Dostarlimab Plus Chemotherapy Extends Progression-Free Survival in Advanced Endometrial Cancer

Written by The Life Science Feed Editorial Team · Published 27 August 2026 · Edited by William Lopes

Endometrial cancer is a common gynecologic malignancy, and treatment options for advanced or recurrent disease have historically been limited. The RUBY trial investigated the efficacy and safety of adding the immune-checkpoint inhibitor dostarlimab to standard chemotherapy for these patients. The findings suggest a notable improvement in progression-free survival, especially for a specific patient subgroup.

KEY TAKEAWAYS

- The Pivot: Adding dostarlimab to chemotherapy significantly improved progression-free survival in primary advanced or recurrent endometrial cancer.
- The Data: In dMMR-MSI-H tumors, 24-month progression-free survival was 61.4% with dostarlimab vs. 15.7% with placebo (HR 0.28).
- The Action: Consider dMMR/MSI-H status in advanced endometrial cancer to identify patients who may derive substantial benefit from dostarlimab-chemotherapy combination therapy.

Background on Endometrial Cancer and Immunotherapy

Endometrial cancer is the most common gynecologic cancer in many developed countries, with incidence rates rising. While early-stage disease is often curable with surgery, prognosis for primary advanced (stage III or IV) or recurrent endometrial cancer remains challenging. Standard first-line treatment typically involves platinum-based chemotherapy, often carboplatin and paclitaxel. Immune-checkpoint inhibitors, such as dostarlimab, which targets the programmed cell death 1 (PD-1) receptor, have shown promise in various solid tumors by enhancing the body's immune response against cancer cells. The combination of chemotherapy and immunotherapy is hypothesized to have synergistic effects, potentially improving outcomes beyond either modality alone in endometrial cancer 1.

RUBY Trial Design and Methodology

The RUBY trial (NCT03981796) was a global, phase 3, double-blind, randomized, placebo-controlled study. It enrolled patients with primary advanced stage III or IV or first recurrent endometrial cancer. Participants were randomly assigned in a 1:1 ratio to receive either dostarlimab (500 mg) or placebo, administered concurrently with carboplatin (area under the concentration-time curve, 5 mg per milliliter per minute) and paclitaxel (175 mg per square meter of body-surface area) every 3 weeks for six cycles. Following this initial phase, patients continued with either dostarlimab (1000 mg) or placebo every 6 weeks for up to 3 years. The primary endpoints were progression-free survival (PFS), as assessed by the

investigator according to RECIST version 1.1, and overall survival (OS). Safety profiles were also rigorously evaluated throughout the study 1.

Significant Progression-Free Survival Benefit

A total of 494 patients were randomized in the study. A key finding was the identification of a subgroup with mismatch repair-deficient (dMMR) or microsatellite instability-high (MSI-H) tumors, which constituted 118 (23.9%) of the randomized patients. In this dMMR-MSI-H population, the estimated progression-free survival at 24 months was notably higher in the dostarlimab group at 61.4% (95% confidence interval [CI], 46.3 to 73.4) compared to 15.7% (95% CI, 7.2 to 27.0) in the placebo group. This translated to a hazard ratio for progression or death of 0.28 (95% CI, 0.16 to 0.50; P1.

Outcomes in the Overall Patient Population

Beyond the dMMR-MSI-H subgroup, the study also demonstrated a significant benefit in the overall patient population. At 24 months, progression-free survival was 36.1% (95% CI, 29.3 to 42.9) in the dostarlimab group, versus 18.1% (95% CI, 13.0 to 23.9) in the placebo group. The hazard ratio for progression or death in the overall population was 0.64 (95% CI, 0.51 to 0.80; P1.

Safety Profile and Adverse Events

The safety analysis revealed that the most common adverse events that occurred or worsened during treatment in both groups included nausea (53.9% in the dostarlimab group vs. 45.9% in the placebo group), alopecia (53.5% vs. 50.0%), and fatigue (51.9% vs. 54.5%). While these common events were generally comparable, severe and serious adverse events were reported more frequently in the dostarlimab group than in the placebo group. Clinicians should be aware of the potential for increased adverse events when combining dostarlimab with chemotherapy 1.

Clinical Implications for Practice Today

The RUBY trial results suggest that adding dostarlimab to carboplatin-paclitaxel chemotherapy can significantly improve progression-free survival for patients with primary advanced or recurrent endometrial cancer. The pronounced benefit observed in the dMMR-MSI-H population underscores the importance of molecular testing to identify patients most likely to respond to this immunotherapy approach. This finding supports the integration of PD-1 inhibition into the first-line treatment paradigm for this specific subgroup.

Why this matters for clinical practice today: This study provides compelling evidence for incorporating dostarlimab into the initial treatment strategy for advanced or recurrent endometrial cancer, particularly for patients with dMMR-MSI-H tumors. For clinicians, this means that comprehensive molecular profiling, including mismatch repair status, should become a standard part of the diagnostic workup for these patients. Identifying dMMR-MSI-H status early can guide treatment decisions, potentially leading to significantly improved progression-free survival and offering a new, effective therapeutic option where historical outcomes have been poor. While the overall survival data are still maturing, the substantial PFS benefit is a critical step forward in managing this challenging disease.

Limitations and Future Research Directions

While the RUBY trial demonstrated significant benefits, some limitations should be considered. The overall survival data, though promising, were not yet mature at the time of this publication, and longer follow-up is needed to fully

assess the long-term impact on survival. Additionally, while the dMMR-MSI-H subgroup showed a dramatic benefit, further research is warranted to identify other biomarkers that might predict response to dostarlimab in the mismatch repair-proficient population. Future studies could also explore the optimal duration of immunotherapy and investigate potential combinations with other agents to further enhance efficacy and manage adverse events 1.

EDITORIAL & AI STANDARDS

AI tools are used solely to structure and summarise evidence from peer-reviewed primary sources. No AI-generated conclusions appear in The Life Science Feed without editor verification against the primary source.

REFERENCES

1. 1. Mirza MR, Chase DM, Slomovitz BM, et al. Dostarlimab for Primary Advanced or Recurrent Endometrial Cancer. N Engl J Med. 2023;388(23):2145-2158. doi:10.1056/NEJMoa2216334

LICENCE & RIGHTS

MEDICAL DISCLAIMER

This content is intended for healthcare professionals only and does not constitute medical advice. Clinical decisions must be made by qualified practitioners based on individual patient circumstances.

FOLLOW THE LIFE SCIENCE FEED

Instagram @lifesciencefeed **LinkedIn** linkedin.com/company/thelifesciencefeed

thelifesciencefeed.com