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Dostarlimab (endometrial cancer) –

Addendum to Commission A21-84[1]

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List of abbreviations

Abbreviation	Meaning
BMI	Body-Mass-Index
dMMR	mismatch repair deficiency
ECOG PS	Eastern Cooperative Oncology Group Performance Status
EORTC QLQ-C30	European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire – Core 30
EPAR	European Public Assessment Report
FIGO	Fédération Internationale de Gynécologie et d'Obstétrique (Federation of Gynecology and Obstetrics)
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
IPD	individual patient data
IPTW	inverse probability of treatment weighting
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
MAIC	matching-adjusted indirect comparison
MSI	Mikrosatelliteninstabilität
MSI-H	high microsatellite instability
NCRAS	National Cancer Registration and Analysis Service
SGB	Sozialgesetzbuch (Social Code Book)

1 Background

On 26 October 2021, the Federal Joint Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to conduct supplementary assessments for Commission A21-84 (Dostarlimab – benefit assessment according to §35a Social Code Book V) [1].

In its dossier for the assessment of dostarlimab in endometrial cancer, the pharmaceutical company (hereinafter referred to as the "company") exclusively presented comparisons of the single-arm study GARNET with dostarlimab with individual arms of different studies. In the dossier, the company only used a method based on individual patient data (IPD) for one of these comparisons (GARNET compared to the doxorubicin arm of the ZoptEC study). In doing so, the company conducted a propensity score analysis using inverse probability of treatment weighting (IPTW) for the IPD-based indirect comparison. All other comparisons used the matching-adjusted indirect comparison (MAIC) method without common comparator on the basis of aggregate data. This method is generally not an adequate option for confounder adjustment [2]. With its comments, the company presented another comparison on the basis of IPD (GARNET compared to registry study 216960).

The G-BA commissioned IQWiG to assess the two indirect comparison on the basis of IPD under consideration of the analyses presented in the commenting procedure and the information provided in the dossier:

- GARNET study versus ZoptEC study
- GARNET study versus registry study 216960

The responsibility for the present assessment and the assessment result lies exclusively with IQWiG. The assessment is forwarded to the G-BA. The G-BA decides on the added benefit.

2 Assessment

The two comparisons described in this addendum are non-randomized comparisons of individual arms from different studies without common comparator. In this context, the company conducted an IPTW analysis each for the IPD-based comparisons of cohort A1 (mismatch repair deficiency [dMMR]/high microsatellite instability [MSI-H]) from the GARNET study versus the doxorubicin arm of the ZoptEC study and versus the National Cancer Registration and Analysis Service (NCRAS) database (registry study 216960). In the analysis of such comparisons, the aim is to achieve structural equality of the treatment groups by adjusting for potential confounders. For this purpose, it is necessary to systematically identify relevant confounders before conducting the analysis.

Since the quality of the confounder adjustment significantly determines the informative value of the analyses presented, the assessment of the adjustment in the comparisons presented is first described. This is followed by further comments on the two analyses on the comparison of individual arms from different studies.

2.1 Confounder adjustment

The company identified the potential confounders for the comparison of individual arms from different studies via a literature search conducted in May 2020 and subsequent expert discussion. This approach is appropriate. The following Table 1 shows the relevant confounders identified by this procedure.

Table 1: Expert assessment of prognostic variables in advanced and/or recurrent endometrial cancer[a]

Pathological factor and grouping	Rated as important prognostic factor					
	Expert 1	Expert 2	Expert 3	Expert 4	Expert 5	Number of experts with rating important (max = 5)
Family origin: white [non-Hispanic] vs. black vs other	Yes	Yes	Yes	Yes	Yes	5
Increased age: ≥ 65 years vs. < 65 years	Yes	Yes	Yes	Yes	Yes	5
ECOG status: 0 or 1 vs. 2	Yes	Yes	Yes	Yes	Yes	5
Histology: endometrioid vs. non-endometrioid	Yes	Yes	No	Yes	Yes	4
Most current FIGO stage: I/II vs. III/IV	Yes	Yes	NR	Yes	NR	3
BMI	No	No	Yes	Yes	Yes	excluded[b]
Grade of disease at diagnosis: grade 1 and 2 vs. grade 3 and 4	Yes	Yes	Yes	Yes	Yes	5
Number of previous antineoplastic therapy regimens: 0 or 1 vs. ≥ 2	Yes	Yes	Yes	Yes	Yes	5
Proportion of patients with previous surgery (for study indication): 0–89% 89–100%	Yes (indirect)	Yes[c]	NR[d]	Yes	NR[e]	3[f]
Other important prognostic factors:[g] MMR/MSI (molecular profile)	Yes	Yes	Yes	Yes	Yes	5

a. The table (including the further footnotes) was taken from the company's study report on the comparison of GARNET vs. ZoptEC. The list of abbreviations comes from IQWiG.
b. The BMI is a risk factor for endometrial cancer, but patients with a high BMI may have a better prognosis because of the association with type 1 endometrial cancer. On the other hand, these patients may have comorbidities. Overall, the prognostic value and the direction are unclear.
c. If resection is possible at the start of the study and there is no distal metastasis.
d. Cannot be delimited from histological factors.
e. Not applicable in later stage/metastatic disease.
f. Indirect factor, previous surgery may indicate less advanced disease, lower tumour load or longer disease-free interval before relapse – all lead to better prognosis.
g. Direction of the prognosis in advanced stage unclear.

BMI: body mass index; ECOG: Eastern Cooperative Oncology Group; FIGO: Fédération Internationale de Gynécologie et d'Obstétrique; max: maximum; MMR: mismatch repair; MSI: microsatellite instability; NR: unclear whether "not reported" or "not relevant"

Of the factors identified in the literature, only the body mass index (BMI) was excluded after the survey of experts. Previous surgeries were classified as indirect factor. For the current International Federation of Gynecology and Obstetrics (FIGO) stage, it remains unclear whether 2 of the 5 experts assessed the factor as not relevant or whether there was no assessment, however, the factor was not excluded. 4 of 5 experts define the tumour histology as relevant factor. All other factors (family origin, increased age, Eastern Cooperative Oncology Group performance status (ECOG PS), degree of the disease, number of previous antineoplastic therapies, other important prognostic factors - MMR/MSI (molecular profile) were classified as relevant prognostic factors by all 5 experts. Thus, the analyses on the comparison of the individual study arms should be adjusted for all non-excluded factors.

The company presented no analysis for either of the two comparisons of individual arms that takes into account all confounders classified as relevant. This deficiency is not addressed in the study report on the comparison of GARNET vs. ZoptEC, nor in that on the comparison of GARNET vs. the registry study. The following Table 2 shows which adjustments were planned and carried out.

Table 2: Confounder adjustment in the analyses presented on the comparison of individual arms of different studies without common comparator

Comparison analysis	**Family origin**	**Age**	**ECOG status**	**Histology**	**Most current FIGO stage**	**Grade of disease at diagnosis**	**Number of previous antineoplastic therapies**	**Prior surgery**	**MMR/MSI**
GARNET vs. ZotpEC									
Propensity score model 1	X	X	X	X	(X)[a]	(X)[b]		X	
GARNET vs. registry study 216960									
Propensity score model 1				X		X	(X)[c]		
Propensity score model 2				X			(X)[c]		
Propensity score model 3	X		(X)[d]	X	(X)[e]			X	

a. Approach for the adjustment not appropriate – see text.
b. Was planned, but could not be considered, because, according to the company, the assumption of positivity was violated.
c. Not relevant in the cohorts used by the company, because only patients with one prior therapy were included.
d. Is only used in the sensitivity analysis of patients with ECOG ≤ 1, because in the total cohort of the registry study, information on the ECOG is missing for 50% of the patients.
e. FIGO stage at first diagnosis (deviating from expert recommendation: current FIGO status).

ECOG: Eastern Cooperative Oncology Group; FIGO: Fédération Internationale de Gynécologie et d'Obstétrique; MMR: mismatch repair; MSI: microsatellite instability

GARNET vs. ZoptEC

In the study report for the indirect comparison of the GARNET study with the doxorubicin arm of the ZoptEC study, the company stated that it would restrict the confounders for the adjustment to a selection from the list determined by the expert survey. It selected the confounders for which data are available in the ZoptEC study. This approach is not appropriate, because it does not lead to a sufficient adjustment for confounders and thus not to a sufficient comparability of the treatment groups. If a data set does not contain the information on the relevant confounders, the corresponding research question cannot be answered adequately [3].

The comparison GARNET vs. ZoptEC completely ignores 2 confounders identified as relevant (number of prior neoplastic therapies, MMR/MSI status). Furthermore, although the adjustment for disease severity at diagnosis was planned, according to the company it was not taken into account due to violation of the positivity assumption. The company did not provide an precise justification for this.

Moreover, the adjustment for the FIGO stage is not appropriate. In the GARNET study, the FIGO stage at first diagnosis was used for the adjustment, while in the ZoptEC study the data on the FIGO stage at study entry were included in the adjustment. In addition, the company assigned patients in the ZoptEC study with the dimension "advanced (stage III and IV)" to the dimension "FIGO stage III and IV" for the adjustment. It assigned the remaining patients to FIGO stages I and II using the formula "FIGO stages I and II are equal to N - stages III and IV". This approach is not appropriate as, among other things, it assigns patients with metastatic disease to FIGO stages I and II (see Table 5 and Table 6 in Appendix A).

Table 4 and Table 5 in Appendix A show the patient characteristics of the studies GARNET and ZoptEC each for the total population and for the analysis population for the IPTW comparison before adjustment was performed. The populations are not balanced for essential factors. The company did not present a complete description of the patient characteristics for the patient population intended for the analysis after adjustment. It only described the factors used by it in the adjustment (see Table 6 in Appendix A). Thus, the balance of the treatment groups cannot be assessed for all (recorded) patient characteristics and especially not for all relevant confounders after adjustment.

Overall, the adjustment for confounders for the comparison of the dostarlimab arm of the GARNET study with the doxorubicin arm of the ZoptEC study must be rated as insufficient. The results of the adjusted analysis are thus not informative.

Table 7 in Appendix A shows the results for overall survival from the comparison of dostarlimab from the GARNET study with doxorubicin from the ZoptEC study. For the reasons mentioned above, these results are not meaningful.

GARNET vs. registry study 216960

For the comparison of the dostarlimab arm of the GARNET study with a cohort from the NCRAS (registry study 216960) from England, the company presented 3 propensity score models in which it considered different confounders for the IPTW analysis (see Table 2). Also for this comparison, none of the models contains all the confounders identified as relevant.

In each case, the company analysed the 3 models for the comparison of the complete cohorts from the two studies (GARNET N = 129, NCRAS N = 999) and in a sensitivity analysis for cohorts of patients for whom data on the ECOG status are available and for whom the ECOG is ≤ 1 (GARNET N = 129, NCRAS N = 501).

The company described that the 3 propensity score models corresponded to those planned for the originally conducted MAIC.

- Model 1: According to the company, this model includes the confounders considered the most important ones by the experts. This is not comprehensible, as the systematic confounder identification of the company contains far more confounders (see Table 2). Irrespective of this, the handling of missing data (more than 30%) for the confounder "disease severity" is not appropriate. The artificial characteristic "unknown" was used for the missing data. This approach is not an adequate method for dealing with missing data in non-randomized studies [4], even in the context of using propensity scores [5].
- Model 2: According to the company, model 2 corresponds to model 1 without the confounder "disease severity". "Disease severity" was removed from the model because data on disease severity were not available for 34% (total cohort) and 31% (cohort ECOG ≤ 1) of patients in the cohorts of the registry study (missing data in GARNET: 5%). The company describes that an analysis with inclusion of patients without information on the disease severity results in unstable effects. This is correct (and applies to model 1). At the same time, model 2 thus lacks another important confounder and cannot deliver meaningful results.
- Model 3: contains confounders that were determined by a regression analysis with backward selection. For the same reason as with model 2, the confounder "disease severity" was also removed. This approach is not appropriate. The adjustment must take into account all confounders identified as relevant. These cannot be removed by subsequent regression analyses.

In models 1 and 2, patients with no or more than one previous antineoplastic therapy are also removed. Nevertheless, the listing still contains the confounder "number of previous antineoplastic therapies". This is misleading because adjustment is not made for different distributions of this confounder (with all characteristics), but the population is restricted instead.

The adjustment for confounders for the comparison of the dostarlimab arm of the GARNET study with the comparator arm from the registry study is also incomplete and, overall, must be classified as insufficient. The results of the adjusted analysis are thus not informative.

For the comparison of the GARNET study with the registry study, the company presented patient characteristics of the study populations before adjustment and after adjustment in the 3 models (see Table 8 to Table 15 in Appendix A). The data show that the treatment groups in both cohorts (complete cohort and patients with ECOG ≤ 1) differed relevantly before adjustment. After adjustment, an approximation of the adjusted characteristics was achieved in most cases, but relevant differences remain for the non-adjusted characteristics. None of the 3 models achieved the necessary comparable treatment groups in the two cohorts. This is another reason why the results of the comparison of dostarlimab from the GARNET study with the registry study are not informative.

Table 16 in Appendix A shows the results for overall survival from the comparison of dostarlimab from the GARNET study with the registry study. For the reasons mentioned above, these results are not meaningful.

2.2 Further comments on the analysis GARNET versus ZoptEC

Analysis population

For the comparisons of the dostarlimab arm from the GARNET study with the doxorubicin arm of the ZoptEC study, the population in both studies was first reduced to the patients who fulfilled the inclusion criteria of both GARNET and ZoptEC. Subsequently, a weighting was carried out using IPTW on the basis of the IPD from both studies.

For the reduction of the population, 37 patients from the GARNET study who had more than one platinum-based prior therapy were not included in the analysis (starting from 129 patients [safety population]).

Based on 255 patients in the ZoptEC study, 22 patients were not included in the analysis who either did not receive study medication (N = 6), whose follow-up was > 36 weeks (information from Module 4 A, deviating information in the study report: > 36 months, N = 4) or whose ECOG score was > 2 or missing (N = 12). The exclusion of patients with long observation periods from the control arm (> 36 weeks or months, N = 4) is not appropriate and distorts the effect estimation because patients with a long survival period in a treatment group are selectively excluded from the analysis. The company does not justify why it excluded these patients and did not censor them at the end of the planned observation.

Results on morbidity and health-related quality of life

In both the GARNET study and the ZoptEC study, outcomes on morbidity and health-related quality of life were assessed using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) questionnaire. Irrespective of the deficiencies in the confounder adjustment described above, which make the interpretation

of the comparison of the study arms impossible, the analysis of the EORTC QLQ-C30 data has further deficiencies. In Module 4 A, the company states to censor patient events in the GARNET arm (but not in the ZoptEC arm) after 28 weeks in the analysis of time to deterioration. It did not provide any reasons for this approach. This analysis also deviates from that in the study report of the comparison of GARNET and ZoptEC, in which this censoring was not carried out. The analysis from the study report is presented by the company in an appendix to Module 4 A.

Moreover, < 70% of the original population is included in the analysis. The results of the outcomes on morbidity and health-related quality of life are thus not usable.

Results on AEs

Irrespective of the deficiencies of the confounder adjustment described above, the analyses of the AEs cannot be interpreted because the two studies have different observation periods, but the company only presents the relative risk on the basis of the number of patients with an event.

In Module 4 A, the company describes that in the GARNET study, AEs were documented during treatment and until 90 days after the end of treatment or until the initiation of alternative anticancer therapy, whichever occurred earlier. For the ZoptECT study, the company stated that the follow-up observation was 30 days after the last dose of study treatment. In Module 4 A, the company did not provide any information on the actual observation period in the studies. According to the information in the European Public Assessment Report (EPAR), the median treatment duration in the GARNET study was about 26 weeks and according to the information in the study report, the median treatment duration in the ZoptEC study was about 10 weeks. Including the follow-up observation periods, the observation periods in the two studies differ relevantly; the effect estimation via relative risks is therefore not appropriate.

Subgroup analyses on tumour histology

With its comment, the company presented subgroup analyses by tumour histology (endometrioid and non-endometrioid tumours) for the comparison of the GARNET study with the ZoptEC study. Regardless of the relevance of considering these subgroups, given the shortcomings of the indirect comparison, these subgroup analyses are also not interpretable.

2.3 Further comments on GARNET versus registry study 216960

With its comment, the company presented subgroup analyses by tumour histology (endometrioid and non-endometrioid tumours) for the comparison of the GARNET study with the registry study. Regardless of the relevance of considering these subgroups, given the shortcomings of the indirect comparisons, these subgroup analyses are also not interpretable.

Furthermore, as with the comparison of GARNET vs. ZoptEC, the claim to adjust for the number of prior therapies is misleading because patients with > 1 platinum-based prior therapy were excluded from the analysis. The use of the category "unknown" for missing values for confounders is also not suitable (see above).

2.4 Summary

The data subsequently submitted by the company in the commenting procedure have not changed the conclusion on the added benefit of dostarlimab from dossier assessment A21-84.

The following Table 3 shows the result of the benefit assessment of dostarlimab under consideration of dossier assessment A21-84 and the present addendum.

Table 3: Dostarlimab – probability and extent of added benefit

Therapeutic indication	**ACT**[a]	**Probability and extent of added benefit**
Adult patients with dMMR/MSI-H recurrent or advanced endometrial cancer that has progressed during or following prior treatment with a platinum-containing regimen	Treatment of physician's choice[b]	Added benefit not proven

a. Presented is the respective ACT specified by the G-BA.
b. Overall, the following treatment options are considered suitable comparators within the framework of the treatment of physician's choice: endocrine therapy (medroxyprogesterone acetate, megestrol acetate), systemic chemotherapy, which can also be a platinum-based retreatment (cisplatin [monotherapy or in combination with doxorubicin], doxorubicin [monotherapy or in combination with cisplatin], carboplatin + paclitaxel), and BSC alone. BSC refers to the therapy that provides the patient with the best possible, individually optimized, supportive treatment to alleviate symptoms and improve the quality of life.

BSC: best supportive care; dMMR: mismatch repair deficiency; G-BA: Federal Joint Committee; MSI-H: microsatellite instability-high

The G-BA decides on the added benefit.

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Appendix A Results of indirect comparison of individual arms of different studies without common comparator

Table 4: Characteristics of the study populations (not adjusted) – Non-RCT, indirect comparison of individual arms from different studies without common comparator (safety analysis set): GARNET vs. ZoptEC (IDP) (multipage table)

Study characteristic category	Dostarlimab	Doxorubicin
	GARNET	ZoptEC
	N[a] = 129	N[a] = 249
Age [years]		
< 65 years, n (%)	66 (51.2)	133 (53.4)
≥ 65 years, n (%)	63 (48.8)	116 (46.6)
Mean (SD)	63 (9)	64 (9)
Median [min; max]	64 [39; 80]	64 [28; 87]
Family origin, n (%)		
White	98 (76.0)	234 (94.0)
Native Americans or Alaskans	3 (2.3)	1 (0.4)
Asian	5 (3.9)	5 (2.0)
Black or African American	3 (2.3)	7 (2.8)
Not reported	19 (14.7)	0 (0)
Other	0 (0)	2 (0.8)
Unknown	1 (0.8)	0 (0)
ECOG performance status, n (%)		
0	55 (42.6)	121 (48.6)
1	74 (57.4)	116 (46.6)
2	0 (0)	11 (4.4)
Missing	0 (0)	1 (0.4)
Histology, n (%)		
Endometrioid (type I)	85 (65.9)	159 (63.9)
Clear-cell carcinoma	1 (0.8)	4 (1.6)
Mixed carcinoma	7 (5.4)	0 (0)
Serous carcinoma	5 (3.9)	64 (25.7)
Squamous carcinoma	1 (0.8)	0 (0)
Undifferentiated carcinoma	5 (3.9)	0 (0)
Other/unspecified	24 (18.6)	22 (8.8)
Unknown	1 (0.8)	0 (0)

Table 4: Characteristics of the study populations (not adjusted) – Non-RCT, indirect comparison of individual arms from different studies without common comparator (safety analysis set): GARNET vs. ZoptEC (IDP) (multipage table)

Study characteristic category	**Dostarlimab**	**Doxorubicin**
	GARNET	**ZoptEC**
	N[a] = 129	**N[a] = 249**
FIGO stage at first diagnosis[b], n (%)		
Stage I	47 (36.4)	ND
Stage II	10 (7.8)	ND
Stage III	47 (36.4)	ND
Stage IV	25 (19.4)	ND
Advanced (stage III or IV)	ND	ND
Metastatic disease	ND A.	ND
recurrent disease	ND	ND
FIGO stage at (most current)[b], n (%)		
Stage I	13 (10.1)	ND
Stage II	4 (3.1)	ND
Stage III	24 (18.6)	ND
Stage IV	86 (66.7)	ND
Unknown	2 (1.6)	ND
Advanced (stage III or IV)	ND	91 (36.5)
Metastatic disease	ND	90 (36.1)
Recurrent disease	ND	68 (27.3)
Number of prior therapies, n (%)		
1	82 (63.6)	ND
2	32 (24.8)	ND
3	11 (8.5)	ND
≥ 4	4 (3.1)	ND
Prior adjuvant chemotherapy, n (%)	129 (100)	92 (36.9)
Prior surgery, n (%)	116 (89.9)	223 (89.6)
Prior radiotherapy n (%)	94 (72.9)	138 (55.4)

a. Number of included patients (GARNET) or randomized (ZoptEC) patients, who had received at least one dose of the respective study medication. Originally, 129 patients in the GARNET study and 255 patients in the ZoptEC study had been randomized into the doxorubicin arm.
b. FIGO stage at study inclusion.

ECOG: Eastern Cooperative Oncology Group; FIGO: Fédération Internationale de Gynécologie et d'Obstétrique; IPD: individual patient data; max: maximum; min: minimum; N: number of randomized (or included) patients; ND: no data; RCT: randomized controlled trial; SD: standard deviation

Table 5:Characteristics of the study populations (not adjusted) – Non-RCT, indirect comparison of individual arms from different studies without common comparator (main analysis set - analysis population of the IPTW comparison): GARNET vs. ZoptEC (IDP) (multipage table)

Study	**Dostarlimab**	**Doxorubicin**
Characteristic	**GARNET**	**ZoptEC**
Category	**N[a] = 92**	**N[a] = 233**
Age [years]		
< 65 years, n (%)	47 (51.1)	124 (53.2)
≥ 65 years, n (%)	45 (48.9)	109 (46.8)
Mean (SD)	63.3 (8.62)	63.7 (8.89)
Median [min; max]	64.0 [41; 80]	64.0 [28; 87]
Family origin, n (%)		
White	73 (79.3)	218 (93.6)
Native Americans or Alaskans	3 (3.3)	1 (0.4)
Asian	2 (2.2)	5 (2.1)
Black or African American	2 (2.2)	7 (3.0)
Not reported	12 (13.0)	0 (0)
Other	0 (0)	2 (0.9)
ECOG performance status, n (%)		
0	38 (41.3)	119 (51.1)
1	54 (58.7)	114 (48.9)
Histology, n (%)		
Endometrioid (type I)	63 (68.5)	147 (63.1)
Clear-cell carcinoma	1 (1.1)	4 (1.7)
Mixed carcinoma	1 (1.1)	0 (0)
Serous carcinoma	4 (4.3)	61 (26.2)
Squamous carcinoma	1 (1.1)	0 (0)
Undifferentiated carcinoma	4 (4.3)	0 (0)
Other/unspecified	17 (18.5)	21 (9.0)
Unknown	1 (1.1)	0 (0)
FIGO stage at first diagnosis, n (%)		
Stage I	39 (42.4)	ND
Stage II	7 (7.6)	ND
Stage III	30 (32.6)	ND
Stage IV	16 (17.4)	ND
Advanced (stage III or IV)	ND	ND
Metastatic disease	ND	ND
Recurrent disease	ND	ND

Table 5:Characteristics of the study populations (not adjusted) – Non-RCT, indirect comparison of individual arms from different studies without common comparator (main analysis set - analysis population of the IPTW comparison): GARNET vs. ZoptEC (IDP) (multipage table)

Study	**Dostarlimab**	**Doxorubicin**
Characteristic	**GARNET**	**ZoptEC**
Category	**N[a] = 92**	**N[a] = 233**
FIGO stage at (most current)[b], n (%)		
Stage I	ND	ND
Stage II	ND	ND
Stage III	ND	ND
Stage IV	ND	ND
Advanced (stage III or IV)	ND	87 (37.3)
Metastatic disease	ND	82 (35.2)
Recurrent disease	ND	64 (27.5)
Number of prior therapies, n (%)		
1	65 (70.7)	ND
2	21 (22.8)	ND
3	4 (4.3)	ND
≥ 4	2 (2.2)	ND
Prior adjuvant chemotherapy, n (%)	92 (100)	87 (37.3)
Prior surgery, n (%)	83 (90.2)	209 (89.7)
Prior radiotherapy n (%)	65 (70.7)	126 (54.1)

a. Main analysis set: Number of patients included in the IPTW comparison. 37 (29%) patients who had received more than one prior line of platinum therapy were excluded from the GARNET study. 22 (9%) patients were excluded from the ZoptEC study for the following reasons: 6 (2%) had not received study medication, 4 (2%) had been observed for longer than 36 months, 11 (4%) had an ECOG status of 2 and 1 (0.4%) patient had an unknown ECOG status.
b. FIGO stage at study inclusion.

ECOG: Eastern Cooperative Oncology Group; FIGO: Fédération Internationale de Gynécologie et d'Obstétrique; IPD: individual patient data; IPTW: inverse probability of treatment weighting; max: maximum; min: minimum; N: number of patients included in the IPTW comparison; ND: no data; RCT: randomized controlled trial; SD: standard deviation

Table 6: Individual characteristics of the study population (before and after IPTW) – Non-RCT, indirect comparison of individual arms from different studies without common comparator (main analysis set - analysis population of the IPTW comparison): GARNET vs. ZoptEC (IDP)

Covariable	Before IPTW			After IPTW		
	GARNET dostarlimab %[a]	ZoptEC doxorubicin %[a]	standardized difference	GARNET dostarlimab %[a]	ZoptEC doxorubicin %[a]	standardized difference
Family origin: non-white	20.7	6.4	0.42	10.4	10.3	0.00
Age: < 65 years	51.1	53.2	0.04	52.8	53.3	0.01
ECOG: 0	41.3	51.1	0.20	46.1	48.0	0.04
Histology: endometrioid	68.5	63.1	0.11	66.4	64.7	0.04
FIGO: I and II[b]	*50.0*	*62.7*	*0.26*	*56.8*	*58.6*	*0.04*
Prior surgery: no	9.8	10.3	0.02	9.0	10.0	0.03
Disease severity	ND	ND	-	ND	ND	-
Number of previous antineoplastic therapies	ND	ND	-	ND	ND	-
MMR/MSI: yes	100	ND	-	ND	ND	-

a. Based on patients who were included into the IPTW comparison (dostarlimab: N = 92 and doxorubicin: N = 233).
b. In the GARNET study, the FIGO stage at diagnosis was used, while in the ZoptEC study the data on the FIGO stage at study entry were included in the adjustment. In addition, the company assigned patients in the ZoptEC study with the dimension "advanced (stage III and IV) to the dimension "FIGO stage III and IV" for the adjustment. It assigned the remaining patients to FIGO stages I and II using the formula "FIGO stages I and II are equal to N - stages III and IV". This approach is not appropriate as, among other things, it assigns patients with metastatic disease to FIGO stages I and II.

ECOG: Eastern Cooperative Oncology Group; FIGO: Fédération Internationale de Gynécologie et d'Obstétrique; IPD: individual patient data; IPTW: inverse probability of treatment weighting; RCT: randomized controlled trial

Table 7: Results on "overall survival" (time to event) – Non-RCT, indirect comparison of individual arms from different studies without common comparator: GARNET vs. ZoptEC (IDP)

Outcome category outcome	GARNET dostarlimab		ZoptEC doxorubicin		Dostarlimab vs. doxorubicin
	N[a]	median time to event in months [95% CI] patients with event n (%)	N[a]	median time to event in months [95% CI] patients with event n (%)	HR [95% CI]; p-value[b]
Mortality					
Overall survival	92	NA [18.00; NC] 31 (33.7)	233	11.17 [9.99; 13.08] 177 (76.0)	0.41 [0.28; 0.61]; < 0.001

a. Number of patients included in the IPTW comparison.
b: HR and 95% CI and p-value: weighted Cox proportional hazards model with weights after stabilized IPTW.

CI: confidence interval; HR: hazard ratio; IPD: individual patient data; IPTW: inverse probability of treatment weighting; n: number of patients with event; N: number of analysed patients; NC: not calculable; NR: not reached; RCT: randomized controlled trial

Table 8: Characteristics of the study populations (before IPTW) – Non-RCT, indirect comparison of individual arms without common comparator: GARNET vs. registry cohort 1 (IPD) (multipage table)

Study characteristic category	GARNET	NCRAS (England) cohort 1	Standardized difference	p-value[a]
	dostarlimab	comparator		
	N = 129	N = 999		
Age, n (%)				
< 65 years	66 (51.2)	445 (44.5)	0.13	0.184
≥ 65 years	63 (48.8)	554 (55.5)	-0.13	
Family origin, n (%)				
White	98 (76.0)	841 (84.2)	-0.21	< 0.001
Black	3 (2.3)	55 (5.5)	-0.16	
Other	8 (6.2)	78 (7.8)	-0.06	
Unknown	20 (15.5)	25 (2.5)	0.47	
ECOG performance status, n (%)				
0	55 (42.6)	320 (32.0)	0.22	< 0.001
1	74 (57.4)	181 (18.1)	0.89	
Unknown	0 (0)	498 (49.8)	ND	
Histology at first diagnosis, n (%)				
Endometrioid	90 (69.8)	424 (42.4)	0.57	< 0.001
Non-endometrioid	38 (29.5)	575 (57.6)	-0.59	
Unknown	1 (0.8)	0 (0)		

Table 8: Characteristics of the study populations (before IPTW) – Non-RCT, indirect comparison of individual arms without common comparator: GARNET vs. registry cohort 1 (IPD) (multipage table)

Study characteristic category	GARNET	NCRAS (England) cohort 1	Standardized difference	p-value[a]
	dostarlimab	comparator		
	N = 129	N = 999		
FIGO stage at first diagnosis, n (%)				
Stage I/II	57 (44.2)	221 (22.1)	0.48	< 0.001
Stage III/IV	72 (55.8)	778 (77.9)	-0.48	
FIGO stage (most current), n (%)				
Stage I/II	17 (13.2)[b]	ND	–	–
Stage III/IV	110 (85.3)[b]	ND	–	
Unknown	2 (1.6)	ND	–	
Disease stage at first diagnosis, n (%)				
Grade 1/2	87 (67.4)	274 (27.4)	0.87	< 0.001
Grade 3/4	36 (27.9)	389 (38.9)	-0.24	
Unknown	6 (4.7)	336 (33.6)	-0.79	
Number of platinum-based therapies in an advanced/recurrent stage, n (%)				
0	2 (1.6)	0 (0)	ND	< 0.001
1	110 (85.3)	999 (100.0)	-0.59	
≥ 2	17 (13.2)	0 (0)	ND A.	
Surgery for advanced or recurrent endometrial cancer, n (%)				
Yes	116 (89.9)	815 (81.6)	0.24	0.026
No	13 (10.1)	184 (18.4)	-0.24	

a. Chi-square test.
b. Institute's calculation.

ECOG: Eastern Cooperative Oncology Group; FIGO: Fédération Internationale de Gynécologie et d'Obstétrique; IPD: individual patient data; IPTW: inverse probability of treatment weighting; N: number of patients included; NCRAS: National Cancer Registration and Analysis Service; ND: not data; RCT: randomized controlled trial

Table 9: Characteristics of the study populations (before IPTW) – Non-RCT, indirect comparison of individual arms without common comparator: GARNET vs. registry cohort 2, ECOG ≤ 1 (IPD) (multipage table)

Study Characteristic Category	GARNET	NCRAS (England) cohort 2, ECOG ≤ 1	Standardized difference	p-value[a]
	Dostarlimab	Comparator		
	N = 129	N = 501		
Age, n (%)				
< 65 years	66 (51.2)	211 (42.1)	0.18	0.081
≥ 65 years	63 (48.8)	290 (57.9)	-0.18	
Family origin, n (%)				
White	98 (76.0)	439 (87.6)	-0.31	< 0.001
Black	3 (2.3)	19 (3.8)	-0.09	
Other	8 (6.2)	33 (6.6)	-0.02	
Unknown	20 (15.5)	10 (2.0)	0.49	
ECOG performance status, n (%)				
0	55 (42.6)	320 (63.9)	-0.44	< 0.001
1	74 (57.4)	181 (36.1)	0.44	
Histology at first diagnosis, n (%)				
Endometrioid	90 (69.8)	213 (42.5)	0.57	< 0.001
Non-endometrioid	38 (29.5)	288 (57.5)	-0.59	
Unknown	1 (0.8)	0 (0)	ND	
FIGO stage at first diagnosis, n (%)				
Stage I/II	57 (44.2)	121 (24.2)	0.43	< 0.001
Stage III/IV	72 (55.8)	380 (75.8)	-0.43	
FIGO stage (most current), n (%)				
Stage I/II	17 (13.2)[b]	ND	–	–
Stage III/IV	110 (85.3)[b]	ND	–	
Unknown	2 (1.6)	ND	–	
Disease stage at first diagnosis, n (%)				
Grade 1/2	87 (67.4)	141 (28.1)	0.86	< 0.001
Grade 3/4	36 (27.9)	206 (41.1)	-0.28	
Unknown	6 (4.7)	154 (30.7)	-0.73	
Number of platinum-based therapies in an advanced/recurrent stage, n (%)				
0	2 (1.6)	0 (0)	ND	< 0.001
1	110 (85.3)	501 (100.0)	-0.59	
≥ 2	17 (13.2)	0 (0)	ND	
Surgery for advanced or recurrent endometrial cancer, n (%)				
Yes	116 (89.9)	413 (82.4)	0.22	0.053
No	13 (10.1)	88 (17.6)	-0.22	

Table 9: Characteristics of the study populations (before IPTW) – Non-RCT, indirect comparison of individual arms without common comparator: GARNET vs. registry cohort 2, ECOG ≤ 1 (IPD) (multipage table)

Study Characteristic Category	GARNET	NCRAS (England) cohort 2, ECOG ≤ 1	Standardized difference	p-value[a]
	Dostarlimab	Comparator		
	N = 129	N = 501		

a. Chi-square test.
b. Institute's calculation.

ECOG: Eastern Cooperative Oncology Group; FIGO: Fédération Internationale de Gynécologie et d'Obstétrique; IPD: individual patient data; IPTW: inverse probability of treatment weighting; N: number of patients included; NCRAS: National Cancer Registration and Analysis Service; ND: not data; RCT: randomized controlled trial

Table 10: Characteristics of the study populations (after IPTW) – Non-RCT, indirect comparison of individual arms without common comparator: GARNET vs. registry cohort 1 (IPD) (Propensity Score Model 1a – ATE) (multipage table)

Study characteristic category	GARNET	NCRAS (England) cohort 1	Standardized difference	p-value[c]
	dostarlimab	comparator		
	N[b] = 109	N = 999		
Age, %				
< 65 years	45.4	45.5	-0.00	> 0.999
≥ 65 years	54.6	54.5	0.00	
Family origin, %				
White	72.7	84.3	-0.28	< 0.001
Black	1.8	5.4	-0.19	
Other	5.5	7.8	-0.09	
Unknown	19.9	2.6	0.57	
ECOG PS, %				
0	51.3	32.2	0.39	< 0.001
1	48.7	18.1	0.69	
Unknown	0	49.7	ND	
Histology at first diagnosis, %				
Endometrioid	55.7	45.4	0.21	< 0.001
Non-endometrioid	44.3	54.6	-0.21	
FIGO stage at first diagnosis, %				
Stage I/II	34.3	22.9	0.25	< 0.001
Stage III/IV	65.7	77.1	-0.25	

Table 10: Characteristics of the study populations (after IPTW) – Non-RCT, indirect comparison of individual arms without common comparator: GARNET vs. registry cohort 1 (IPD) (Propensity Score Model 1a – ATE) (multipage table)

Study characteristic category	GARNET	NCRAS (England) cohort 1	Standardized difference	p-value[c]
	dostarlimab	comparator		
	N[b] = 109	N = 999		
FIGO stage (most current), %	ND	ND	–	–
Disease stage at first diagnosis, %				
Grade 1/2	31.7	31.5	0.01	0.758
Grade 3/4	38.8	37.6	0.02	
Unknown	29.5	30.9	-0.03	
Number of platinum-based therapies in an advanced/recurrent stage, %				
1	100	100	0	–
Surgery for advanced or recurrent endometrial cancer, %				
Yes	79.9	81.8	-0.05	0.273
No	20.1	18.2	0.05	

a. The following covariates were used for IPTW in scenario 1: stage of disease at first diagnosis, histology at first diagnosis and number of platinum-based therapies in an advanced/recurrent stage. However, the variable "number of platinum-based therapies in the advanced/recurrent stage" has no influence, as all patients in the analysis population received one therapy.
b. One patient with missing histology and 19 patients with 0 or ≥ 2 platinum-based therapies were excluded from the GARNET study.
c. Chi-square test.

ATE: average treatment effect; ECOG: Eastern Cooperative Oncology Group; FIGO: Fédération Internationale de Gynécologie et d'Obstétrique; IPD: individual patient data; IPTW: inverse probability of treatment weighting; N: number of patients included; NCRAS: National Cancer Registration and Analysis Service; ND: not data; RCT: randomized controlled trial

Table 11: Characteristics of the study populations (after IPTW) – Non-RCT, indirect comparison of individual arms without common comparator: GARNET vs. registry cohort 1 (IPD) (Propensity Score Model 2a – ATE) (multipage table)

Study characteristic category	GARNET	NCRAS (England) cohort 1	Standardized difference	p-value[c]
	dostarlimab	comparator		
	N[b] = 109	N = 999		
Age, %				
< 65 years	49.0	45.2	0.08	0.077
≥ 65 years	51.0	54.8	-0.08	

Table 11: Characteristics of the study populations (after IPTW) – Non-RCT, indirect comparison of individual arms without common comparator: GARNET vs. registry cohort 1 (IPD) (Propensity Score Model 2a – ATE) (multipage table)

Study characteristic category	GARNET	NCRAS (England) cohort 1	Standardized difference	p-value[c]
	dostarlimab	comparator		
	N[b] = 109	N = 999		
Family origin, %				
White	77.6	84.2	-0.17	< 0.001
Black	2.4	5.4	-0.16	
Other	7.2	7.9	-0.03	
Unknown	12.8	2.6	0.39	
ECOG PS, %				
0	41.3	32.1	0.19	< 0.001
1	58.7	18.0	0.92	
Unknown	0	49.8	ND	
Histology at first diagnosis, (%)				
Endometrioid	45.4	45.4	0.00	> 0.99
Non-endometrioid	54.6	54.6	-0.00	
FIGO stage at first diagnosis, (%)				
Stage I/II	41.7	22.6	0.42	< 0.001
Stage III/IV	58.3	77.4	-0.42	
FIGO stage (most current), (%)	ND	ND	–	–
Disease stage at first diagnosis, (%)				
Grade 1/2	50.6	28.9	0.45	< 0.001
Grade 3/4	43.5	38.9	0.09	
Unknown	5.9	32.2	-0.71	
Number of platinum-based therapies in an advanced/recurrent stage, (%)				
1	100	100	0	–
Surgery for advanced or recurrent endometrial cancer, %				
Yes	89.9	81.7	0.24	< 0.001
No	10.1	18.3	-0.24	

a. The following covariates were used for IPTW in scenario 2: histology at first diagnosis and number of platinum-based therapies in an advanced/recurrent stage. However, the variable "number of platinum-based therapies in the advanced/recurrent stage" has no influence, as all patients in the analysis population received one therapy.
b. One patient with missing histology and 19 patients with 0 or ≥ 2 platinum-based therapies were excluded from the GARNET study.
c. Chi-square test.

ATE: average treatment effect; ECOG: Eastern Cooperative Oncology Group; FIGO: Fédération Internationale de Gynécologie et d'Obstétrique; IPD: individual patient data; IPTW: inverse probability of treatment weighting; N: number of patients included; NCRAS: National Cancer Registration and Analysis Service; ND: not data; RCT: randomized controlled trial

Table 12: Characteristics of the study populations (after IPTW) – Non-RCT, indirect comparison of individual arms without common comparator: GARNET vs. registry cohort 1 (IPD) (Propensity Score Model 3a – ATE) (multipage table)

Study characteristic category	GARNET	NCRAS (England) cohort 1	Standardized difference	p-value[c]
	dostarlimab	comparator		
	N[b] = 128	N = 999		
Age, %				
< 65 years	55.9	45.4	0.21	< 0.001
≥ 65 years	44.1	54.6	-0.21	
Family origin, %				
White	83.7	83.3	0.01	0.889
Black	4.6	5.1	-0.03	
Other	8.0	7.5	0.02	
Unknown	3.8	4.1	-0.01	
ECOG PS, %				
0	38.9	32.3	0.14	< 0.001
1	61.1	18.0	0.98	
Unknown	0	49.8	ND	
Histology at first diagnosis, (%)				
Endometrioid	42.4	45.6	-0.06	0.137
Non-endometrioid	57.6	54.4	0.06	
FIGO stage at first diagnosis, (%)				
Stage I/II	23.4	24.8	-0.03	0.467
Stage III/IV	76.6	75.2	0.03	
FIGO stage (most current), (%)	ND	ND	–	–
Disease stage at first diagnosis, (%)				
Grade 1/2	45.8	29.3	0.35	< 0.001
Grade 3/4	48.6	38.9	0.20	
Unknown	5.6	31.9	-0.71	
Number of platinum-based therapies in an advanced/recurrent stage, (%)				
0	1.9	0	–	< 0.001
1	79.7	100	-0.71	
≥ 2	18.4	0	–	
Surgery for advanced or recurrent endometrial cancer, %				
Yes	82.2	82.6	-0.01	0.848
No	17.8	17.4	0.01	

Table 12: Characteristics of the study populations (after IPTW) – Non-RCT, indirect comparison of individual arms without common comparator: GARNET vs. registry cohort 1 (IPD) (Propensity Score Model 3a – ATE) (multipage table)

Study characteristic category	GARNET	NCRAS (England) cohort 1	Standardized difference	p-value[c]
	dostarlimab	comparator		
	N[b] = 128	N = 999		

a. The following covariates were used for IPTW in scenario 3: family origin, FIGO stage at first diagnosis, histology at first diagnosis and prior surgery for the advanced/recurrent endometrial cancer.
b. One patient with missing histology was excluded from the GARNET study.
c. Chi-square test.

ATE: average treatment effect; ECOG: Eastern Cooperative Oncology Group; FIGO: Fédération Internationale de Gynécologie et d'Obstétrique; IPD: individual patient data; IPTW: inverse probability of treatment weighting; N: number of patients included; NCRAS: National Cancer Registration and Analysis Service; ND: not data; RCT: randomized controlled trial

Table 13; Characteristics of the study populations (after IPTW) – Non-RCT, indirect comparison of individual arms without common comparator: GARNET vs. registry cohort 2, ECOG ≤ 1 (IPD) (Propensity Score Model 1a – ATE) (multipage table)

Study characteristic category	GARNET	NCRAS (England) cohort 2, ECOG ≤ 1	Standardized difference	p-value[c]
	dostarlimab	comparator		
	N[b] = 109	N = 501		
Age, %				
< 65 years	46.2	43.7	0.05	0.418
≥ 65 years	53.8	56.3	-0.05	
Family origin, %				
White	73.6	87.9	-0.37	< 0.001
Black	2.0	3.5	-0.09	
Other	5.9	6.5	-0.02	
Unknown	18.6	2.1	0.56	
ECOG PS, %				
0	49.6	64.2	-0.30	< 0.001
1	50.4	35.8	0.30	
Histology at first diagnosis, (%)				
Endometrioid	54.9	47.8	0.14	0.016
Non-endometrioid	45.1	52.2	-0.14	
FIGO stage at first diagnosis, (%)				
Stage I/II	35.9	26.1	0.21	< 0.001
Stage III/IV	64.1	73.9	-0.21	

Table 13; Characteristics of the study populations (after IPTW) – Non-RCT, indirect comparison of individual arms without common comparator: GARNET vs. registry cohort 2, ECOG ≤ 1 (IPD) (Propensity Score Model 1a – ATE) (multipage table)

Study characteristic category	**GARNET**	**NCRAS (England) cohort 2, ECOG ≤ 1**	**Standardized difference**	**p-value[c]**
	dostarlimab	**comparator**		
	N[b] = 109	**N = 501**		
FIGO stage (most current), (%)	ND	ND	–	–
Disease stage at first diagnosis, (%)				
Grade 1/2	35.8	35.4	0.01	0.652
Grade 3/4	40.2	38.4	0.04	
Unknown	24.0	26.2	-0.05	
Number of platinum-based therapies in an advanced/recurrent stage, (%)				
1	100	100	0	–
Surgery for advanced or recurrent endometrial cancer, %				
Yes	82.2	82.9	-0.02	0.788
No	17.8	17.1	0.02	

a. The following covariates were used for IPTW in scenario 1: stage of disease at first diagnosis, histology at first diagnosis and number of platinum-based therapies in an advanced/recurrent stage. However, the variable "number of platinum-based therapies in the advanced/recurrent stage" has no influence, as all patients in the analysis population received one therapy.
b. One patient with missing histology and 19 patients with 0 or ≥ 2 platinum-based therapies were excluded from the GARNET study.
c. Chi-square test.

ATE: average treatment effect; ECOG: Eastern Cooperative Oncology Group; FIGO: Fédération Internationale de Gynécologie et d'Obstétrique; IPD: individual patient data; IPTW: inverse probability of treatment weighting; N: number of patients included; NCRAS: National Cancer Registration and Analysis Service; ND: not data; RCT: randomized controlled trial

Table 14: Characteristics of the study populations (after IPTW) – Non-RCT, indirect comparison of individual arms without common comparator: GARNET vs. registry cohort 2, ECOG ≤ 1 (IPD) (Propensity Score Model 2a – ATE) (multipage table)

Study characteristic category	GARNET	NCRAS (England) cohort 2, ECOG ≤ 1	Standardized difference	p-value[c]
	dostarlimab	comparator		
	N[b] = 109	N = 501		
Age, %				
< 65 years	49.2	43.3	0.12	0.046
≥ 65 years	50.8	56.7	-0.12	
Family origin, %				
White	77.5	87.7	-0.27	< 0.001
Black	2.3	3.5	-0.07	
Other	7.0	6.7	-0.01	
Unknown	13.2	2.0	0.43	
ECOG PS, %				
0	41.5	64.2	-0.47	< 0.001
1	58.5	35.8	0.47	
Histology at first diagnosis, (%)				
Endometrioid	47.9	47.9	0.00	> 0.999
Non-endometrioid	52.1	52.1	-0.00	
FIGO stage at first diagnosis, (%)				
Stage I/II	42.3	25.2	0.37	< 0.001
Stage III/IV	57.7	74.8	-0.37	
FIGO stage (most current), (%)	ND	ND	–	–
Disease stage at first diagnosis, (%)				
Grade 1/2	52.2	30.8	0.45	< 0.001
Grade 3/4	41.9	40.7	0.02	
Unknown	5.9	28.5	-0.63	
Number of platinum-based therapies in an advanced/recurrent stage, (%)				
1	100	100	0	–
Surgery for advanced or recurrent endometrial cancer, %				
Yes	89.9	82.6	0.21	< 0.001
No	10.1	17.4	-0.21	

Table 14: Characteristics of the study populations (after IPTW) – Non-RCT, indirect comparison of individual arms without common comparator: GARNET vs. registry cohort 2, ECOG ≤ 1 (IPD) (Propensity Score Model 2a – ATE) (multipage table)

Study characteristic category	GARNET	NCRAS (England) cohort 2, ECOG ≤ 1	Standardized difference	p-value[c]
	dostarlimab	comparator		
	N[b] = 109	N = 501		

a. The following covariates were used for IPTW in scenario 2: histology at first diagnosis and number of platinum-based therapies in an advanced/recurrent stage. However, the variable "number of platinum-based therapies in the advanced/recurrent stage" has no influence, as all patients in the analysis population received one therapy.
b. One patient with missing histology and 19 patients with 0 or ≥ 2 platinum-based therapies were excluded from the GARNET study.
c. Chi-square test.

ATE: average treatment effect; ECOG: Eastern Cooperative Oncology Group; FIGO: Fédération Internationale de Gynécologie et d'Obstétrique; IPD: individual patient data; IPTW: inverse probability of treatment weighting; N: number of patients included; NCRAS: National Cancer Registration and Analysis Service; ND: not data; RCT: randomized controlled trial

Table 15: Characteristics of the study populations (after IPTW) – Non-RCT, indirect comparison of individual arms without common comparator: GARNET vs. registry cohort 2, ECOG ≤ 1 (IPD) (Propensity Score Model 3a – ATE) (multipage table)

Study characteristic category	GARNET	NCRAS (England) cohort 2, ECOG ≤ 1	Standardized difference	p-value[c]
	dostarlimab	comparator		
	N[b] = 128	N = 501		
Age, %				
< 65 years	47.8	44.0	0.08	0.195
≥ 65 years	52.2	56.0	-0.08	
Family origin, %				
White	84.0	84.8	-0.02	0.702
Black	4.5	3.5	0.05	
Other	6.9	6.3	0.02	
Unknown	4.7	5.4	-0.04	
ECOG PS, %				
0	60.0	59.0	0.02	0.766
1	40.0	41.0	-0.02	
Histology at first diagnosis, (%)				
Endometrioid	43.7	48.2	-0.09	0.116
Non-endometrioid	56.3	51.8	0.09	
FIGO stage at first diagnosis, (%)				
Stage I/II	26.2	29.2	-0.07	0.242
Stage III/IV	73.8	70.8	0.07	

Table 15: Characteristics of the study populations (after IPTW) – Non-RCT, indirect comparison of individual arms without common comparator: GARNET vs. registry cohort 2, ECOG ≤ 1 (IPD) (Propensity Score Model 3a – ATE) (multipage table)

Study characteristic category	**GARNET**	**NCRAS (England) cohort 2, ECOG ≤ 1**	**Standardized difference**	**p-value[c]**
	dostarlimab	**comparator**		
	N[b] = 128	**N = 501**		
FIGO stage (most current), (%)	ND	ND	–	–
Disease stage at first diagnosis, (%)				
Grade 1/2	43.3	31.5	0.25	< 0.001
Grade 3/4	50.6	40.6	0.20	
Unknown	6.1	27.9	-0.61	
Number of platinum-based therapies in an advanced/recurrent stage, (%)				
0	1.2	0	ND	< 0.001
1	83.2	100	-0.64	
2	15.6	0	ND	
Surgery for advanced or recurrent endometrial cancer, %				
Yes	81.6	84.1	-0.07	0.260
No	18.4	15.9	0.07	

a. The following covariates were used for IPTW in scenario 3: family origin, ECOG PS, FIGO stage at first diagnosis, histology at first diagnosis and prior surgery for the advanced/recurrent endometrial cancer.
b. One patient with missing histology was excluded from the GARNET study.
c. Chi-square test.

ATE: average treatment effect; ECOG: Eastern Cooperative Oncology Group; FIGO: Fédération Internationale de Gynécologie et d'Obstétrique; IPD: individual patient data; IPTW: inverse probability of treatment weighting; N: number of patients included; NCRAS: National Cancer Registration and Analysis Service; ND: not data; RCT: randomized controlled trial

Table 16: Results on "overall survival" (time to event) – Non-RCT, indirect comparison of individual arms without common comparator: GARNET vs. registry (IPD)

Cohort	Median time to event in months [95 % CI] ATE GARNET/dostarlimab	Median time to event in months [95 % CI] ATE registry study	HR [95% CI][a] ATE	P-value[a] ATE
Cohort 1[b], unadjusted	NA [18.4; NC]	10.3 [9.2; 11.1]	0.38 [0.27; 0.53]	< 0.001
Cohort 1[b], scenario 1[b]	NA [15.4; NC]	10.3 [9.3; 11.1]	0.44 [0.39; 0.50]	< 0.001
Cohort 1[b], scenario 2[b]	NA [18.0; NC]	10.3 [9.2; 11.1]	0.35 [0.30; 0.40]	< 0.001
Cohort 1[b], scenario 3[b]	NA [21.6; NC]	10.3 [9.2; 11.1]	0.31 [0.27; 0.36]	< 0.001
Cohort 2[b], unadjusted	NA [18.4; NC]	10.3 [9.0; 11.1]	0.38 [0.27; 0.53]	< 0.001
Cohort 2[b], scenario 1[b]	NA [15.4; NC]	10.3 [9.1; 11.2]	0.41 [0.35; 0.49]	< 0.001
Cohort 2[b], scenario 2[b]	NA [18.0; NC]	10.3 [9.1; 11.1]	0.35 [0.29; 0.42]	< 0.001
Cohort 2[b], scenario 3[b]	NA [21.6; NC]	10.3 [8.9; 11.1]	0.25 [0.21; 0.31]	< 0.001

b: HR, 95% CI and p-value: weighted Cox proportional hazards model with weights after stabilized IPTW with the covariables of the respective scenario.
b. Cohort 1 of the registry included patients whose ECOG status was 0, 1 or not documented (N = 999). Cohort 2 of the registry only included patients whose ECOG status was ≤ 1 (N = 501). The used prognostic factors in the individual scenarios were:
Scenario 1: disease stage at first diagnosis, histology at first diagnosis and number of prior platinum-based chemotherapies. However, the variable "number of platinum-based therapies in the advanced/recurrent stage" has no influence, as all patients in the analysis population received one therapy.
Scenario 2: histology at first diagnosis and number of prior platinum-based chemotherapies. However, the variable "number of platinum-based therapies in the advanced/recurrent stage" has no influence, as all patients in the analysis population received one therapy.
Scenario 3: family origin, ECOG PS (only for cohort 2), FIGO stage at first diagnosis, histology at first diagnosis and prior surgery for the advanced/recurrent endometrial cancer.

ATE: average treatment effect; CI: confidence interval; ECOG: Eastern Cooperative Oncology Group; HR: hazard ratio; IPD: individual patient data; N: number of analysed patients; NA: not reached; NC: not calculable; RCT: randomized controlled trial