

Supplementary Materials

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Supplementary Methods

Datasets

Patient diagnoses, characteristics, and vital stats data were selected from the National Cancer Registration and Analysis Service dataset,[1] with linked systemic anti-cancer therapy data coming from the Systemic Anti-Cancer Therapy dataset.[2] The data collected by the National Cancer Registration and Analysis Service comes from several sources such as multidisciplinary team meetings, pathology reports, molecular testing results, treatment records, hospital records and patient administration systems and operational standards such as cancer waiting times. Patients are primarily identified via their National Health Service number. The Office for National Statistics supplies the cause and date of death for deceased patients.[1]

Algorithm for approximation of lines of therapy

An algorithm was used to approximate lines of therapy for the data extracted from the Systemic Anti-Cancer Therapy dataset [1] and the rules are summarized as follows:

- 1) A treatment switch was identified if the following applied:
 - a. The treatment-free period between two consecutive regimens totaled ≤ 90 days in duration; and,
 - b. One or more drugs prescribed in the previous regimen were no longer prescribed at the subsequent regimen; and,
 - c. One or more drugs not prescribed in the previous regimen were initiated at the subsequent regimen
- 2) An add-on was identified if the following applied:
 - a. The treatment-free period between two consecutive regimens totalled ≤ 90 days in duration; and,
 - b. All drugs from the previous regimen are still prescribed in the subsequent regimen; and,
 - c. One or more drugs not prescribed at the previous regimen were initiated.
- 3) No change in treatment-line was identified in two instances if the following applied:
 - a. The treatment-free period between two regimens totalled ≤ 90 days in duration; and,

- b. There was no change in the drug(s) prescribed between two consecutive regimens; or,
 - c. One or more drugs prescribed in the previous regimen were no longer prescribed at the subsequent regimen, but no other drugs are initiated.
- 4) Treatment discontinuation was identified if the following applied:
- a. Any treatment, whether similar or different, initiated >90 days after a treatment discontinuation, and thereby considered initiation of a new line of therapy.

As Systemic Anti-Cancer Therapy does not include dates that patients stopped receiving treatments, the treatment-free period between consecutive regimens was defined as the interval in days between the start date of a regimen, which is recorded within Systemic Anti-Cancer Therapy, and the date of the last known administration (or cycle) within that regimen.

Definitions of endpoints

Overall survival was defined as the time from initiation of dostarlimab (GARNET cohort) or second-line therapy (overall real-world cohort) to the date of death by any cause.

For the GARNET cohort, progression-free survival was defined as the date of first dostarlimab dose to earliest date of assessment of progression or death by any cause in the absence of progression according to Response Evaluation Criteria in Solid Tumors v1.1 by blinded independent central review.

Time-to-next treatment was defined from the date of initiation of second-line therapy until failure (the earliest date of all-cause death or the start of a new line of treatment). Time-to-treatment discontinuation was defined from the initiation of second-line therapy to the earliest of the end date of second-line treatment followed by a gap in systemic therapy treatment that was >90 days, or death.

Selection of matching variables

A targeted literature review was conducted in May 2020 to identify prognostic variables associated with endometrial cancer survival.[3-14] The list of prognostic variables was validated by a panel of oncologists from Germany, the UK, and Canada. The factors deemed important were race, age, Eastern Cooperative Oncology Group (ECOG) performance status, histology at diagnosis, Federation of Gynecology and Obstetrics (FIGO) stage, disease grade at diagnosis, number of prior platinum-based chemotherapies in the advanced/recurrent setting, and prior surgery. Mismatch repair/microsatellite

instability status was also deemed important but was not included as a matching variable due to limiting reporting in the National Cancer Registration and Analysis Service.

Matching scenarios

Scenario 1 included the matching variables of histology, disease grade, and number of prior platinum-based chemotherapies. Scenario 2 also included histology and number of prior platinum-based chemotherapies, but not disease grade since this was poorly recorded in constituent datasets of the National Cancer Registration and Analysis Service. Scenario 3 included variables identified as statistically significant by empirical regression analyses for overall survival and progression-free survival (and progression-free survival proxies), which were race, ECOG performance status, histology, FIGO stage at initial diagnosis, and surgery.

Statistical analysis

A Cox proportional-hazards with weights obtained by the matching-adjusted indirect comparison method was used to re-estimate overall survival hazard ratios for the GARNET cohort versus the real-world cohorts; this assumption was tested prior to estimating overall survival hazard ratios by log cumulative hazard plots and Schoenfeld residual plots. In addition, overall survival and secondary endpoints were summarized descriptively using Kaplan-Meier methodology, with weighted GARNET individual patient data from the matched real-world populations versus the real-world cohort. A Cox proportional-hazards comparison was not used for secondary endpoints due to both the use of time-to-next treatment and time-to-treatment discontinuation as a proxy for progression-free survival and the time-period of evaluations for the real-world cohort being too dissimilar to those in GARNET. All analyses, including calculation of matching-adjusted indirect comparison weights, were performed in R language, version 3.6.2.

Supplementary Tables

Supplementary Table 1. Overall survival for overall real-world cohort and the real-world cohort of patients with known ECOG performance status ≤ 1

Overall real-world cohort* (N=999)				
	GARNET (dostarlimab) cohort before matching (N=153)	Scenario 1 (ESS=18)	Scenario 2 (ESS=62)	Scenario 3 (ESS=67)
OS HR (95% CI)	0.32 (0.24–0.42)	0.47 (0.22–0.99)	0.30 (0.20–0.47)	0.31 (0.21–0.46)
P-value	<0.0001	0.0481	<0.0001	<0.0001
Real-world cohort ECOG performance status ≤ 1 (N=501)				
	GARNET (dostarlimab) cohort before matching (N=153)	Scenario 1 (ESS=21)	Scenario 2 (ESS=62)	Scenario 3 (ESS=52)
OS HR (95% CI)	0.32 (0.24–0.42)	0.45 (0.22–0.95)	0.30 (0.20–0.47)	0.26 (0.17–0.40)
P-value	<0.0001	0.0357	<0.0001	<0.0001

Scenario 1: Matching variables are histology, grade, and number of prior platinum-based therapies; scenario 2: Matching variables are histology and number of prior platinum-based therapies; scenario 3: Matching variables are race, histology, stage at initial diagnosis, and surgery (ECOG performance status was not included as a matching variable due to patients with unknown status). *Including patients with unknown ECOG performance status.

CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; ESS, effective sample size; HR, hazard ratio; OS, overall survival.

Supplementary Table 2. Overall survival for real-world comparator treatments and the GARNET (dostarlimab, ITT) cohort after matching

	Real-world cohort (95% CI)	GARNET (dostarlimab) cohort (95% CI)		
	Paclitaxel monotherapy (N=116)	Scenario 1 (ESS=16)	Scenario 2 (ESS=59)	Scenario 3 (ESS=50)
Median OS, months	6.6 (5.7–8.0)	19.5 (6.4–NE)	40.5 (19.4–NE)	NE (21.6–NE)
OS rate				
6 months	0.54 (0.44–0.62)	0.88 (0.71–0.95)	0.88 (0.77–0.94)	0.92 (0.85–0.96)
12 months	0.28 (0.20–0.37)	0.58 (0.27–0.80)	0.75 (0.62–0.84)	0.79 (0.66–0.88)
18 months	0.15 (0.09–0.23)	0.55 (0.26–0.77)	0.70 (0.56–0.80)	0.72 (0.58–0.82)
HR for OS	-	0.36 (0.16–0.83)	0.21 (0.12–0.36)	0.18 (0.11–0.31)
<i>P-value</i>	-	0.0155	<0.0001	<0.0001
	Carboplatin + paclitaxel (N=279)	Scenario 1 (ESS=20)	Scenario 2 (ESS=61)	Scenario 3 (ESS=64)
Median OS, months	14.2 (12.4–16.1)	39.9 (6.4–NE)	40.5 (19.4–NE)	NE (21.6–NE)
OS rate				
6 months	0.83 (0.78–0.87)	0.88 (0.73–0.95)	0.88 (0.78–0.93)	0.91 (0.81–0.96)
12 months	0.58 (0.51–0.64)	0.60 (0.30–0.80)	0.75 (0.62–0.84)	0.79 (0.67–0.87)
18 months	0.37 (0.31–0.44)	0.57 (0.29–0.77)	0.70 (0.57–0.80)	0.69 (0.55–0.79)
HR for OS	-	0.61 (0.28–1.32)	0.40 (0.26–0.63)	0.42 (0.26–0.62)
<i>P-value</i>	-	0.2120	<0.0001	<0.0001
	Carboplatin + liposomal doxorubicin (N=141)	Scenario 1 (ESS=14)	Scenario 2 (ESS=57)	Scenario 3 (ESS=63)
Median OS, months	13.9 (11.2–15.7)	19.5 (6.4–NE)	40.5 (19.4–NE)	40.5 (21.6–NE)
OS rate				
6 months	0.86 (0.79–0.91)	0.88 (0.71–0.96)	0.88 (0.77–0.94)	0.91 (0.82–0.95)
12 months	0.57 (0.48–0.65)	0.56 (0.23–0.79)	0.75 (0.62–0.84)	0.78 (0.66–0.87)
18 months	0.39 (0.30–0.47)	0.53 (0.22–0.76)	0.70 (0.56–0.81)	0.70 (0.56–0.80)
HR for OS	-	0.66 (0.26–1.65)	0.37 (0.22–0.63)	0.38 (0.23–0.61)
<i>P-value</i>	-	0.3710	0.0002	<0.0001
	Liposomal doxorubicin monotherapy (N=130)	Scenario 1 (ESS=21)	Scenario 2 (ESS=65)	Scenario 3 (ESS=67)

Median OS, months	4.9 (4.2–6.1)	39.9 (6.4–NE)	40.5 (19.4–NE)	39.9 (21.6–NE)
OS rate				
6 months	0.41 (0.33–0.50)	0.87 (0.72–0.95)	0.87 (0.78–0.93)	0.90 (0.83–0.94)
12 months	0.16 (0.10–0.23)	0.60 (0.32–0.80)	0.75 (0.62–0.84)	0.76 (0.63–0.85)
18 months	-	0.57 (0.30–0.77)	0.70 (0.57–0.80)	0.69 (0.56–0.79)
HR for OS	-	0.29 (0.13–0.63)	0.17 (0.10–0.29)	0.16 (0.09–0.27)
<i>P-value</i>	-	0.0016	<0.0001	<0.0001
	Carboplatin monotherapy (N=93)	Scenario 1 (ESS=12)	Scenario 2 (ESS=55)	Scenario 3 (ESS=62)
Median OS, months	8.3 (6.7–11.4)	18.3 (6.4–NE)	40.5 (19.4–NE)	39.9 (21.6–NE)
OS rate				
6 months	0.68 (0.57–0.77)	0.88 (0.72–0.96)	0.88 (0.77–0.94)	0.90 (0.81–0.95)
12 months	0.35 (0.25–0.45)	0.55 (0.21–0.79)	0.75 (0.61–0.85)	0.78 (0.65–0.87)
18 months	0.24 (0.15–0.34)	0.52 (0.20–0.76)	0.70 (0.56–0.81)	0.68 (0.54–0.79)
HR for OS	-	0.55 (0.22–1.33)	0.28 (0.16–0.50)	0.28 (0.16–0.48)
<i>P-value</i>	-	0.1830	<0.0001	<0.0001

Scenario 1: Matching variables are histology, grade, and number of prior platinum-based therapies; scenario 2: Matching variables are histology and number of prior platinum-based therapies; scenario 3: Matching variables are race, histology, stage at initial diagnosis, and surgery (ECOG PS was not included as a matching variable due to patients with unknown status).

CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; ESS, effective sample size; HR, hazard ratio; NE, non-estimable; OS, overall survival.

Supplementary Table 3. Progression-free survival for real-world comparator treatments and the GARNET (dostarlimab, ITT) cohort after matching. A) time-to-next treatment used as a proxy for progression-free survival for real-world cohort and B) time-to-treatment discontinuation used as a proxy for real-world cohort

A)

	PFS (95% CI): TTNT as a proxy			
	Real-world cohort	GARNET (dostarlimab) cohort		
	Paclitaxel monotherapy (N=116)	Scenario 1 (ESS=16)	Scenario 2 (ESS=59)	Scenario 3 (ESS=50)
Median PFS, months	5.8 (3.9–6.5)	4.2 (2.7–16.6)	8.1 (4.2–37.3)	16.6 (5.2–NE)
PFS rate				
6 months	0.45 (0.36–0.54)	0.44 (0.22–0.65)	0.53 (0.39–0.65)	0.62 (0.48–0.74)
12 months	0.20 (0.13–0.28)	0.37 (0.18–0.56)	0.49 (0.35–0.61)	0.58 (0.43–0.70)
18 months	-	0.31 (0.15–0.49)	0.41 (0.28–0.54)	0.48 (0.32–0.62)
	Carboplatin + paclitaxel (N=279)	Scenario 1 (ESS=20)	Scenario 2 (ESS=61)	Scenario 3 (ESS=64)
Median PFS, months	10.0 (9.0–11.3)	4.5 (2.7–16.6)	8.1 (4.2–37.3)	16.3 (5.2–37.3)
PFS rate				
6 months	0.74 (0.68–0.79)	0.45 (0.24–0.64)	0.53 (0.39–0.64)	0.61 (0.48–0.71)
12 months	0.37 (0.31–0.43)	0.38 (0.20–0.56)	0.49 (0.36–0.61)	0.55 (0.41–0.66)
18 months	0.19 (0.14–0.25)	0.33 (0.17–0.50)	0.42 (0.29–0.54)	0.42 (0.29–0.55)
	Carboplatin + liposomal doxorubicin (N=141)	Scenario 1 (ESS=14)	Scenario 2 (ESS=57)	Scenario 3 (ESS=63)
Median PFS, months	9.9 (8.3–11.2)	3.9 (2.7–16.6)	8.1 (4.2–37.3)	16.3 (5.2–37.3)
PFS rate				
6 months	0.78 (0.70–0.84)	0.43 (0.19–0.65)	0.53 (0.39–0.65)	0.60 (0.47–0.71)
12 months	0.38 (0.30–0.46)	0.35 (0.16–0.55)	0.49 (0.35–0.61)	0.54 (0.41–0.66)
18 months	0.20 (0.13–0.27)	0.30 (0.13–0.49)	0.41 (0.28–0.54)	0.44 (0.30–0.56)
	Liposomal doxorubicin monotherapy (N=130)	Scenario 1 (ESS=21)	Scenario 2 (ESS=65)	Scenario 3 (ESS=67)

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Median PFS, months	4.1 (3.4–4.6)	4.5 (2.7–16.6)	8.1 (4.2–37.3)	13.8 (4.2–37.3)
PFS rate				
6 months	0.30 (0.22–0.38)	0.46 (0.25–0.65)	0.53 (0.40–0.64)	0.56 (0.43–0.67)
12 months	-	0.38 (0.21–0.56)	0.49 (0.36–0.61)	0.52 (0.39–0.63)
18 months	-	0.33 (0.17–0.50)	0.42 (0.29–0.54)	0.42 (0.29–0.54)
	Carboplatin monotherapy (N=93)	Scenario 1 (ESS=12)	Scenario 2 (ESS=55)	Scenario 3 (ESS=62)
Median PFS, months	6.9 (5.8–8.3)	3.0 (2.7–16.6)	8.1 (4.2–37.3)	13.8 (4.2–37.3)
PFS rate				
6 months	0.59 (0.48–0.69)	0.41 (0.17–0.63)	0.53 (0.39–0.65)	0.59 (0.46–0.70)
12 months	0.18 (0.10–0.27)	0.34 (0.15–0.55)	0.49 (0.35–0.62)	0.53 (0.39–0.65)
18 months	-	0.30 (0.13–0.49)	0.41 (0.28–0.54)	0.41 (0.28–0.54)

B)

	PFS (95% CI): TTD as a proxy			
	Real-world cohort	GARNET (dostarlimab) cohort		
	Paclitaxel monotherapy (N=116)	Scenario 1 (ESS=16)	Scenario 2 (ESS=59)	Scenario 3 (ESS=50)
Median PFS, months	3.2 (2.5–3.7)	4.2 (2.7–16.6)	8.1 (4.2–37.3)	16.6 (5.2–NE)
PFS rate				
6 months	0.11 (0.06–0.18)	0.44 (0.22–0.65)	0.53 (0.39–0.65)	0.62 (0.48–0.74)
12 months	-	0.37 (0.18–0.56)	0.49 (0.35–0.61)	0.58 (0.43–0.70)
18 months	-	0.31 (0.15–0.49)	0.41 (0.28–0.54)	0.48 (0.32–0.62)
	Carboplatin + paclitaxel (N=279)	Scenario 1 (ESS=20)	Scenario 2 (ESS=61)	Scenario 3 (ESS=64)
Median PFS, months	3.4 (3.4–3.5)	4.5 (2.7–16.6)	8.1 (4.2–37.3)	16.3 (5.2–37.3)
PFS rate				
6 months	0.13 (0.09–0.18)	0.45 (0.24–0.64)	0.53 (0.39–0.64)	0.61 (0.48–0.71)
12 months	-	0.38 (0.20–0.56)	0.49 (0.36–0.61)	0.55 (0.41–0.66)
18 months	-	0.33 (0.17–0.50)	0.42 (0.29–0.54)	0.42 (0.29–0.55)

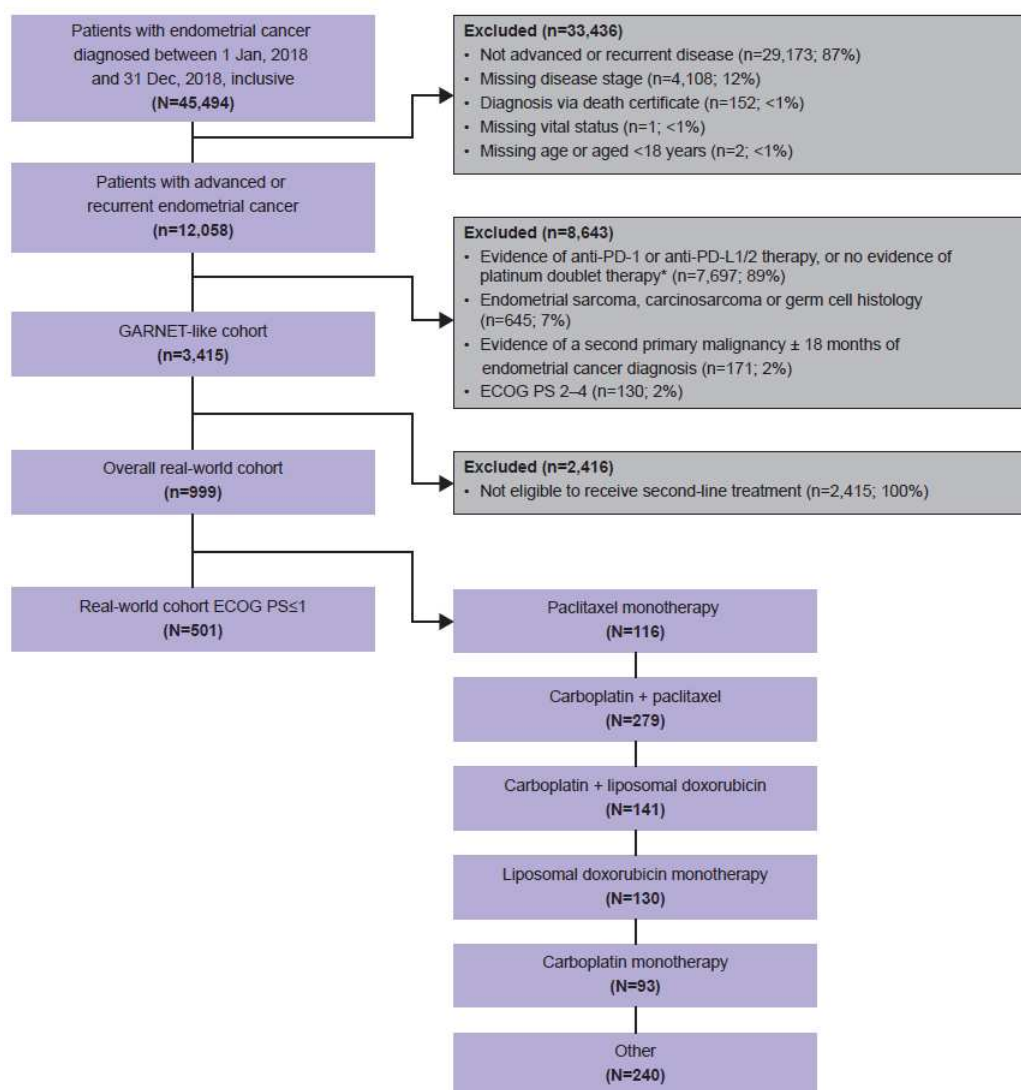
	Carboplatin + liposomal doxorubicin (N=141)	Scenario 1 (ESS=14)	Scenario 2 (ESS=57)	Scenario 3 (ESS=63)
Median PFS, months	4.6 (4.0–4.6)	3.9 (2.7–16.6)	8.1 (4.2–37.3)	16.3 (5.2–37.3)
PFS rate				
6 months	0.14 (0.09–0.21)	0.43 (0.19–0.65)	0.53 (0.39–0.65)	0.60 (0.47–0.71)
12 months	-	0.35 (0.16–0.55)	0.49 (0.38–0.61)	0.54 (0.41–0.66)
18 months	-	0.30 (0.13–0.49)	0.41 (0.28–0.54)	0.44 (0.30–0.56)
	Liposomal doxorubicin monotherapy (N=130)	Scenario 1 (ESS=21)	Scenario 2 (ESS=65)	Scenario 3 (ESS=67)
Median PFS, months	2.8 (2.1–2.9)	4.5 (2.7–16.6)	8.1 (4.2–37.3)	13.8 (4.2–37.3)
PFS rate				
6 months	0.12 (0.07–0.19)	0.46 (0.25–0.65)	0.53 (0.40–0.64)	0.56 (0.43–0.67)
12 months	-	0.38 (0.21–0.56)	0.49 (0.36–0.61)	0.52 (0.39–0.63)
18 months	-	0.33 (0.17–0.50)	0.42 (0.29–0.54)	0.42 (0.29–0.54)
	Carboplatin monotherapy (N=93)	Scenario 1 (ESS=12)	Scenario 2 (ESS=55)	Scenario 3 (ESS=62)
Median PFS, months	3.4 (2.8–3.5)	3.0 (2.7–16.6)	8.1 (4.2–37.3)	13.8 (4.2–37.3)
PFS rate				
6 months	-	0.41 (0.17–0.63)	0.53 (0.39–0.65)	0.59 (0.46–0.70)
12 months	-	0.34 (0.15–0.55)	0.49 (0.35–0.62)	0.53 (0.39–0.65)
18 months	-	0.30 (0.13–0.49)	0.41 (0.28–0.54)	0.41 (0.23–0.54)

Scenario 1: Matching variables are histology, grade, and number of prior platinum-based therapies; scenario 2: Matching variables are histology and number of prior platinum-based therapies; scenario 3: Matching variables are race, histology, stage at initial diagnosis, and surgery (ECOG PS was not included as a matching variable due to patients with unknown status).

CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; ESS, effective sample size; NE, not explained; PFS, progression-free survival; TTD, time-to-discontinuation; TTNT, time-to-next treatment.

Supplementary Figures

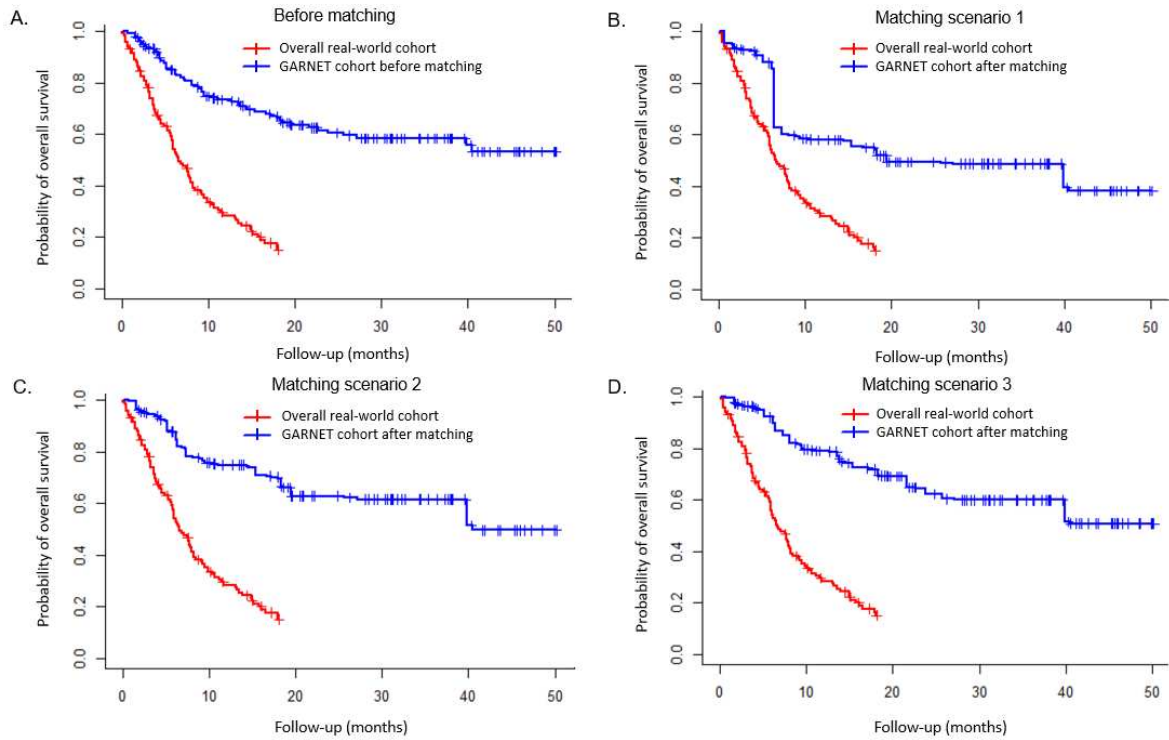
Supplementary Figure 1. UK real-world cohort patient flow diagram. Purple boxes indicate the number of patients within each cohort and subgroup; grey boxes indicate patients that were excluded from each cohort and the breakdown of reasons for exclusion.



*Prior treatment with hormone therapies was acceptable but did not count towards lines of therapy.

ECOG PS, Eastern Cooperative Oncology Group performance status; PD-1, programmed cell death protein 1; PD-L1/2, programmed death-ligand 1/2.

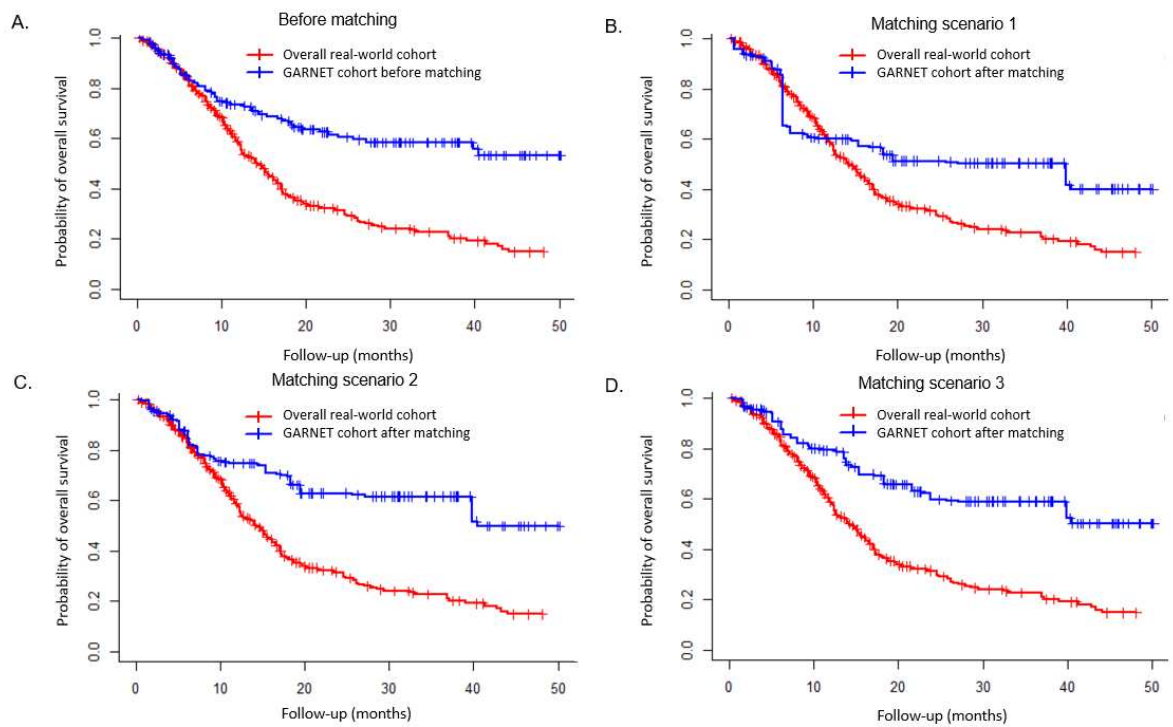
Supplementary Figure 2. Kaplan Meier curves for overall survival comparing the GARNET (dostarlimab, ITT) cohort and paclitaxel monotherapy real-world cohort. A) before matching, B) matching scenario 1*, C) matching scenario 2[†], D) matching scenario 3[‡]. Tick marks represent censored data.



*Matching variables: histology, grade, and number of prior platinum-based therapies; [†]matching variables: histology and number of prior platinum-based therapies; [‡]matching variables: race/ethnicity, histology, stage at initial diagnosis, and surgery

ITT, intention to treat

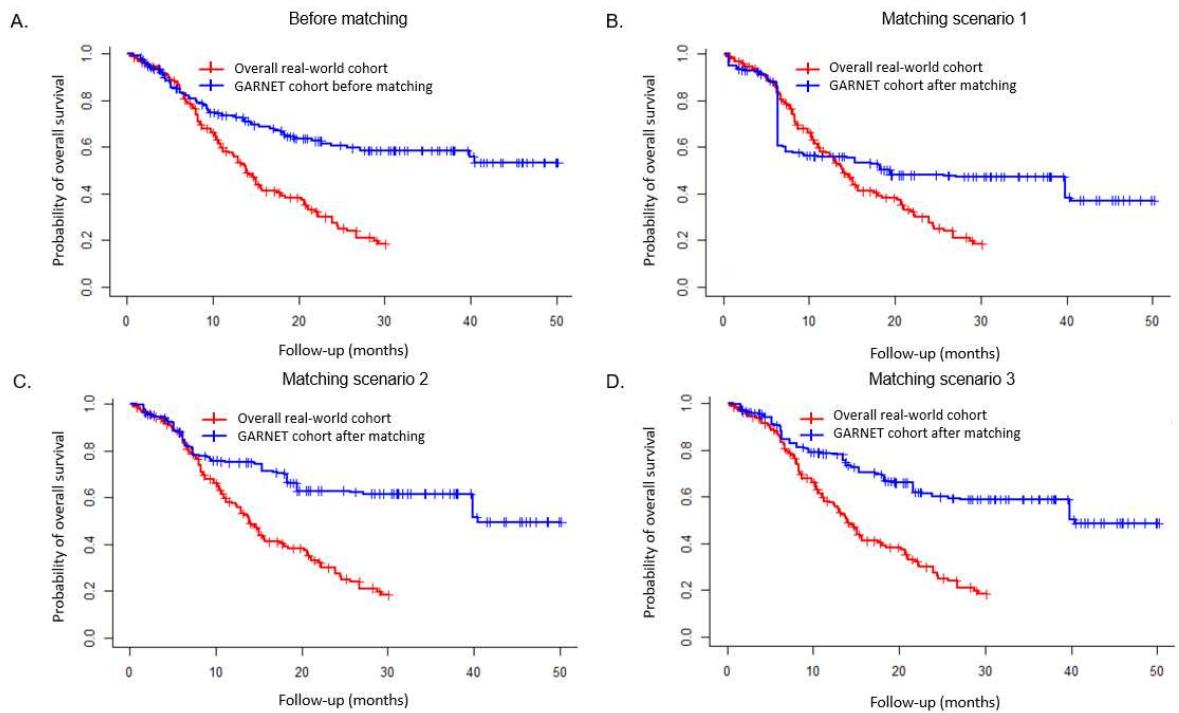
Supplementary Figure 3. Kaplan Meier curves for overall survival comparing the GARNET (dostarlimab, ITT) cohort and carboplatin + paclitaxel real-world cohort. A) before matching, B) matching scenario 1*, C) matching scenario 2[†], D) matching scenario 3[‡]. Tick marks represent censored data.



*Matching variables: histology, grade, and number of prior platinum-based therapies; [†]matching variables: histology and number of prior platinum-based therapies; [‡]matching variables: race/ethnicity, histology, stage at initial diagnosis, and surgery

ITT, intention to treat

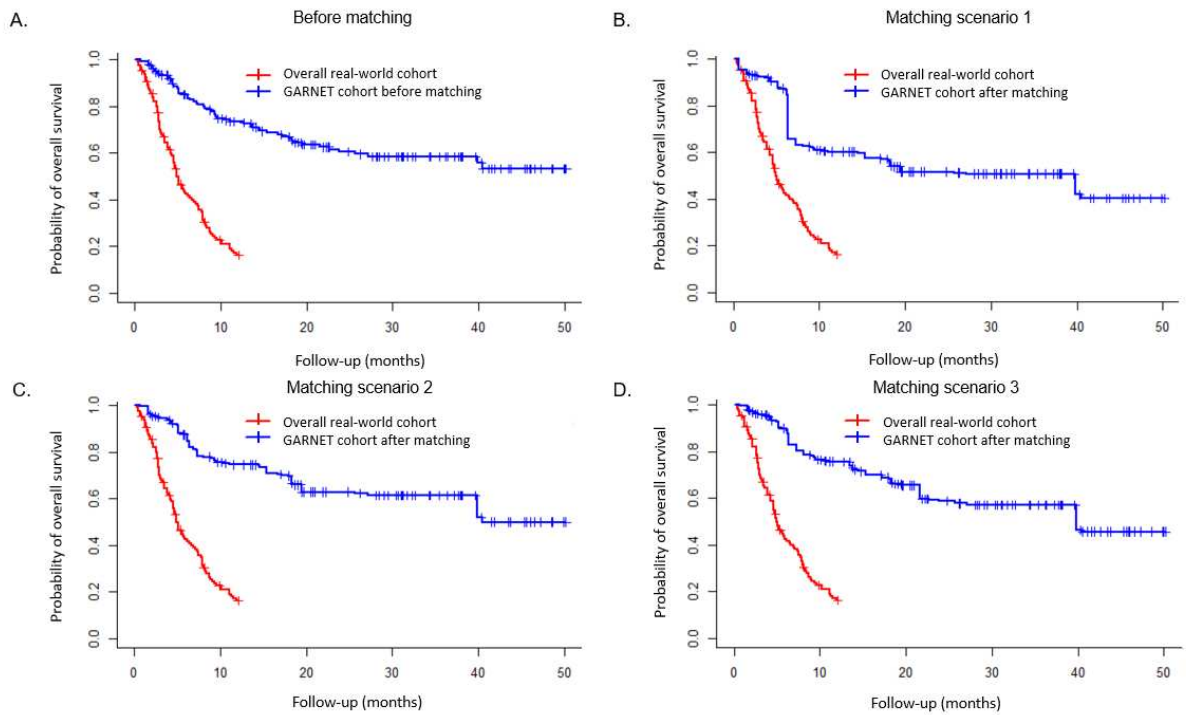
Supplementary Figure 4. Kaplan Meier curves for overall survival comparing the GARNET (dostarlimab, ITT) cohort and carboplatin + liposomal doxorubicin real-world cohort. A) before matching, B) matching scenario 1*, C) matching scenario 2[†], D) matching scenario 3[‡]. Tick marks represent censored data.



*Matching variables: histology, grade, and number of prior platinum-based therapies; [†]matching variables: histology and number of prior platinum-based therapies; [‡]matching variables: race/ethnicity, histology, stage at initial diagnosis, and surgery

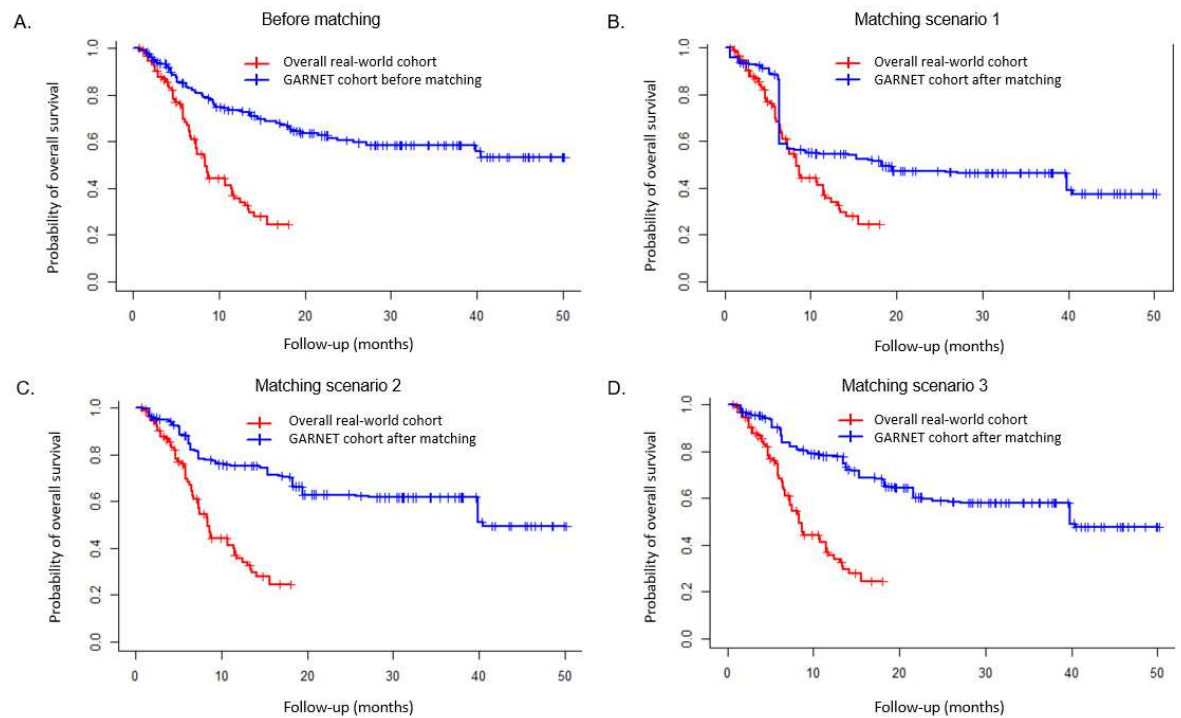
ITT, intention to treat

Supplementary Figure 5. Kaplan Meier curves for overall survival comparing the GARNET (dostarlimab, ITT) cohort and liposomal doxorubicin real-world cohort. A) before matching, B) matching scenario 1*, C) matching scenario 2[†], D) matching scenario 3[‡]. Tick marks represent censored data.



*Matching variables: histology, grade, and number of prior platinum-based therapies; [†]matching variables: histology and number of prior platinum-based therapies; [‡]matching variables: race/ethnicity, histology, stage at initial diagnosis, and surgery
ITT, intention to treat

Supplementary Figure 6. Kaplan Meier curves for overall survival comparing the GARNET (dostarlimab, ITT) cohort and carboplatin real-world cohort. A) before matching, B) matching scenario 1*, C) matching scenario 2[†], D) matching scenario 3[‡]. Tick marks represent censored data.



*Matching variables: histology, grade, and number of prior platinum-based therapies; [†]matching variables: histology and number of prior platinum-based therapies; [‡]matching variables: race/ethnicity, histology, stage at initial diagnosis, and surgery

ITT, intention to treat

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