NICE National Institute for Health and Care Excellence

NICE guidance

Dostarlimab with platinum-containing chemotherapy for treating primary advanced or recurrent endometrial cancer with microsatellite stability or mismatch repair proficiency

Technology appraisal guidance
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Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

1 Recommendations

1.1 Dostarlimab plus platinum-containing chemotherapy can be used as an option to treat primary advanced or recurrent endometrial cancer with microsatellite stability (MSS) or mismatch repair proficiency (MMRp) in adults when systemic treatment is suitable.

Dostarlimab plus platinum-containing chemotherapy can only be used if the company provides it according to the commercial arrangement.

1.2 This recommendation is not intended to affect treatment with dostarlimab plus platinum-containing chemotherapy that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS healthcare professional consider it appropriate to stop.

What this means in practice

Dostarlimab plus platinum-containing chemotherapy must be funded in the NHS in England for the condition and population in the recommendations, if it is considered the most suitable treatment option. It must be funded in England within 90 days of final publication of this guidance.

There is enough evidence to show that dostarlimab plus platinum-containing chemotherapy provides benefits and value for money, so it can be used routinely across the NHS in this population.

NICE has produced tools and resources to support the implementation of this guidance.

Why the committee made these recommendations

Usual treatment for primary advanced or recurrent endometrial cancer with MSS or MMRp is platinum-containing chemotherapy (for example, carboplatin and paclitaxel).

Evidence from an ongoing clinical trial suggests that dostarlimab plus carboplatin and paclitaxel may increase the time before a person's cancer gets worse more than placebo plus carboplatin and paclitaxel. It is unclear whether adding dostarlimab to usual treatment increases how long people live.

There are also uncertainties in the economic model. But the cost-effectiveness estimates for dostarlimab plus platinum-containing chemotherapy are within the range that NICE considers an acceptable use of NHS resources. So, it can be used.

2 Information about dostarlimab

Marketing authorisation indication

2.1 Dostarlimab (Jemperli, GlaxoSmithKline) is indicated 'in combination with platinum-containing chemotherapy for the treatment of adult patients with primary advanced or recurrent endometrial cancer (EC) and who are candidates for systemic therapy'.

Dosage in the marketing authorisation

2.2 The dosage schedule is available in the summary of product characteristics for dostarlimab.

Price

2.3 The list price for dostarlimab is £5,887.33 per 500-mg vial (excluding VAT; BNF online accessed November 2025).

2.4 The company has a commercial arrangement. This makes dostarlimab available to the NHS with a discount. The size of the discount is commercial-in-confidence.

Carbon Reduction Plan

2.5 For information, GlaxoSmithKline did not disclose its Carbon Reduction Plan for UK carbon emissions.

3 Committee discussion

The evaluation committee considered evidence submitted by GlaxoSmithKline, a review of this submission by the external assessment group (EAG) and responses from stakeholders. See the committee papers for full details of the evidence.

The condition

Impact on quality of life

3.1 Endometrial cancer starts in the lining of the uterus and is the most common type of uterine cancer. At diagnosis, primary advanced endometrial cancer refers to stage 3 or 4 disease that has spread beyond the uterus. Recurrent endometrial cancer refers to cancer that is detected either radiologically or histologically, when there has been remission after initial treatment. Mismatch repair (MMR) status, the functionality of the DNA MMR system in tumours, is routinely tested in endometrial cancer. About 75% of people with endometrial cancer have tumours that are MMR proficient (MMRp) or microsatellite stable (MSS). In MMRp, the DNA repair mechanisms are intact and mutations can be corrected. In MSS, the length of microsatellites remains unchanged. People from Black ethnic backgrounds have a higher incidence of the p53-abnormal (p53abn) subtype of endometrial cancer with MSS or MMRp. This may correlate with TP53-mutated (TP53mut) tumours (see section 3.4). This represents a small proportion of all endometrial cancers, but is often more aggressive and associated with poorer outcomes.

The clinical experts explained that endometrial cancer with MSS or MMRp is a molecularly heterogeneous group. They suggested that routinely available molecular testing cannot further identify subgroups of endometrial cancer with MSS or MMRp. They highlighted that the median survival for people with endometrial cancer with MSS or MMRp is usually less than 2 years. The patient experts explained that living with stage 3 or 4 endometrial cancer with MSS or MMRp has a substantial impact on all aspects of life for both the person and their family. This includes debilitating physical symptoms, psychological distress from the uncertainty of disease progression and financial burden. The committee concluded that primary advanced or recurrent endometrial cancer with MSS or

MMRp can have a negative impact on people with the condition, as well as on their families and carers.

Clinical management

Treatment options

3.2 Standard care for primary advanced or recurrent endometrial cancer is platinum-containing chemotherapy, typically a combination of carboplatin and paclitaxel, followed by surveillance scans every 12 weeks. People whose cancer progresses after chemotherapy may be offered immunotherapy, further chemotherapy or, for a very small proportion, maintenance hormone treatment. Pembrolizumab plus lenvatinib is available as an option for people who have had treatment for endometrial cancer (see NICE's technology appraisal guidance on pembrolizumab with lenvatinib for previously treated advanced or recurrent endometrial cancer). The clinical experts explained that, once cancer has progressed after chemotherapy, about 35% to 40% of people are unable to tolerate further treatment at second line, including immunotherapy. They highlighted that the side effects are more often related to lenvatinib than to pembrolizumab.

The patient experts agreed and emphasised the high unmet need. They highlighted the limited treatment options for endometrial cancer with MSS or MMRp at this stage, which can leave people feeling frustrated, hopeless and abandoned. At the second committee meeting, NHS England's Cancer Drugs Fund lead noted that people with endometrial cancer with MSS or MMRp can now access immunotherapy at first line. This is because, since the first committee meeting, NICE recommended pembrolizumab with carboplatin and paclitaxel for untreated primary advanced or recurrent endometrial cancer. The committee noted the limited first-line treatment options available for endometrial cancer with MSS or MMRp. It concluded that people with the condition, and their families, would welcome safe and effective treatments that offer durable responses and are well tolerated.

Positioning of dostarlimab plus platinum-containing chemotherapy

3.3 For this evaluation, the company positioned dostarlimab as an add-on treatment to platinum-containing (also referred to as platinum-based) chemotherapy as a first-line option for primary advanced or recurrent endometrial cancer with MSS or MMRp, when systemic treatment is suitable. The company explained that its target population is narrower than the marketing authorisation. The committee noted that dostarlimab is recommended for a different subpopulation in NICE's technology appraisal guidance on dostarlimab with platinum-based chemotherapy for treating primary advanced or recurrent endometrial cancer with high MSS or MMR deficiency.

At the first committee meeting, the company explained that the only relevant comparator was carboplatin plus paclitaxel. This is standard NHS care for primary advanced or recurrent endometrial cancer with MSS or MMRp (see section 3.2). It also highlighted that, if recommended, people with primary advanced or recurrent endometrial cancer with MSS or MMRp who have had dostarlimab plus platinum-containing chemotherapy at first line would not be able to have pembrolizumab-based regimens at second line. This is because immunotherapies are not offered more than once for this condition in the NHS. At the first committee meeting, the clinical experts confirmed that the choice of comparator aligns with NHS practice for the company's target population.

The committee agreed with the company's positioning of dostarlimab plus platinum-containing chemotherapy. It noted that 5 days before the second committee meeting, NICE had recommended pembrolizumab with carboplatin and paclitaxel for people with untreated primary advanced or recurrent endometrial cancer (TA1092; see section 3.2), which would be considered a relevant comparator for the company's target population. The committee noted that NICE technology appraisal and highly specialised technologies guidance: the manual states that a comparator should be established clinical practice in the NHS for the population. But it concluded that the timing of TA1092 meant that, for this evaluation, the relevant comparator is carboplatin plus paclitaxel.

Clinical effectiveness

Key clinical-effectiveness evidence for dostarlimab plus platinum-containing chemotherapy

3.4 The key clinical-effectiveness evidence used in the company's submission and economic model came from RUBY-1, an ongoing phase 3 multinational double-blind randomised trial. It compared 18 weeks of dostarlimab plus carboplatin and paclitaxel (from now, platinum-containing chemotherapy) followed by dostarlimab monotherapy for up to 3 years (from now, the dostarlimab arm) with 18 weeks of placebo plus platinum-containing chemotherapy followed by placebo for up to 3 years (from now, the placebo arm). Randomisation was stratified by MMR and MSS status, prior external pelvic radiotherapy and disease status. The trial included 494 adults (18 years and over) with primary stage 3 or 4, or recurrent endometrial cancer, and an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1. Of these, 76% (376 of 494) had endometrial cancer with MSS or MMRp. Mutational data was available for 400 people, of which 88 people had TP53mut tumours. The primary endpoints were overall survival (OS) and progression-free survival (PFS), assessed by the investigator according to Response Evaluation Criteria in Solid Tumors version 1.1. The company presented results from 2 planned interim data cuts, which were used in the economic model:

- IA1 (28 September 2022) was done for PFS, health-related quality of life and time to treatment discontinuation at the first committee meeting The company considers the median follow-up for IA1 to be commercial-in-confidence, so this information cannot be reported here. In response to the draft guidance consultation, the company used PFS data at the IA2 data cut in its updated base case.
- IA2 (22 September 2023) had a median follow-up of 37.5 months for OS and adverse events.

Generalisability of results from the RUBY-1 population

3.5 The clinical experts noted that people in RUBY-1 were generally younger than

people likely to have dostarlimab in the NHS. But they thought that the RUBY-1 population was broadly representative of NHS clinical practice. This was because people in the NHS would typically need to have an ECOG performance status of 0 or 1 to be considered fit enough for triplet therapy (chemotherapy and immunotherapy). About 64% (239 of 376) of people with endometrial cancer with MSS or MMRp in RUBY-1 had a subsequent treatment after disease progression. These treatments included chemotherapy, immunotherapy (such as pembrolizumab plus lenvatinib and pembrolizumab monotherapy), radiation therapy, hormone treatment and bevacizumab. At the IA2 data cut, more people in the placebo arm (73%, 134 of 184) had a subsequent treatment compared with the dostarlimab arm (55%, 105 of 192). About 27% (102 of 376) of people with endometrial cancer with MSS or MMRp had subsequent immunotherapy. This was more common in the placebo arm (37%, 68 of 184) than in the dostarlimab arm (18%, 34 of 192).

The committee noted that some of the subsequent treatments used in RUBY-1 were not fully representative of NHS practice. Specifically, bevacizumab monotherapy is not used for endometrial cancer in the NHS, and people whose cancer progresses after first-line immunotherapy would not usually have further immunotherapy. The EAG noted that few people had bevacizumab and, because proportions were similar between arms, this was unlikely to have affected outcomes. It agreed with the company that subsequent immunotherapy use in the placebo arm was similar to that seen in UK clinical practice. But it highlighted that the proportion of people having subsequent immunotherapies in the dostarlimab arm was higher than would be expected in NHS clinical practice. So, the treatment effect of the dostarlimab arm in the NHS may be lower than what was seen in RUBY-1. This introduced uncertainty about the generalisability of the OS results (see section 3.7). The committee noted that RUBY-1 was broadly representative of people likely to have dostarlimab in the NHS, But it concluded that differences in subsequent treatment use and retreatment with immunotherapy introduced uncertainty about the generalisability of the trial's findings to NHS clinical practice.

RUBY-1 PFS and PFS2 results

3.6 At the first committee meeting, the company presented PFS results from the IA1

and IA2 data cuts. At IA1, the median PFS was 9.9 months in the dostarlimab arm compared with 7.9 months in the placebo arm. The difference was statistically significant (hazard ratio [HR] 0.76, 95% confidence interval [CI] 0.59 to 0.98). But the difference in PFS was not statistically significant at the IA2 data cut. The company considers the PFS results at IA2 to be commercial-in-confidence, so they cannot be reported here. The company also presented results for PFS2. This was defined as the time from treatment randomisation to the date of assessment of progression on the first subsequent anticancer treatment after study treatment or death by any cause (whichever is earlier). Median PFS2 at IA2 was 24.6 months in the dostarlimab arm compared with 15.9 months in the placebo arm (HR 0.74, 95% CI 0.57 to 0.97). The committee noted the difference in whether there was a statistically significant benefit for dostarlimab in PFS between IA1 and IA2. It concluded that there was uncertainty about the clinical effectiveness of dostarlimab plus platinum-containing chemotherapy in improving PFS in people with endometrial cancer with MSS or MMRp compared with platinum-containing chemotherapy.

RUBY-1 OS results and impact of subsequent immunotherapy

3.7 In its submission, the company did not present OS results at IA1. At IA2, the median OS was 34 months in the dostarlimab arm compared with 27 months in the placebo arm. But the difference was not statistically significant (HR 0.79, 95% CI 0.60 to 1.04). The company highlighted that the OS data at this interim analysis was still immature, with 54.8% data maturity. The clinical experts thought that the OS data was relatively mature and that it was unlikely that the OS estimates would change substantially by the final follow-up in 2026. The EAG highlighted concerns about the reliability of the OS data from RUBY-1, particularly the data beyond 30 months, because of heavy censoring. The committee noted the use of subsequent treatments in RUBY-1 and questioned their potential impact on OS (see section 3.5). The company explained that, for most people in RUBY-1, the cancer had progressed in the first 12 months. So, it thought that the impact of subsequent treatments would have been captured in the IA2 post-progression outcomes. The clinical experts highlighted that there was no data on the clinical effectiveness of second-line immunotherapy after progression on first-line immunotherapy. But they thought it unlikely that this would have a substantial impact on OS in RUBY-1 because they did not expect later lines of

immunotherapy to be clinically effective. The committee questioned why 18% (34 of 192) of people in the dostarlimab arm of RUBY-1 had subsequent immunotherapy if it was not expected to be clinically effective. The company explained that RUBY-1 was a double-blind trial, so investigators were unaware of treatment group allocations.

In response to the draft guidance consultation, the company reiterated that the proportion of people having subsequent treatment, and the lines and types of regimens in RUBY-1, were largely consistent with what would be expected in clinical practice. The exception was for bevacizumab use. It clarified that RUBY-1's protocol had not included guidelines for post-progression treatment strategies. Instead, decisions on subsequent treatments were based on physicians' clinical judgement. The company also provided post-hoc analyses exploring the effect of subsequent treatments on survival outcomes in RUBY-1:

- An analysis of the treatment effect of dostarlimab plus platinum-containing chemotherapy compared with placebo plus platinum-containing chemotherapy on OS by subsequent immunotherapy or chemotherapy use: The company explained that this suggested that subsequent immunotherapy did not improve OS in the dostarlimab arm compared with subsequent chemotherapy alone. It considers the results to be commercial-in-confidence, so they cannot be reported here. The EAG highlighted limitations of the analysis, including small sample sizes, broken randomisation, lack of baseline comparability and a focus only on pembrolizumab plus lenvatinib immunotherapy. So, it remained unclear whether any differences reflected treatment effects or patient characteristics. The EAG also highlighted that the company had not provided evidence from any previous trials on the impact of retreatment with immunotherapy on post-progression outcomes.

- An analysis of the time between first and second progression event (PFS2 minus PFS1). The company suggested that this showed that upfront use of dostarlimab increases time between first and progression events. This is despite using immunotherapies after progression in people who initially had chemotherapy. The EAG highlighted that PFS2 reflects the time to a person's second progression event, rather than the length of time from controlled disease to a second progression. The EAG explained that post-progression benefit should be interpreted with caution because PFS2 does not isolate the treatment effect of dostarlimab. This is because it includes the additional

effects of different subsequent treatments. Also, the PFS2 analysis included everyone, not just people who had had a first progression event. So, the dostarlimab arm mainly reflected people who had had an early failure on initial dostarlimab treatment. Conversely, the placebo arm likely included a greater number of people who had progressed on initial chemotherapy. So, the populations between arms were not balanced for PFS2.

- An analysis of the treatment effect of dostarlimab plus platinum-containing chemotherapy compared with placebo plus platinum-containing chemotherapy for PFS2 at IA2, by subsequent immunotherapy or any subsequent anticancer treatment use. The company noted that the results suggested that people in the dostarlimab arm who had subsequent immunotherapy had a similar median PFS2 as people in the same arm who had any subsequent anticancer treatment. The company considers the results to be commercial-in-confidence so they cannot be reported here. The EAG highlighted the limitations of the post-hoc subgroup analysis. These limitations included no explanation from the company on choice of subsequent treatment offered to people at disease progression and concerns about using PFS2 as an outcome measure. So, it was also unclear whether any differences in median PFS2 were because of the type of subsequent treatment or differences in patient characteristics.

- Treatment-switching analyses using rank-preserving structural failure time models (RPSTMs) on OS, which adjusted for switching to all subsequent immunotherapies or only pembrolizumab plus lenvatinib in both trial arms. The company explained that, in the analyses, there was a modest reduction in the OS hazard ratio compared with the unadjusted hazard ratios from the trial. These treatment-switching analyses showed that the hazard ratios adjusted for all subsequent immunotherapies (HR 0.76; 95% CI 0.542 to 1.061) and for pembrolizumab plus lenvatinib only (HR 0.77; 95% CI 0.564 to 1.057) were similar to the unadjusted hazard ratios (HR 0.79; 95% CI 0.602 to 1.044) used in the company's base case. The EAG suggested that Inverse Probability of Censoring Weights (IPCW) models may be more appropriate than RPSTMs if immunotherapy effects are likely to vary and treatment is started at different times. At the second committee meeting, the company explained that it had explored both methods but preferred the RPSFTM. This choice reflected a concern that the IPCWs may have been unstable because of the moderate sample size in RUBY-1. Also, there were concerns that the

censoring and treatment switching could have violated the no-unmeasured-confounders assumption essential to IPCWs. The EAG agreed that IPWCs were less sensitive to the 'common treatment-effect' assumption for previous subsequent treatment. But it explained that this assumption remains a critical vulnerability of RPSFTMs.

The committee noted the lack of statistical significance on OS estimates, data immaturity and the issues of subsequent immunotherapy use in RUBY-1. It acknowledged the company's attempts to analyse the impact of subsequent treatments on survival estimates. It also noted that the direction of the treatment effect for dostarlimab plus platinum-containing chemotherapy in these post-hoc analyses was broadly consistent with what had been previously presented in the ITT population. But it thought that there was still uncertainty. The committee concluded that there is uncertainty about the effectiveness of dostarlimab plus platinum-containing chemotherapy in improving OS in people with endometrial cancer with MSS or MMRp compared with platinum-containing chemotherapy alone.

Results of subgroup analyses from RUBY-1

3.8 The committee noted that subgroup analyses in the TP53mut population (see section 3.4) showed better PFS benefit compared with that in the overall population at IA1 (HR 0.55, 95% CI 0.30 to 0.99). But the OS benefit in this subgroup was not statistically significant (HR 0.59, 95% CI 0.33 to 1.03). The committee agreed that these subgroup analyses were post hoc and involved a small cohort, so they were not statistically powered to detect differences. But it recalled that endometrial cancer with the p53abn subtype is associated with poorer outcomes (see section 3.1). Having seen the relative clinical-effectiveness evidence from RUBY-1 for the TP53mut subgroup, the committee thought that it would be useful to see exploratory analyses in the p53abn and TP53mut subgroups. In response to the draft guidance consultation, the company explained that it was not informative to explore cost-effectiveness scenarios in any subgroup, including p53abn. This was because it did not think that the potential for dostarlimab to disproportionately benefit a single subgroup in endometrial cancer with MMRp or MSS was supported by evidence from RUBY-1, external expert opinion, underlying clinical rationale or external evidence. The

committee acknowledged the company's rationale but concluded that they would preferred to have seen analyses specific to this subgroup.

Economic model

Company's modelling approach

3.9 The company used a partitioned survival model to estimate the cost effectiveness of adding dostarlimab to platinum-containing chemotherapy. This had 3 health states (progression-free, progressed disease and death), a 1-week cycle with no half-cycle correction and a 36-year time horizon. Data from the placebo arm of RUBY-1 was used to inform the comparator arm in the model (that is, platinum-containing chemotherapy). In line with the marketing authorisation, a 3-year stopping rule was applied for dostarlimab (see section 2.2). The committee concluded that the company's model was suitable for decision making.

Extrapolating survival over time

3.10 The company extrapolated the long-term effects of dostarlimab plus platinum-containing chemotherapy, and of platinum-containing chemotherapy alone, on PFS and OS in people with primary advanced or recurrent endometrial cancer with MSS or MMRp beyond the trial data. It assumed non-proportional hazards for PFS and OS. This was because dostarlimab has a different mechanism of action than platinum-containing chemotherapy. There was a longer time on treatment with dostarlimab but only 6 cycles of platinum-containing chemotherapy in RUBY-1. There was also the commonly observed delayed response with immunotherapies. To extrapolate the long-term effects, the company fitted independent parametric distributions to model PFS and OS in the 2 treatment arms. The EAG agreed with the company that the proportional hazard assumption did not hold. It also agreed that fitting independent parametric distributions to model PFS and OS in the 2 arms was reasonable. The committee concluded that using independent parametric distributions to model PFS and OS was appropriate for decision making.

Extrapolating PFS

3.11 At the first committee meeting, the company used PFS data at IA1 from RUBY-1 to inform the extrapolation of PFS in the model. This was because statistical significance for PFS was reached at IA1 in the trial (see section 3.4 and section 3.5). The EAG thought that the company's approach to modelling PFS was appropriate. It noted that the Kaplan–Meier curves for PFS at IA2 showed that the tail of the curve (from 32 months onwards) appeared to plateau for both treatment arms. So, it also thought that the company's approach of extrapolating PFS in the model based on PFS data at IA1 from RUBY-1 was reasonable. This was because modelling a long-term plateau in PFS would not be appropriate because outcomes for the endometrial cancer with MSS or MMRp population tend to be poor and relapses are likely. The EAG thought that the PFS curves at IA2 were more uncertain because of the censoring in RUBY-1. But the committee noted that censoring existed both at IA1 and IA2 data cuts, even though at different time points. The committee did not think that the PFS curve at IA2 was more uncertain than at IA1. This was because the observed plateau on the PFS Kaplan–Meier curves at IA1 was likely related to censoring. The committee noted that the PFS hazard rate plot was similar in both arms around year 2 in the model but the hazard rate plot for OS diverged. The EAG explained that this was likely because of the impact of subsequent immunotherapies on OS in the platinum-containing chemotherapy arm. It also noted that there was no impact of subsequent immunotherapies on the PFS curves.

The committee thought that modelling based on longer follow-up would be more informative and reliable. So, it asked to see analyses using the more mature and most recent IA2 data cut to extrapolate PFS. In response to the draft guidance consultation, the company updated its base case to include PFS extrapolations using data from IA2. Because standard parametric distributions did not provide plausible extrapolations, the company selected the Odds k=1 flexible spline models for both the dostarlimab and platinum-containing chemotherapy arms. The EAG thought that the company's approach to modelling PFS using the updated data cut at IA2 was appropriate. The committee concluded that the company's approach of modelling PFS using updated data at IA2 was appropriate for decision making.

Extrapolating OS

3.12 The company used OS data at IA2 from RUBY-1 to inform the extrapolation of OS. To model OS over time, it selected the log-normal distribution for the dostarlimab arm and the log-logistic distribution for the platinum-containing chemotherapy arm. This was based on statistical and visual fit, and clinical validation of the extrapolated OS curves. The EAG agreed with the company's selection of curves. The EAG explained that the hazard rate plot based on the company's selected OS curves showed that the risk of death in the 2 arms gradually converged around year 15 and became similar after that. The EAG considered that the convergence of the risk of death was likely because of the impact of subsequent immunotherapies in arms. This was because subsequent immunotherapies may not have had a substantial impact on OS in the dostarlimab arm. But they may have improved OS in the platinum-containing chemotherapy arm. This led to similar risks of death in the 2 arms over time.

The committee recalled its discussion on the uncertainties in the treatment effect of dostarlimab on OS (see section 3.7) and the impact of subsequent treatments on OS seen in RUBY-1. At the first committee meeting, it thought that there was high uncertainty in the modelling of OS. So, it asked for the subsequent treatments' effects on OS to be further explored. In response to the draft guidance consultation, the company provided additional analyses of the impact of subsequent treatments on OS (see section 3.7). It continued to use the unadjusted OS data from IA2 because the treatment-switching analyses showed that the adjusted and unadjusted hazard ratios were similar. The EAG highlighted that the methods used for the adjusted OS analysis were uncertain and agreed with the company's use of OS extrapolations in its base case. The committee concluded that the company's approach to OS extrapolation using data from IA2 was acceptable for decision making.

Treatment-effect waning

3.13 In its base case, the company assumed that treatment-effect waning was captured in the modelled OS. This assumption was based on RUBY-1, which the company suggested had shown a sustained OS benefit in the dostarlimab arm compared with the placebo arm. The company also highlighted that its

independent modelling of OS curves should have implicitly captured any waning of the treatment effect. The EAG thought that the company's modelling of OS was generally appropriate, and agreed with the company that treatment-effect waning was likely captured in the OS extrapolations. This was because the PFS plots showed that the risk of progression was similar for both arms after about 2 years. But the EAG noted that, at IA2, the Kaplan–Meier curve for OS in the 2 treatment arms appeared to converge from month 30 then diverge again from month 36 onwards. So, it thought that a scenario of gradual treatment-effect waning may be informative. The company also provided 2 treatment-effect waning scenarios:

- a scenario with a 2-year stopping rule
- a scenario with a 3-year stopping rule that was in line with dostarlimab's marketing authorisation (see section 2.2).

The committee did not think that treatment-effect waning was implicitly captured in the model. This was because the company's extrapolated OS curves with and without incorporated treatment-effect waning were different. The committee recalled the uncertainties associated with the evidence on OS (see section 3.7 and section 3.12). It thought that there was high uncertainty related to the treatment-effect waning assumptions. At the first committee meeting, the committee requested additional evidence and analyses in which:

- including or excluding treatment-effect waning in the model was sufficiently justified
- the impact of second-line treatment effect on OS was adjusted for the potential interplay between the impact of subsequent treatments on OS and treatment-effect waning is explored.

In response to the draft guidance consultation, the company reiterated that fitting independent OS curves implicitly captured treatment-effect waning in the model, as evidenced by the hazard ratios for OS over time. These OS estimates were consistent with clinical expectation and RUBY-1 data. It noted that this approach was consistent with previous NICE appraisals in similar indications with less mature OS data. But it also provided scenarios of gradual treatment-effect waning. These reduced the treatment effect to the

same level as the platinum-containing chemotherapy arm after 3 years, and at 3 and 5 years after dostarlimab's stopping rule (that is, 6 to 8 years and 8 to 10 years after starting dostarlimab).

The company provided analyses in which the waning assumptions were applied to everyone and also just to people without a complete response (74.2% in dostarlimab arm). The EAG suggested that treatment-effect waning was likely captured in the data for the observed period of RUBY-1 that informed the PFS and OS extrapolations. It explained that the main effect of dostarlimab is to reduce the risk of progression. It highlighted that the hazard rate plot for PFS showed that treatment effect peaks at about 1 year and then diminishes, until it is equal to the platinum-containing chemotherapy arm. It also noted that the follow-up period for RUBY-1 was about 4 years and that most people in the dostarlimab arm had stopped treatment before the maximum duration of 3 years. So, the EAG did not apply any additional treatment-effect waning assumptions in its base case. The committee noted that the implied hazard ratio over time showed that the relative treatment effect over time increased sharply then decreased during the observed period of RUBY-1 at 4 years. The company explained that the implied hazard ratio reached 1 at about 20 years, meaning no difference in treatment effect in the 2 arms. The committee acknowledged that treatment-effect waning may have been largely captured during the observed period of RUBY-1 and the independent extrapolations. But it considered that there was uncertainty in assuming that dostarlimab benefit would continue for up to about 15 years after stopping treatment. So, the committee preferred not to apply any additional treatment-effect waning assumptions in the base case. But it concluded that treatment-effect waning was unlikely to have been fully captured in the modelled OS estimates and took this into account in its decision making.

Time on treatment

3.14 The company modelled time on treatment by using weighted completion rates for platinum-containing chemotherapy from RUBY-1 for the first 6 cycles across both treatment arms. For dostarlimab, it used completion rates for the first 6 cycles, followed by time to treatment discontinuation Kaplan–Meier data adjusted for

relative dose intensity up to 3 years. The EAG thought that using completion rates did not fully capture the cost of starting treatment in either arm. This was because the intention-to-treat population included people who were randomised but did not start treatment. So, the completion rate for the first treatment cycle in the model was less than 100%. To capture the full treatment costs in its base case, the EAG preferred to use time to treatment discontinuation Kaplan–Meier data for both arms. In addition, for dostarlimab, it used the relative dose intensity from cycle 1 up to 3 years. The committee concluded that the EAG's approach to modelling time on treatment was appropriate.

Resource use

Health-state resource use for the dostarlimab arm

3.15 In its original base case, the company modelled health-state resource use for the dostarlimab arm based on advice from 6 UK healthcare professionals. It assumed that, after the first 18 weeks of treatment, people having dostarlimab who were progression-free would have specific resource use that differed from people in the platinum-containing chemotherapy arm. The EAG disagreed and thought that, after 3 years of dostarlimab monotherapy, resource use would be the same. The clinical experts thought that the level of surveillance would be similar for people who are progression-free after treatment, regardless of whether they have had had dostarlimab or platinum-containing chemotherapy. At the committee meeting, the company explained that it agreed with the EAG's modelling. In response to the draft guidance consultation, the company adopted the EAG's approach to modelling health-state resource use for the dostarlimab arm. The committee concluded that the EAG's approach to modelling health-state resource use for the dostarlimab arm in the company's updated base case was appropriate for decision making.

Costs

Oral administration cost for lenvatinib

3.16 The company's original base case included an oral administration cost for lenvatinib to account for specialist oversight related to procurement, prescribing, dispensing and administration. The EAG disagreed and excluded this cost from its base case. It noted that, based on published advice, people are likely to take lenvatinib at home. So, there would likely be no administration cost to the NHS. It highlighted that these administration costs only affect the platinum-containing chemotherapy arm because pembrolizumab plus lenvatinib is not used after dostarlimab treatment. The clinical experts agreed that there is likely no cost associated with administering lenvatinib. But they noted there would be costs related to managing its side effects. The EAG confirmed that these were accounted for in the monitoring costs already included in the model. The committee thought that the oral administration cost of lenvatinib should be excluded from the model. In response to the draft guidance consultation, the company adopted the EAG's approach of excluding the oral administration cost of lenvatinib from the model. The committee concluded that the company's updated base case excluding oral administration cost of lenvatinib was appropriate for decision making.

Severity

3.17 NICE's methods on conditions with a high degree of severity did not apply.

Cost-effectiveness estimates

Committee's preferred assumptions

3.18 At the second committee meeting, the company's updated base case included:

- PFS extrapolations using more mature data from IA2 (see section 3.11)

- subsequent treatment proportions from the IA2 data cut
- the committee's preferences from the first committee meeting in modelling time on treatment (see section 3.14)
- health-state resource use for dostarlimab arm (see section 3.15)
- excluding the cost for oral administration of lenvatinib (see section 3.16).

The EAG's preferred base case was mostly aligned with the company's updated base case, except for corrections it had done in the first committee meeting. These were to:

- use the Office for National Statistics life tables from 2017-2019 (see guidance in NICE's Decision Support Unit's technical support document 23)
- source nurse and GP costs directly from the Unit Costs of Health and Social Care Manual, 2023
- use the unit cost of carboplatin 450 mg for subsequent treatment cost.

The committee noted the uncertainty in the clinical evidence (see section 3.5, section 3.6 and section 3.7) and economic modelling (see section 3.12). But it concluded that the EAG's preferred base case including the corrections to the company's updated base case, reflected its preferred assumptions.

Acceptable ICER

3.19 NICE technology appraisal and highly specialised technologies guidance: the manual notes that, above a most plausible incremental cost-effectiveness ratio (ICER) of £20,000 per quality-adjusted life year (QALY) gained, judgements about the acceptability of a technology as an effective use of NHS resources will take into account the degree of certainty around the ICER. The committee will be more cautious about recommending a technology if it is less certain about the ICERs presented. But it will also take into account other aspects including uncaptured health benefits. The committee noted the substantial uncertainty in the evidence and company's modelling, specifically:

- that the longer data cut of PFS was not statistically significant and OS data was immature (see section 3.6)
- that subsequent treatments from RUBY-1 may not be generalisable to NHS clinical practice and may affect the OS estimates (see section 3.5 and section 3.7)
- whether treatment-effect waning has been fully captured in the company's base case (see section 3.13).

The committee considered the uncertainties in the evidence and modelling and whether there are any benefits not fully captured (see section 3.22). It concluded that an acceptable ICER would be towards the lower end of the range NICE considers a cost-effective use of NHS resources, that is, around £20,000 per QALY gained.

Company and EAG cost-effectiveness estimates

3.20 The committee noted that there was little difference between the cost-effectiveness estimates in the company's updated base case and the EAG's preferred base case. The exact figures cannot be reported because of confidential discounts for dostarlimab, pembrolizumab and lenvatinib. Both the company's and EAG's updated base case ICERs were within the range that NICE normally considers an acceptable use of NHS resources.

Other factors

Equality

3.21 Stakeholders highlighted that people from Black ethnic backgrounds have a higher incidence of the more aggressive p53-abn subtype of endometrial cancer with MSS or MMRp, which is associated with poorer outcomes (see section 3.1). Although the committee requested further analyses for consideration in the p53-abnormal or TP53mut subgroups, the company did not provide these (see

section 3.8). The committee noted that the company's target population meant this subgroup would have been included. So, the recommendations would apply to everyone with endometrial cancer with MMRp or MSS. The committee thought that equality issues relating to differences in incidence of a condition cannot be addressed in a technology appraisal. It concluded that although the incidence of p53-abnormal subtype was higher in people from Black ethnic backgrounds, there were no equality issues that would need changes to the recommendation.

Uncaptured benefits

3.22 The committee acknowledged that there are limited options for early treatment of primary advanced or recurrent endometrial cancer with MSS or MMRp (see section 3.2). It considered whether there were any uncaptured benefits of dostarlimab plus platinum-containing chemotherapy and did not identify additional benefits not captured in the economic modelling. So, it concluded that all additional benefits of dostarlimab plus platinum-containing chemotherapy had already been taken into account.

Conclusion

Recommendation

3.23 The most likely cost-effectiveness estimates were within the range considered to be a cost-effective use of NHS resources. So, dostarlimab plus platinum-containing chemotherapy can be used to treat primary advanced or recurrent endometrial cancer with MSS or MMRp in adults when systemic treatment is suitable.

4 Implementation

4.1 Section 7 of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires integrated care boards, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this evaluation within 90 days of its date of publication.

4.2 Chapter 2 of Appraisal and funding of cancer drugs from July 2016 (including the new Cancer Drugs Fund) – A new deal for patients, taxpayers and industry states that for those drugs with a draft recommendation for routine commissioning, interim funding will be available (from the overall Cancer Drugs Fund budget) from the point of marketing authorisation, or from release of positive draft guidance, whichever is later. Interim funding will end 90 days after positive final guidance is published (or 30 days in the case of drugs with an Early Access to Medicines Scheme designation or cost comparison evaluation), at which point funding will switch to routine commissioning budgets. The NHS England Cancer Drugs Fund list provides up-to-date information on all cancer treatments recommended by NICE since 2016. This includes whether they have received a marketing authorisation and been launched in the UK.

4.3 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal guidance recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 60 days of the first publication of the final draft guidance.

4.4 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has primary advanced or recurrent endometrial cancer with microsatellite stability or mismatch repair proficiency and the healthcare professional responsible for their care thinks that dostarlimab with platinum-containing chemotherapy is the right treatment, it should be available for use, in line with NICE's recommendations.

5 Evaluation committee members and NICE project team

Evaluation committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee A.

Committee members are asked to declare any interests in the technology being evaluated. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

The minutes of each evaluation committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

Chair

Radha Todd
Chair, technology appraisal committee A

NICE project team

Each evaluation is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the evaluation), a technical adviser, a project manager and an associate director.

Sharlene Ting
Technical lead

Yelan Guo
Technical adviser

Jennifer Upton and Greg O'Toole

Project managers

Lizzie Walker
Principal technical adviser

Ian Watson
Associate director

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