Long-Term Outcomes With Daratumumab, Bortezomib, Lenalidomide, and Dexamethasone (Dara-VRd) Versus VRd in Transplant-Eligible Newly Diagnosed Multiple Myeloma in the Phase 3 PERSEUS Study

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WHAT DO THESE RESULTS MEAN?

In the PERSEUS/EMN017 study, the addition of **daratumumab** to standard induction, consolidation, and maintenance therapy helped more transplant-eligible patients with multiple myeloma (MM) achieve **deeper responses** and remain free of detectable cancer cells in the bone marrow for longer than standard treatment alone. After almost 7 years of follow-up, these **deeper and longer-lasting responses** were associated with a lower risk of the disease worsening and allowed patients to **live longer without their MM getting worse**, supporting the potential for long-term disease control in some patients with MM

▶ See glossary below for definitions of key terms

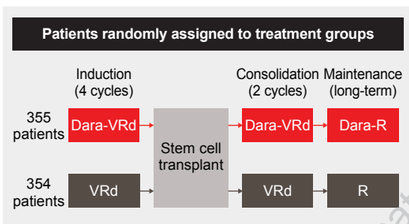
WHAT WAS THE PURPOSE OF THIS STUDY?

- Researchers wanted to see if adding daratumumab to standard induction, consolidation, and maintenance therapy provided a benefit for patients with newly diagnosed MM who could undergo a stem cell transplant

WHO WAS IN THE STUDY AND HOW WAS IT CARRIED OUT?

- The PERSEUS/EMN017 study (NCT03710603) was conducted by randomly assigning 709 transplant-eligible patients with newly diagnosed MM to receive induction and consolidation therapy with bortezomib, lenalidomide, and dexamethasone followed by lenalidomide maintenance (VRd/R), or daratumumab plus bortezomib, lenalidomide, and dexamethasone followed by daratumumab plus lenalidomide maintenance (Dara-VRd/Dara-R)

Patients 18–70 years of age who had a new diagnosis of MM and were considered able to undergo a stem cell transplant



Primary study assessment was the length of time until the return, growth, or spread of MM or the patient died

WHAT WERE THE RESULTS?

After almost 7 years of follow-up, patients who received Dara-VRd/Dara-R had deeper and more durable responses, as cancer cells could not be detected by very sensitive minimal residual disease (MRD) testing, compared with patients who received VRd/R. As a result, patients who received Dara-VRd/Dara-R lived longer without their MM getting worse

Figure 1: No cancer cells detected in the bone marrow (MRD negativity with complete response or better)

More patients who received Dara-VRd/Dara-R achieved complete response or better and had **no cancer cells detected in their bone marrow** by very sensitive MRD testing, suggesting deeper responses compared with VRd/R

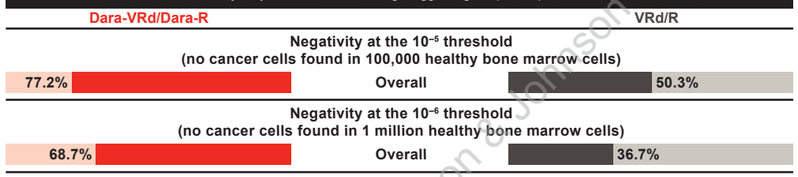


Figure 2: Continued control of MM over time (durable MRD negativity with complete response or better)

Some patients had MRD negativity that lasted for up to 3 years. In this study, more patients who received Dara-VRd/Dara-R achieved complete response or better and had **no cancer cells detected in their bone marrow for 1, 2, and 3 years**, suggesting more durable responses compared with VRd/R

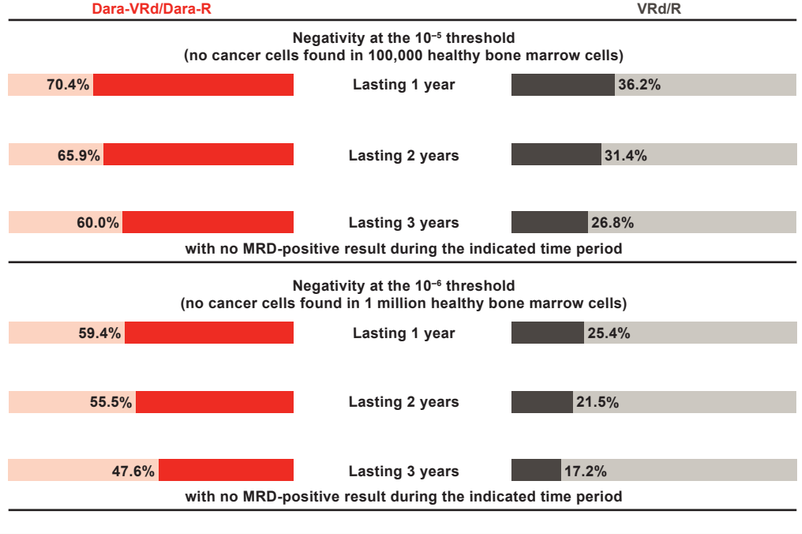


Figure 3: Ability to stop daratumumab maintenance in patients with continued control of MM over time

In total, almost 3 out of 4 patients (**73%**) who completed at least 2 years of maintenance with Dara-R and had achieved durable MRD negativity lasting at least 1 year with a complete response or better were able to stop daratumumab treatment per study criteria — **73%**

Until now, almost 3 out of 4 patients (**74%**) who had stopped daratumumab maintenance kept their response without restarting daratumumab, indicating **daratumumab maintenance can be stopped in patients with continued control of MM** — **74%**

Figure 4: Longer time until MM got worse (progression-free survival)

After almost 7 years of follow-up, Dara-VRd/Dara-R **lowered the risk of MM getting worse or death during the study by 65%**, with patients generally living longer before their MM worsened, compared with VRd/R — **Lowered risk by 65%**

Figure 5: Longer time until patients died (overall survival)

Dara-VRd/Dara-R **lowered the risk of death during the study by 43%** compared with VRd/R. However, because many patients were still alive at the time of this analysis, these long-term survival results are not yet final — **Lowered risk by 43%**

There were no new side effects or safety concerns with the daratumumab combination

Glossary of terms

Complete response	Standard signs of MM are gone from the blood and bone marrow after treatment	**Maintenance therapy**	Long-term treatment to help prevent cancer from returning after it has disappeared following induction therapy, stem cell transplant, and consolidation therapy	**Stem cell transplant**	In this procedure, a patient's own healthy stem cells are collected from their blood or bone marrow and stored safely; these cells can make all the different types of blood cells (such as white blood cells, red blood cells, and platelets). After the patient receives high-dose chemotherapy to kill as many remaining cancer cells as possible, the stored stem cells are returned to the patient's body to help the bone marrow recover and start making healthy blood cells again
Induction therapy	First treatment in a multiphase cancer regimen, intended to reduce the number of cancer cells	**Progression-free survival**	Length of time since treatment started that patients have lived without their MM getting worse (return, growth, or spread of MM) or until the patient dies	**Minimal residual disease**	After treatment, there is sometimes a small number of cancer cells still left in the patient's bone marrow that can be detected with very sensitive tests; these remaining cancer cells could potentially cause the disease to come back. "Overall" MRD negativity refers to achievement of MRD negativity at any time during the study • Negativity at the 10^{-5} threshold: No cancer cells found in a sample of 100,000 healthy bone marrow cells • Negativity at the 10^{-6} threshold: No cancer cells found in a sample of 1 million healthy bone marrow cells
Overall survival	Length of time the patient is alive after starting treatment	**Consolidation therapy**	A follow-up treatment, occurring after induction therapy and stem cell transplant, meant to kill any cancer cells left in the body	**Durable minimal residual disease negativity**	No cancer cells found below a certain threshold (in a sample of 100,000 [10^{-5} threshold] or 1 million [10^{-6} threshold] healthy bone marrow cells) at 2 consecutive tests for MRD that were separated by the indicated time period, with no positive MRD test result in between. This is also sometimes referred to as "sustained minimal residual disease negativity"

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***AI was used in the preparation of these summaries.**