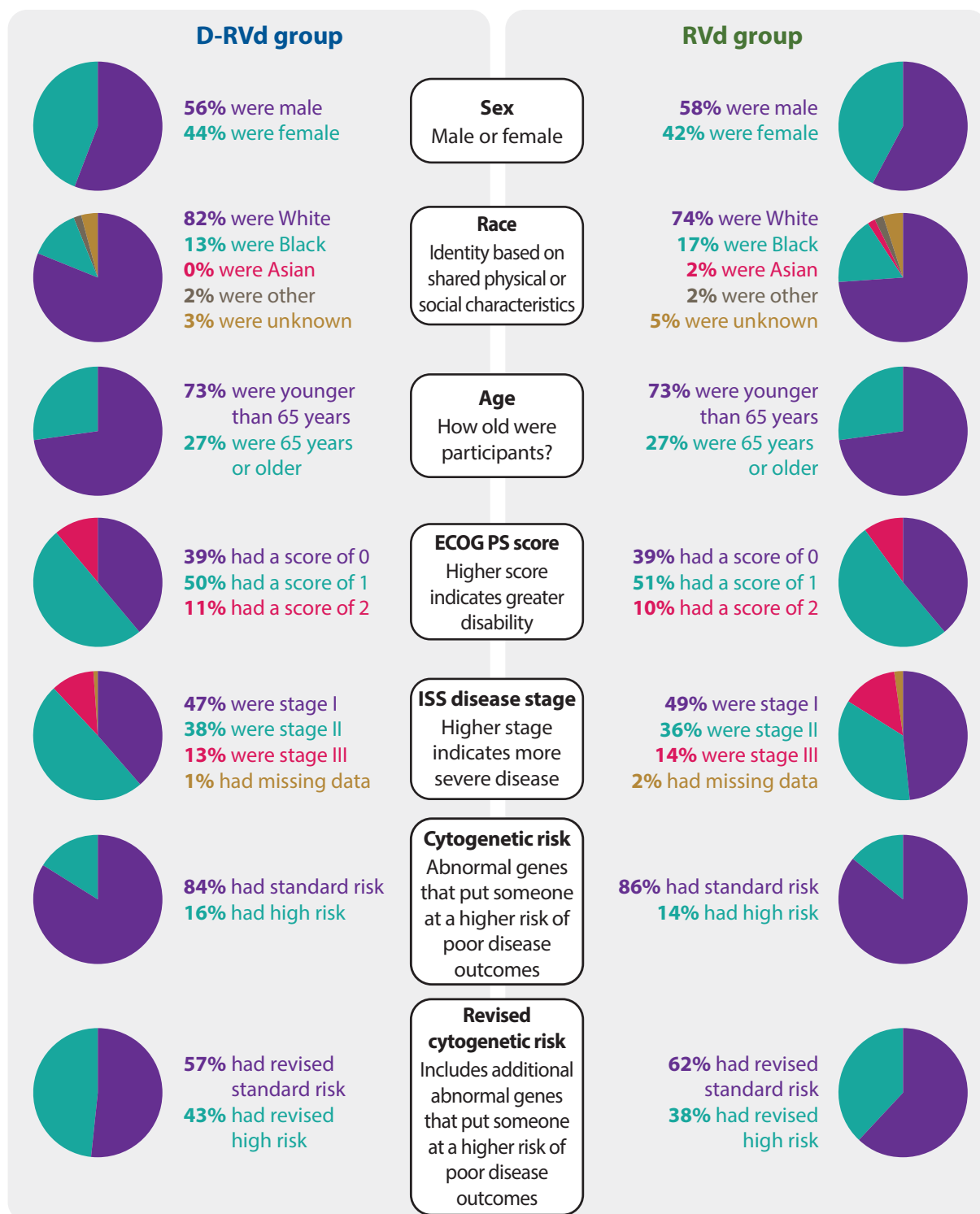
Participants in the GRIFFIN study were treated in oncology (cancer) centers, such as hospitals and clinics, in the United States



Alabama	Nebraska
California	New York
Colorado	North Carolina
Florida	Ohio
Georgia	Oregon
Illinois	Pennsylvania
Kansas	Tennessee
Louisiana	Texas
Maryland	Utah
Massachusetts	Washington
Michigan	Washington, DC
Missouri	Wisconsin



Characteristics of participants who were in the GRIFFIN study



Eastern Cooperative Oncology Group performance status (ECOG PS): The ECOG PS score describes a participant's level of overall functioning. This takes into consideration the participant's ability to care for themselves, their daily activity, and their physical ability (e.g., walking or working). A participant's performance status is graded on a scale from 0 to 4, with higher scores reflecting worse functional performance.

International Staging System (ISS): The ISS is a method used to determine how bad or how aggressive a participant's cancer is. The ISS looks at 2 markers (biological signs) of cancer within a participant's body. The higher the ISS disease stage (e.g., ISS stage III disease), the greater the risk for more severe and aggressive disease.

Cytogenetic risk: An increased chance of having worse disease outcomes and poorer response to treatment due to the presence of broken, missing, rearranged, or extra genes/chromosomes in multiple myeloma cells. A gene holds all the information and instructions for building specific proteins, and a chromosome contains multiple genes. These genetic/chromosome alterations are called 'cytogenetic abnormalities' and can cause multiple myeloma cells to divide faster and potentially become more resistant to treatment. Participants without these specific abnormal genes or abnormal chromosomes are considered as having 'standard risk' multiple myeloma, whereas participants with 1 or more of these abnormal genes or chromosomes are considered as having 'high-risk' multiple myeloma.

Revised cytogenetic risk: The presence of additional cytogenetic abnormalities according to a newer, revised definition. Participants with 'revised high-risk' multiple myeloma have 1 or more abnormal genes or abnormal chromosomes based on this new and updated definition; participants with 'revised standard risk' have none of these.

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

- In the GRIFFIN study, researchers looked at how well D-RVd followed by D-R maintenance and RVd followed by R maintenance worked among all participants who enrolled in the study (i.e., the overall study population), as well as among several groups of participants with multiple myeloma who were at risk for worse outcomes based on specific disease or participant characteristics.
- Participants with multiple myeloma who were specially grouped included:
 - » Participants who were 65 years of age or older
 - » Participants with more advanced disease stage
 - » Participants with multiple myeloma cells that carry specific cytogenetic abnormalities (also referred to as 'high-risk cytogenetic abnormalities' or 'HRCAs') associated with worse disease
 - » Participants who did not achieve a good response early in treatment
- The GRIFFIN study also enrolled a relatively large proportion of Black participants (15%) compared to many clinical studies and evaluated D-RVd followed by R maintenance versus RVd followed by R maintenance among Black and White participants.

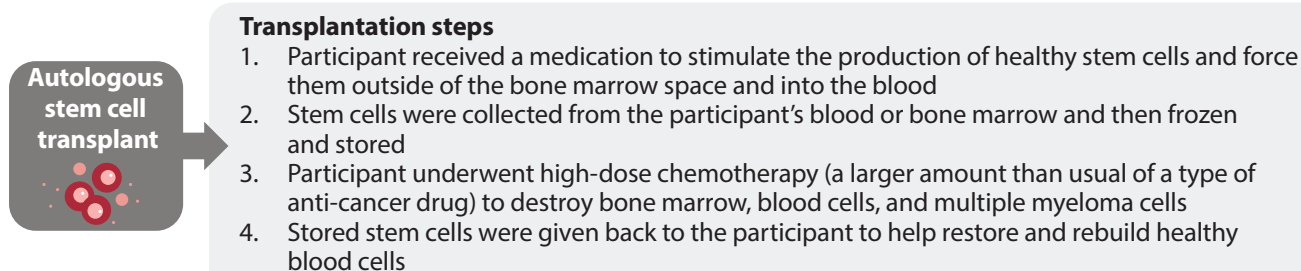
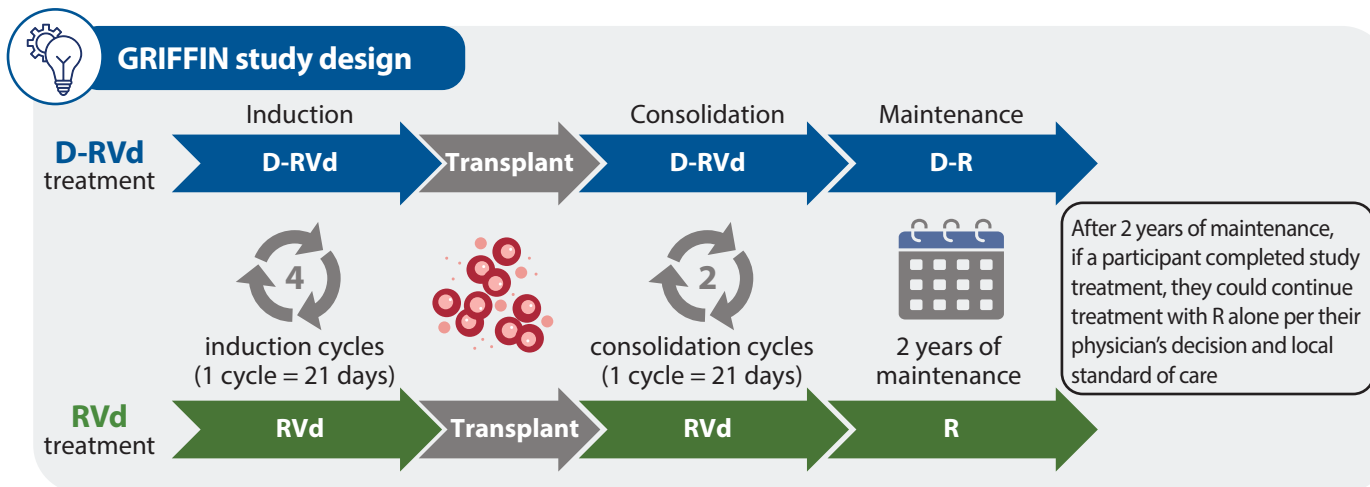
What happened in the study?

How was medicine given in the GRIFFIN study?

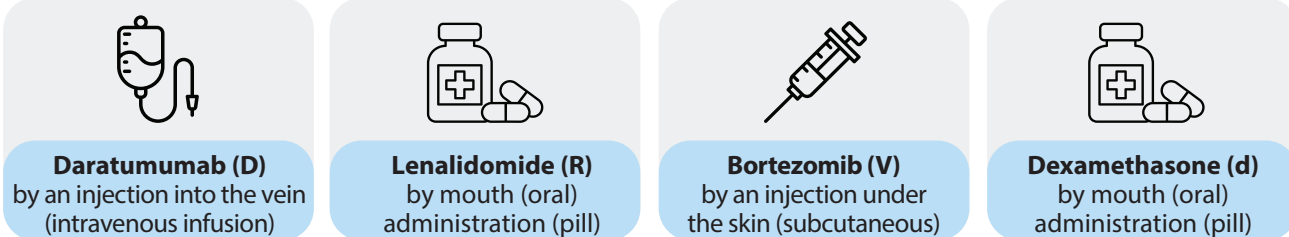
- In order to allow for a fair comparison between treatments, the GRIFFIN study was a randomized study, meaning that researchers used a computer program to randomly (i.e., by chance) select which participants received D-RVd treatment or RVd treatment. In GRIFFIN, about half of the participants received the treatment containing daratumumab (D-RVd treatment followed by D-R maintenance) and half received standard treatment alone (RVd treatment followed by R maintenance).
- The GRIFFIN study was also open label, meaning that both the participant and the doctor knew which treatment the participant was receiving.

- As shown in the study design figure, once participants were randomized, they began treatment in the study, which had 4 treatment phases:

1. D-RVd or RVd induction treatment (4 **cycles** in total)
2. Autologous stem cell transplant
3. D-RVd or RVd consolidation treatment (2 cycles in total)
4. D-R or R maintenance treatment (2 years in total)



How were treatment components given in the GRIFFIN study?



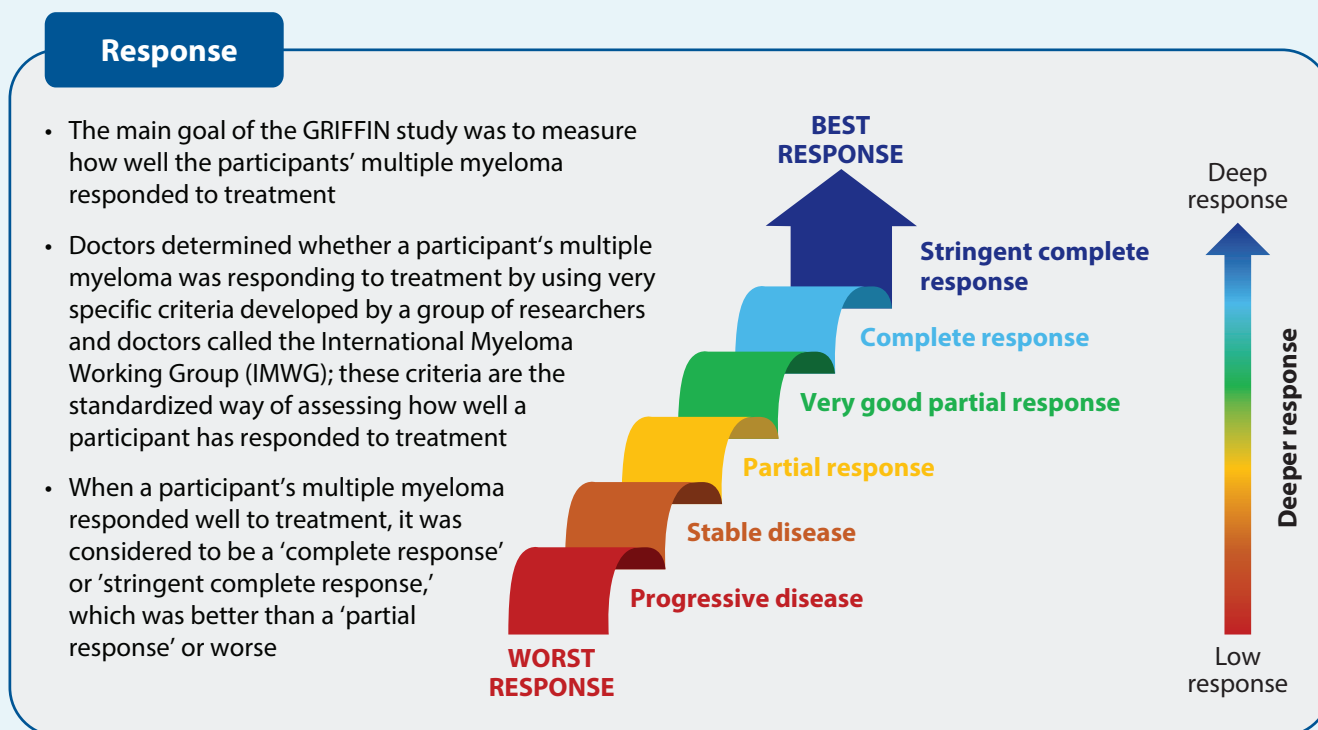
Cycle: A period or length of time (days) that defines a particular treatment schedule and defines treatment time and time spent taking a break from treatment. A cycle of treatment is usually repeated during a particular treatment phase. In the treatment of participants with multiple myeloma who undergo an autologous stem cell transplant, induction typically consists of 4 cycles before the transplant and consolidation of 2 cycles after the transplant.

What were the overall results of the GRIFFIN study?

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

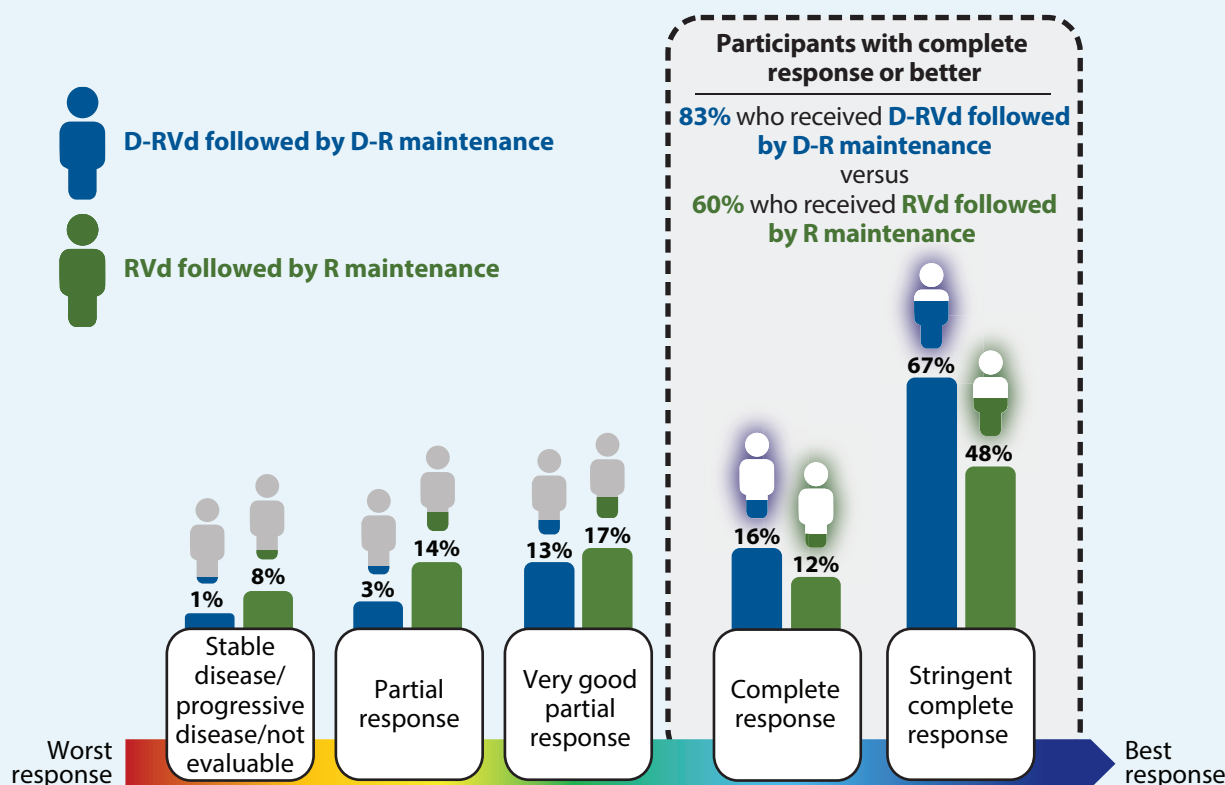
- This was the final, end-of-study GRIFFIN analysis that occurred 1 year after all participants completed their study treatment or discontinued study involvement. At the time of this analysis, a median of 49.6 months had passed since each participant was randomized to a treatment group; this means that half of the participants were followed for at least 49.6 months after they began the study.
- To find out how much the treatment worked, researchers measured the 'treatment response' of the participants' multiple myeloma. To do this, researchers used and measured abnormal markers (biomarkers) made by multiple myeloma cells in samples taken from a participant's blood, urine, and/or bone marrow.
- In addition, researchers looked at how many multiple myeloma cells were left in the participant's bone marrow to see if the multiple myeloma responded after treatment using a test called 'minimal residual disease' or 'MRD'. If a participant's bone marrow sample gave the result of 'MRD negative,' it meant that the participant had very low (undetectable) levels of multiple myeloma. A result of 'MRD positive' meant that the multiple myeloma was still found (detectable) in the participant's bone marrow.
- Researchers also measured the amount of time that a participant lived without their multiple myeloma getting worse, which is known as 'progression-free survival.'

Response results

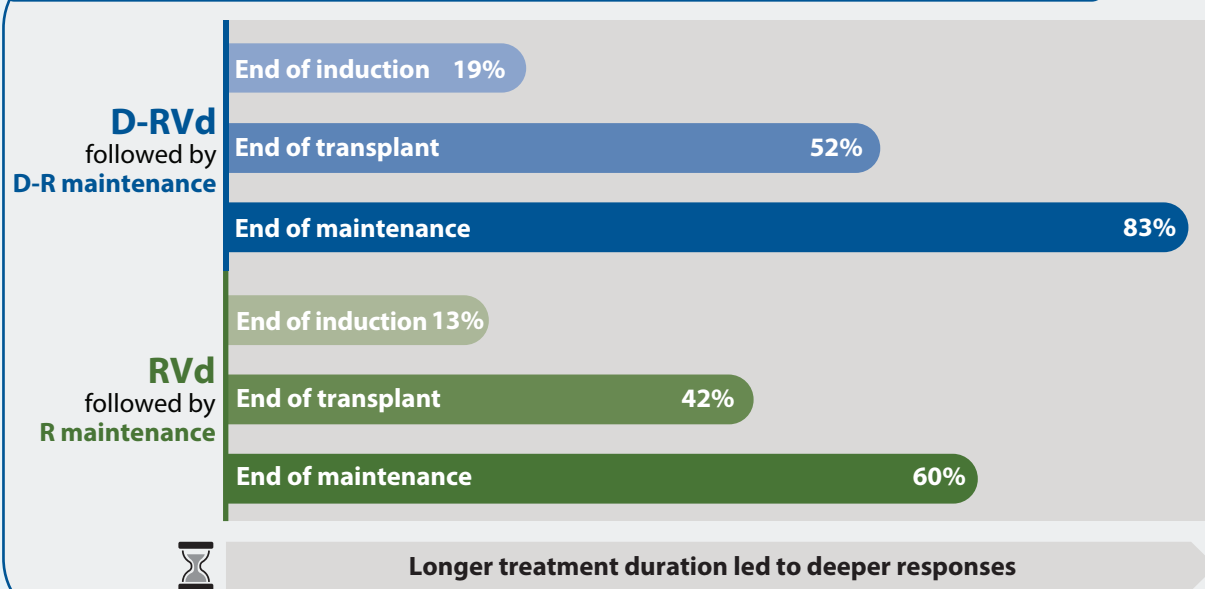


- In the GRIFFIN study, participants who received D-RVd treatment followed by D-R maintenance had a better response to treatment compared with those who received RVd treatment followed by R maintenance; this response improved over time throughout the study and lasted longer than it did for participants who received RVd followed by R maintenance.

Best response achieved among participants in the GRIFFIN study by the end of the study



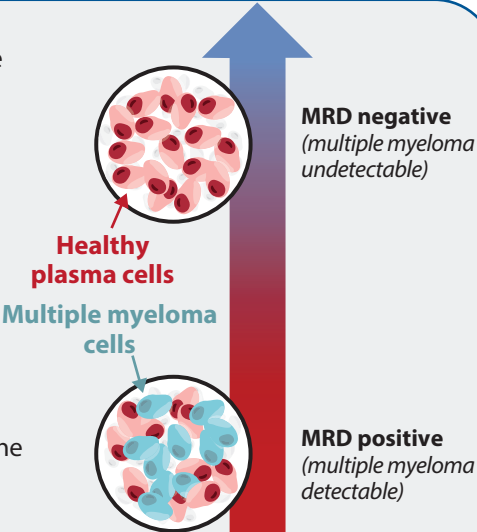
Complete response or better in participants in the GRIFFIN study over time



Minimal residual disease (MRD) results

Minimal residual disease (MRD)

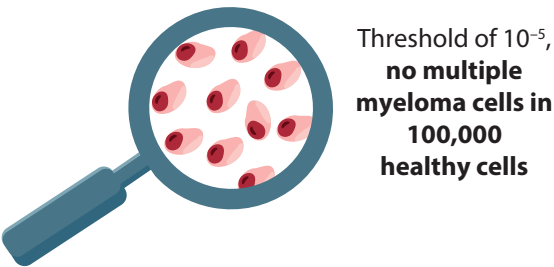
- **MRD** is used to measure whether any multiple myeloma cells are present in a participant’s bone marrow
- Participants were considered MRD negative if no multiple myeloma cells were detected in a sample of:
 - » One hundred thousand (100,000) healthy cells (called the **10⁻⁵ threshold**)or
 - » One million (1,000,000) healthy cells (called the **10⁻⁶ threshold**)
- In the GRIFFIN study, the achievement of MRD-negative status indicated that very few multiple myeloma cells were present in the bone marrow and that multiple myeloma was undetectable



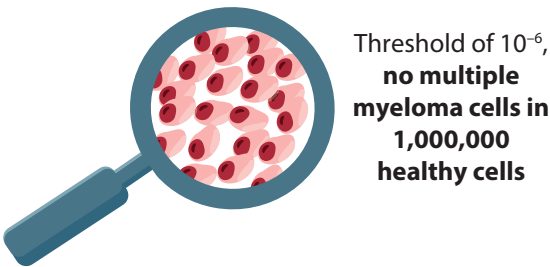
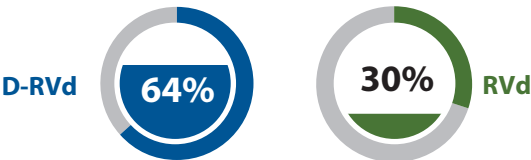
When looking at a bone marrow sample after treatment, did more participants who received D-RVd followed by D-R maintenance have undetectable multiple myeloma?

YES

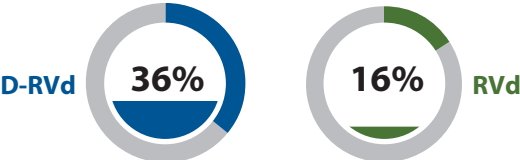
Participants who received **D-RVd followed by D-R maintenance** were more likely to have undetectable multiple myeloma (**MRD negative**) compared with those who received **RVd followed by R maintenance** at both threshold levels



Participants who were MRD negative at 10⁻⁵



Participants who were MRD negative at 10⁻⁶



Progression-free survival (PFS) results

Progression-free survival (PFS)

Researchers also measured the length of time from when a participant was randomized to a treatment to when their disease got worse (progressed) or they died. This was called '**progression-free survival**'



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

YES



After 4 years, **87%** of participants who received **D-RVd followed by D-R maintenance** compared to **70%** of participants who received **RVd followed by R maintenance** were alive and without worsening of multiple myeloma

YES

Participants who received **D-RVd followed by D-R maintenance** were **55%** less likely to die or have their multiple myeloma worsen or return compared with those who received **RVd followed by R maintenance**

D-RVd followed by D-R maintenance reduced the risk of multiple myeloma getting worse or death by

55% ↓

When the researchers looked at all participants and those at risk for worse outcomes based on specific characteristics, did **D-RVd followed by D-R maintenance** help participants live longer without their multiple myeloma getting worse compared with standard **RVd followed by R maintenance**?

All participants

YES

Among all participants enrolled, **D-RVd** reduced the risk of multiple myeloma getting worse or death by

55% ↓

Age

YES

Among participants who were 65 years of age or older, **D-RVd** reduced the risk of multiple myeloma getting worse or death by

71% ↓

ISS disease stage III

YES

Among participants with ISS disease stage III, **D-RVd** reduced the risk of multiple myeloma getting worse or death by

77% ↓

How about the participants who had genes found in multiple myeloma cells that put them at a higher risk for not responding as well to treatment or having poor outcomes?

High cytogenetic risk

YES Among participants with 1 or more of 3 specific abnormal genes, **D-RVd** reduced the risk of multiple myeloma getting worse or death by **46%** ↓

Revised high cytogenetic risk

YES Among participants with 1 or more of the 5 'revised' abnormal genes, **D-RVd** reduced the risk of multiple myeloma getting worse or death by **62%** ↓

0 HRCAs

YES Among participants with no abnormal genes, **D-RVd** reduced the risk of multiple myeloma getting worse or death by **61%** ↓

1 HRCA

YES Among participants with only 1 of the 5 abnormal genes, **D-RVd** reduced the risk of multiple myeloma getting worse or death by **81%** ↓

2 or more HRCAs

NO Among participants with 2 or more of the 5 abnormal genes, there was no benefit with **D-RVd** treatment. The number of participants in this subgroup was small; therefore, larger studies with a greater number of ultra-high-risk participants are needed to make more informed conclusions

Gain/amp(1q21)

YES Among participants with this specific gene associated with worse outcomes, **D-RVd** reduced the risk of multiple myeloma getting worse or death by **58%** ↓

Gain/amp(1q21) + 1 HRCA

YES Among participants with this specific gene and 1 other HRCA, **D-RVd** reduced the risk of multiple myeloma getting worse or death by **19%** ↓

Gain/amp(1q21) isolated

YES Among participants with this specific gene only and no other abnormal gene, **D-RVd** reduced the risk of multiple myeloma getting worse or death by **79%** ↓

How about the participants who did not respond to treatment early on in the GRIFFIN study? Could they still benefit from D-RVd followed by D-R maintenance later on?

Less than VGPR by the end of induction

YES Among participants who did not have a very good partial response (VGPR) or better to treatment by the end of induction, **D-RVd** reduced the risk of multiple myeloma getting worse or death by **71%** ↓

Not MRD negative by the end of consolidation

YES Among participants who had detectable multiple myeloma when they finished consolidation, **D-RVd** reduced the risk of multiple myeloma getting worse or death by **18%** ↓

Not MRD negative after 2 years of maintenance

NO Among participants who had detectable multiple myeloma after 2 years of maintenance, there was no benefit with **D-RVd** treatment. Additional studies are needed to make more informed conclusions

Patient-reported outcomes

- Living with multiple myeloma and going through treatment can greatly impact an individual's quality of life, including their mental health, social life, and physical ability.
- As part of the GRIFFIN study, researchers also explored the impact of receiving D-RVd followed by D-R maintenance or RVd treatment followed by R maintenance on the participants' quality of life by looking at what are called '**patient-reported outcomes**.'
- Researchers asked participants in the GRIFFIN study to complete 3 different questionnaires throughout the study:
 - » A cancer-specific questionnaire
 - » A questionnaire specific to multiple myeloma
 - » A general health-related questionnaire
- Participants were asked questions about the following:
 - » How they felt about their health overall
 - » How they felt emotionally during the study
 - » How much pain they were feeling and how tired they were (fatigue)
 - » How they were managing with everyday activities, such as carrying shopping bags, walking, cleaning the house, eating, bathing, or using the toilet
- Of note, the participants did know which treatment they were receiving, which the researchers mentioned could have impacted some of the answers given to these questionnaires.

How many participants completed the questionnaires at the end of the GRIFFIN study?

After 2 years of maintenance therapy

D-RVd

49%

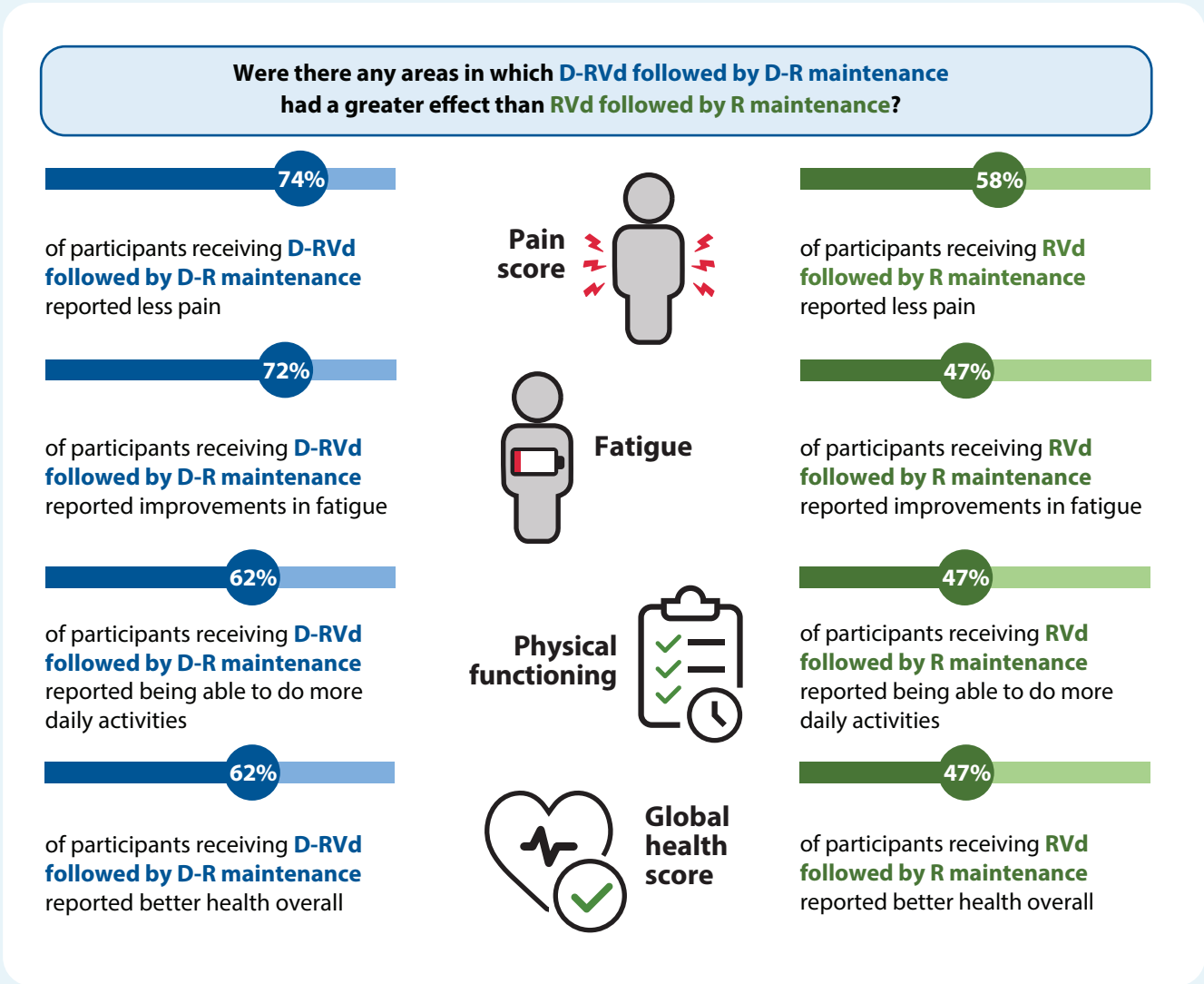
RVd

45%

What did participants have to say about their treatment during the GRIFFIN study?

Overall, after 2 years of maintenance treatment, similar meaningful improvements were reported by participants across most aspects of quality of life and satisfaction for both **D-RVd followed by D-R maintenance** and **RVd followed by R maintenance**; therefore, the addition of **daratumumab did not seem to compromise quality of life**





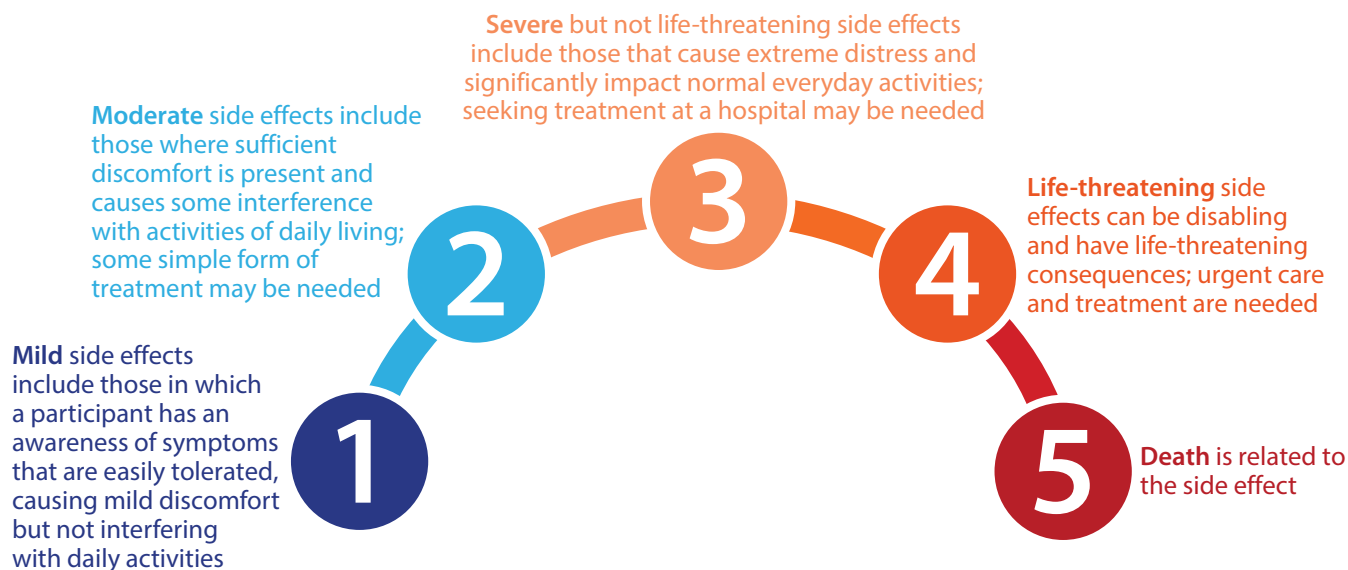
Patient-reported outcomes (PROs): In comparison to clinical assessments gathered by researchers or health care professionals, this type of information is provided directly by the participant. Using a variety of established questionnaires, which in this instance have been specially designed for participants with cancer, a participant can describe their symptoms, how happy they are with their treatment or care, and how the treatment is impacting their quality of life, including aspects of their day-to-day lives such as their physical, emotional, spiritual, or social well-being.

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

- Researchers also wanted to find out if the addition of daratumumab to RVd and R maintenance would result in more side effects (unwanted or unexpected effects of treatment that can be harmful) than RVd followed by R maintenance. To explore this, researchers looked at how common and how severe the side effects were.

SIDE EFFECTS

were measured and graded using a grading scale following these descriptions:



Overall, the frequency of side effects was similar between **D-RVd followed by D-R maintenance** and **RVd followed by R maintenance**, and there were no unexpected or new side effects with either treatment

What were the most common mild to moderate side effects reported in the GRIFFIN study?

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

All side effects were reported by participants as soon as they occurred, and participants were treated as needed and appropriately. Side effects may have been brief and were not necessarily present for the whole duration of the study



Fatigue

an extreme sense of tiredness and a lack of energy

D-RVd

65%

RVd

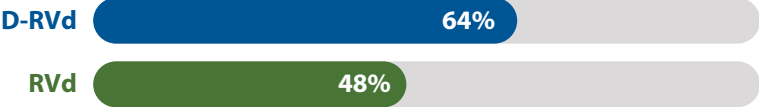
56%

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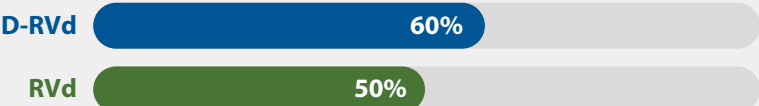
Upper respiratory tract infection

infections of the throat, nose, or sinuses

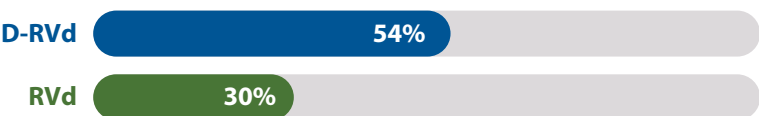


Diarrhea

frequent passing of loose, watery poo

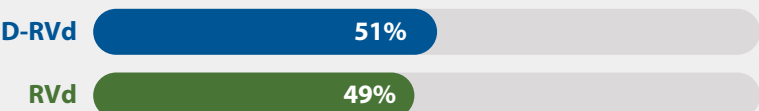


Cough



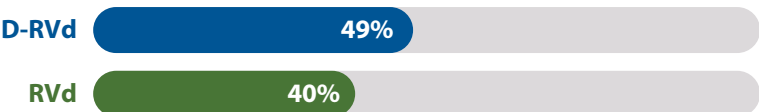
Nausea

sensation of discomfort in the stomach region accompanied by an urge to vomit



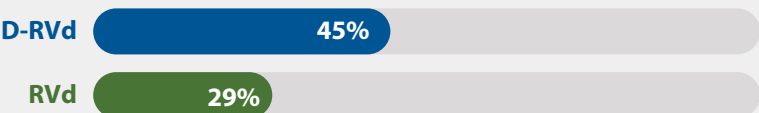
Constipation

infrequent bowel movements and difficulty in passing poo; poo is hard and dry



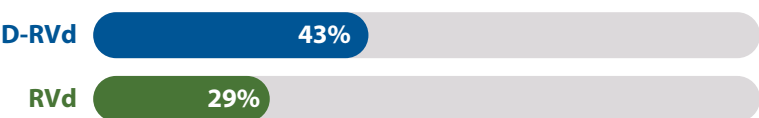
Fever (pyrexia)

an increase in body temperature above normal



Insomnia

difficulty in either falling or staying asleep that often negatively affects how someone can function in the daytime



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

YES

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

D-RVd

86%

RVd

79%

What were the most common severe or life-threatening side effects reported in the GRIFFIN study?
(Reported in more than 10% of participants in either treatment group)



Neutropenia

low number of white blood cells, specifically those called neutrophils, which usually help fight infections

D-RVd

46%

RVd

23%



Lymphopenia

low number of white blood cells, specifically those called lymphocytes, which usually help fight infections

D-RVd

23%

RVd

23%



Leukopenia

low number of white blood cells, specifically those called leukocytes, which usually help fight infections

D-RVd

17%

RVd

8%



Thrombocytopenia

low number of cell fragments called platelets, which usually help control or stop bleeding

D-RVd

16%

RVd

9%

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Pneumonia
an infection that causes inflammation in the lungs



Hypophosphatemia
low level of phosphate, an essential component needed for various body functions, in the blood



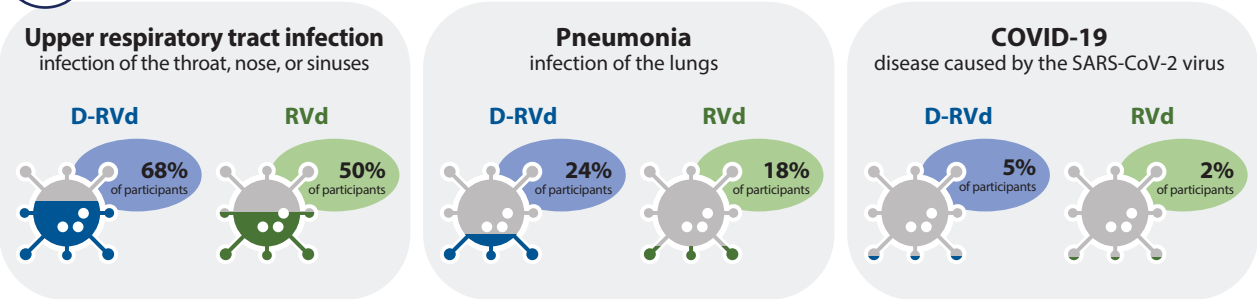
Infections are a common side effect of multiple myeloma therapy.
Did the frequency of infections of any severity differ between participants who received D-RVd followed by D-R maintenance and those who received RVd followed by R maintenance?

YES

Infections of any severity were more common in participants who received **D-RVd followed by D-R maintenance** than in those who received **RVd followed by R maintenance**



Different types of infection of any severity in the GRIFFIN study



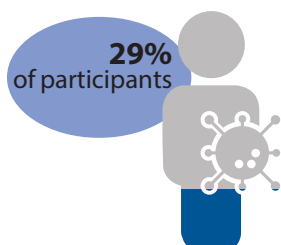
When participants reported an infection, they were treated as needed and appropriately. In the GRIFFIN study, the number of participants who stopped taking their study treatment due to an infection was similar between those in the **D-RVd followed by D-R maintenance** group (2%) and those in the **RVd followed by R maintenance** group (3%)

Were severe or life-threatening infections more common in those who received D-RVd followed by D-R maintenance than in those who received RVd followed by R maintenance?

NO

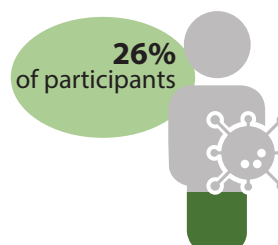
The **incidence** of severe or life-threatening infections **was similar** between participants who received **D-RVd followed by D-R maintenance** and participants who received **RVd followed by R maintenance**

D-RVd



Severe or life-threatening infections

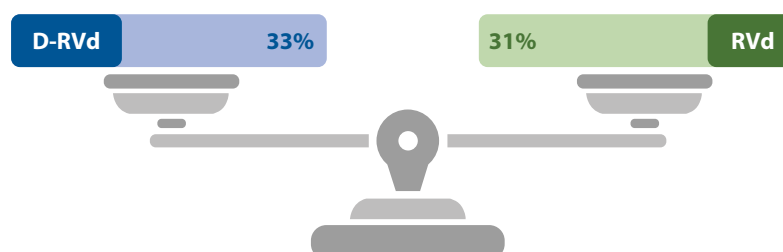
RVd



Some side effects may lead to participants stopping their treatment. Did any participants who received D-RVd followed by D-R maintenance or RVd followed by R maintenance stop taking 1 or more of their treatments due to side effects of any severity?

YES

A **similar** number of participants who received **D-RVd followed by D-R maintenance** and who received **RVd followed by R maintenance** stopped taking 1 or more of their treatments due to side effects of any severity



In the **GRIFFIN** study, did any participants die due to side effects following D-RVd or RVd treatment?



YES
1 participant from each treatment group died due to a side effect (bronchopneumonia in the **D-RVd** group, and an unknown cause in the **RVd** group)

Were other side effects reported among participants in the GRIFFIN study who received daratumumab?

- Sometimes, patients who receive daratumumab can experience unwanted side effects known as infusion-related side effects, which occur as they are receiving daratumumab or some time afterwards.
- Although infusion-related side effects are often mild in severity, participants in the GRIFFIN study who were randomized to receive daratumumab also received some specific medications to take before and after receiving daratumumab to help reduce the frequency or severity of these side effects.

In the GRIFFIN study, how many participants who received **D-RVd followed by D-R maintenance** had an infusion-related side effect?



49%

of participants who received D-RVd followed by D-R maintenance had infusion-related side effects, most of which were generally mild

What impact did daratumumab have on autologous stem cell transplant in GRIFFIN?

- During an autologous stem cell transplant, stem cells are collected, frozen, thawed (unfrozen), and then given back later to the participant after they have received a large dose of an anti-cancer drug, which is used to kill all the cancer cells in the bone marrow. A stem cell transplant can be called successful when all the normal blood cells in the body return to normal levels, which can take several weeks.
- Detailed information on stem cell transplant success in GRIFFIN was previously published.
 - » Participants in the GRIFFIN study who received D-RVd had a slightly lower amount of stem cells collected compared to participants who received RVd treatment alone, but participants in the D-RVd group still collected more than enough stem cells to do the transplant, which means that treatment with D-RVd did not have any harmful effect on the ability to collect stem cells.
 - » Participants who received D-RVd also recovered and got better within a similar amount of time as participants who received RVd treatment, which means that despite the slightly lower amount of stem cells collected, treatment with D-RVd led to a similar success rate of stem cell transplant compared to RVd.

What were the main findings of the GRIFFIN study?

- After an average of more than 4 years, participants who received treatment with D-RVd followed by D-R maintenance had a better response compared with participants who received RVd treatment followed by R maintenance. Importantly, participants who received D-RVd treatment followed by D-R maintenance were 55% less likely to die or have their multiple myeloma worsen compared with those who received RVd treatment followed by R maintenance.
- Participants with specific characteristics associated with worse outcomes (older age, advanced disease stage, abnormal genes, and did not respond early to treatment) also seemed to benefit from D-RVd treatment followed by D-R maintenance, with most groups having a lower chance of multiple myeloma progression than those receiving RVd treatment followed by R maintenance. Some

groups did not seem to experience a benefit; however, the number of participants in these groups was small, so more studies with a greater number of participants are needed to make clear conclusions for these groups.

- Participants receiving either D-RVd followed by D-R maintenance or RVd followed by R maintenance felt better with their treatment, reporting improvements in multiple aspects of their day-to-day lives and concluding that the addition of daratumumab to the current standard of care treatment did not seem to compromise their overall quality of life. Participants receiving D-RVd treatment followed by D-R maintenance reported greater improvements than those receiving RVd treatment followed by R maintenance in certain areas, including pain, fatigue, physical functioning, and overall health.
- In the GRIFFIN study, there were no new or unexpected safety concerns. More participants who received D-RVd followed by D-R maintenance had infections compared to participants who received RVd followed by R maintenance. However, the number of participants who stopped taking their treatment because of side effects was similar in both treatment groups, suggesting participants could tolerate the addition of daratumumab.
- Overall, these results support the use of D-RVd treatment followed by D-R maintenance as a new daratumumab-based treatment option for individuals with transplant-eligible newly diagnosed multiple myeloma.

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

This plain language summary covers information from 3 different GRIFFIN articles, for which the full citations are provided below:

Voorhees PM, Sborov DW, Laubach J, Kaufman JL, Reeves B, Rodriguez C, Chari A, Silbermann R, Costa LJ, Anderson LD Jr, Nathwani N, Shah N, Bumma N, Efebera YA, Holstein SA, Costello C, Jakubowiak A, Wildes TM, Orlowski RZ, Shain KH, Cowan AJ, Dinner S, Pei H, Cortoos A, Patel S, Lin TS, Usmani SZ, Richardson PG. Addition of daratumumab to lenalidomide, bortezomib, and dexamethasone for transplantation-eligible patients with newly diagnosed multiple myeloma (GRIFFIN): final analysis of an open-label, randomised, phase 2 trial. *Lancet Haematol*. 2023 Oct;10(10):e825-e837. doi: 10.1016/S2352-3026(23)00217-X. Epub 2023 Sep 11. PMID: 37708911.

- This is an original article of the final analysis of the GRIFFIN study, written by Voorhees and colleagues, published in *The Lancet Haematology* in October 2023, and can be found and accessed for a fee at: [https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026\(23\)00217-X/abstract](https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026(23)00217-X/abstract).

Chari A, Kaufman JL, Laubach J, Sborov DW, Reeves B, Rodriguez C, Silbermann R, Costa LJ, Anderson LD Jr, Nathwani N, Shah N, Bumma N, Holstein SA, Costello C, Jakubowiak A, Wildes TM, Orlowski RZ, Shain KH, Cowan AJ, Pei H, Cortoos A, Patel S, Lin TS, Voorhees PM, Usmani SZ, Richardson PG. Daratumumab in transplant-eligible patients with newly diagnosed multiple myeloma: final analysis of clinically relevant subgroups in GRIFFIN. *Blood Cancer J*. 2024 Jul 8;14(1):107. doi: 10.1038/s41408-024-01088-6. PMID: 38977707; PMCID: PMC11231363.

- This is an article focusing on specific subgroups of GRIFFIN participants who were at a higher risk of poor response or aggressive disease; this was written by Chari and colleagues and published in *The Blood Cancer Journal* in July 2024. This can be accessed and read without any fee at: <https://www.nature.com/articles/s41408-024-01088-6>.

Silbermann R, Laubach J, Kaufman JL, Sborov DW, Reeves B, Rodriguez C, Chari A, Costa LJ, Anderson LD Jr, Nathwani N, Shah N, Bumma N, Holstein SA, Costello C, Jakubowiak A, Orlowski RZ, Shain KH, Cowan AJ, Gries KS, Pei H, Cortoos A, Patel S, Lin TS, Voorhees PM, Usmani SZ, Richardson PG. Health-related quality of life in transplant-eligible patients with newly diagnosed multiple myeloma treated with daratumumab, lenalidomide, bortezomib, and dexamethasone: Patient-reported outcomes from GRIFFIN. *Am J Hematol*. 2024 Jul;99(7):1257-1268. doi: 10.1002/ajh.27326. Epub 2024 Apr 15. PMID: 38622840.

- This last article focuses on the patient-reported outcomes of participants in the GRIFFIN study; this was written by Silbermann and colleagues and was published in *The American Journal of Hematology* in April 2024. This can be accessed and read for free at: <https://onlinelibrary.wiley.com/doi/10.1002/ajh.27326>.

Additional information relating to the GRIFFIN study is also available. The primary analysis of GRIFFIN, titled 'Daratumumab, lenalidomide, bortezomib, and dexamethasone for transplant-eligible newly diagnosed multiple myeloma: the GRIFFIN trial,' was written by Voorhees and colleagues and published in *Blood* in August 2020 and can be freely accessed at: <https://doi.org/10.1182/blood.2020005288>. An article focusing on the outcomes of Black participants from the GRIFFIN study, titled 'Daratumumab plus lenalidomide/bortezomib/dexamethasone in Black patients with transplant-eligible newly diagnosed multiple myeloma in GRIFFIN,' was written by Nooka and colleagues, published in *The Blood Cancer Journal* in April 2022, and can be found free to access and read at: <https://www.nature.com/articles/s41408-022-00653-1>. A plain language summary of this article was also written by Nooka and colleagues and published in *Future Oncology* in February 2023. This can be accessed and read for free at: <https://www.tandfonline.com/doi/10.2217/fon-2022-0775>.

Additionally, information on stem cell mobilization and feasibility of ASCT can be found in the primary GRIFFIN analysis (mentioned above) as well as in another detailed publication, titled 'Stem Cell Mobilization Yields with Daratumumab- and Lenalidomide-Containing Quadruplet Induction Therapy in Newly Diagnosed Multiple Myeloma: Findings from the MASTER and GRIFFIN Trials,' written by Chhabra and colleagues, published in *Transplantation and Cellular Therapy* in March 2023, and can be found free to read at: <https://doi.org/10.1016/j.jtct.2022.11.029>. Furthermore, a final update of Black participants in the GRIFFIN study, titled 'Post hoc analysis of daratumumab plus lenalidomide, bortezomib and dexamethasone in Black patients from final data of the GRIFFIN study,' was recently written by Nooka and colleagues and published in *The British Journal of Haematology* in March 2024. This can be found free to access and read at: <https://onlinelibrary.wiley.com/doi/10.1111/bjh.19386>.

You can also read more about the GRIFFIN study, which enrolled participants between December 2016 and April 2018, at <http://www.clinicaltrials.gov> by entering the ClinicalTrials.gov Identifier for this study (NCT02874742) into the search field.

The GRIFFIN study protocol and all amendments were approved by the appropriate institutional review boards/independent ethics committees at each participating study site. Additionally, all participants gave written informed consent to participate in this study.

Information provided on the PERSEUS study, mentioned earlier in this summary, was based on the publication titled 'Daratumumab, bortezomib, lenalidomide, and dexamethasone for multiple myeloma' that was written by Sonneveld and colleagues and published in *The New England Journal of Medicine* in January 2024. This can be accessed and read for free at: <https://www.nejm.org/doi/full/10.1056/NEJMoa2312054>. A plain language summary of the first results from the PERSEUS study was also written by Sonneveld and colleagues and published in *Future Oncology* in September 2024 and can be accessed and read for free at: <https://www.tandfonline.com/doi/full/10.1080/14796694.2024.2394323>.

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