# Supplemental Online Content

André T, Berton D, Curigliano G, et al. Antitumor activity and safety of dostarlimab monotherapy in patients with mismatch repair deficient solid tumors: a nonrandomized controlled trial. *JAMA Netw Open.* 2023;6(10):e2341165. doi:10.1001/jamanetworkopen.2023.41165



This supplemental material has been provided by the authors to give readers additional information about their work.

## eAppendix 1. Sites and Investigators and Supplementary Methods

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**Supplemental methods**

*Key inclusion and exclusion criteria*

The key inclusion criteria for cohorts A1 and F were as follows: mismatch repair deficient/microsatellite instability–high (dMMR/MSI-H) solid tumors (with cohort F also including patients with nonendometrial polymerase epsilon mutation [POLE-mut] tumors), at least 1 blinded independent central review (BICR)–confirmed measurable lesion at baseline, no prior treatment with anti–programmed death (ligand) 1 (anti–PD-[L]1) therapy, received no more than 2 prior lines of treatment for recurrent or advanced disease (progression following up to 3 prior lines of therapy is allowed for colorectal cancer [CRC]), disease progression following systemic therapy with no satisfactory alternative treatment options, and submission of 2 scans demonstrating progressive disease (PD) based on BICR per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1) prior to the first dose of dostarlimab.

Patients enrolled on the study based on POLE-mut status must have had local results available showing tumor mutation in the exonuclease domain of the *POLE* gene (amino acid residues 268-471) prior to screening for assignment into cohort F (prospective POLE-mut).

Patients with endometrial cancer (EC) were required to have progression on or after platinum doublet therapy. Patients with CRC must have had progression after, or been intolerant to, fluoropyrimidine, oxaliplatin, and irinotecan, and patients with ovarian cancer with platinum-resistant disease were allowed receipt of up to 1 line of systemic therapy after becoming platinum resistant.

*Enrolling sites*

This is an international trial with 123 sites. Enrolling sites for cohort A1 (dMMR/MSI-H EC) and F (dMMR/MSI-H non-EC solid tumors) are listed previously in the supplemental appendix.

*Sample size*

Cohort A1 had a planned enrollment of approximately 100 participants with dMMR/MSI-H EC, with potential enrollment of up to 165 participants with dMMR/MSI-H EC evaluable for antitumor activity. For cohort A1, the null hypothesis that the true response rate was ≤20% (H0: $P \leq .2$) was tested against a one-sided alternative of ≥40% (Ha: $P \geq .4$). With 65 patients treated, the cohort had a 92% power to rule out a ≤20% objective response rate (ORR; null hypothesis) when the true ORR was 40% at the 2.5% type I error rate (one-sided). The sample size of cohort A1 was increased to 100 patients to allow the lower-limit boundary of the exact 95% confidence interval to exclude a response rate of 25% or less and assume observed ORR was 35%.

Cohort F had a planned enrollment of approximately 100 patients, with potential enrollment of up to 200 patients, with dMMR/MSI-H solid tumors evaluable for antitumor activity. Since cohort A1 and cohort F consist of patients with previously treated dMMR/MSI-H solid tumors, a combined analysis was performed to determine the ORR in the dMMR/MSI-H solid tumor population. The null hypothesis for the combined cohort was that the true response rate was ≤20% (H0: $P \leq .2$) and was tested against a one-sided alternative of ≥30% (Ha: $P \geq .3$). With an expected total of 165 patients (65 from cohort A1, 100 from cohort F), the combined cohort had 85% power to rule out a ≤20%

ORR (null hypothesis) when the true ORR was 30% at the one-sided 2.5% type I error rate.

The sample size was increased to 200 patients under protocol amendment 5. The total sample size of 300 patients evaluable for antitumor activity from cohorts A1 and F combined allowed the lower-limit boundary of the exact 95% CI to exclude a response rate of ≤30%, assuming the observed ORR was 35%.

*Statistics*

All statistical outputs were generated using SAS (version 9.4). Patient demographics, baseline characteristics, safety, and antitumor activity results were summarized descriptively. All patients who received at least 1 dose of dostarlimab by the data cutoff were included in the safety analysis. All patients who received at least 1 dose of dostarlimab, had at least 1 BICR-confirmed measurable lesion at baseline, and had the opportunity to be followed for at least 6 months, as of the data cutoff date, were included in the efficacy population, regardless of whether the patient had a postbaseline tumor assessment.

Point estimates and exact two-sided 95% CIs were provided for ORR; duration of response (DOR) was analyzed using the Kaplan-Meier method. Patients who did not achieve a confirmed response, either complete response (CR) or partial response (PR), were excluded from the DOR analysis. Median follow-up time was calculated using the reverse Kaplan-Meier method. Time-to-event analyses were performed using Kaplan-Meier methods.

ORR per RECIST v1.1 was calculated as the proportion of patients who achieved a best overall response (BOR) of CR or PR. Determination of BOR can be found in the statistical analysis plan, which is available as a supplemental file. Disease control rate was defined as the proportion of patients achieving a BOR of confirmed CR, PR, or stable disease. DOR was defined as the time from first documentation of overall response leading to a confirmed CR or PR when confirmation is required in cohorts A1 and F by RECIST v1.1 until the time of first documentation of overall response of disease progression or death.

Overall survival (OS) was defined as the time from date of first dose of study treatment to the date of death by any cause. Patients last known to be alive will be censored at date of last known contact. OS was calculated as:
OS (days) = date of death/censoring – date of first dose + 1

PFS was defined as the time from date of first dose to the earlier date of assessment of progression or death by any cause in the absence of progression based on the time of first documentation of PD per RECIST v1.1. Only tumor assessments performed before the start of any new anticancer treatment were included in the assessment of PFS. PFS was calculated as:
PFS (days) = date of <PD event or death>/censoring – date of first dose + 1

*Biomarker screening*

Patients were screened prospectively for MMR/MSI status using immunohistochemistry (IHC), polymerase chain reaction, or next-generation sequencing. For patients enrolled

after protocol amendment 5, eligibility was determined by IHC performed in a certified local laboratory or by central testing if local IHC testing was not available. When results from more than 1 test (MMR or MSI) were available for a patient, the patient was classified by their MMR status. In cases where MMR testing was unknown (MMRunk), patients were classified by their MSI status. Patients screened using the MMR IHC testing were not required to have MSI testing performed.

Patients enrolled in the study based on POLE-mut status must have had local results available showing tumor mutation in the exonuclease domain of the *POLE* gene (amino acid residues 268-471) prior to screening for assignment into cohort F (prospective POLE-mut).

PD-L1 expression and TMB were exploratory biomarkers assessed for patients in cohorts A1 and F. TMB status was determined using Foundation One test; TMB-high was defined as ≥10 mutations/Mb. PD-L1 expression was determined by CPS per Ventana assay; PD-L1–high was defined as CPS ≥1.

After enrollment to the study and assignment to cohort based on MMR IHC testing, patients with pathogenic variants in POLE were retrospectively identified by Foundation One test in cohorts A1 (dMMR/MSI-H EC) and cohort A2 (mismatch repair proficient/ microsatellite stable [MMRp/MSS] EC) (retrospective POLE-mut).

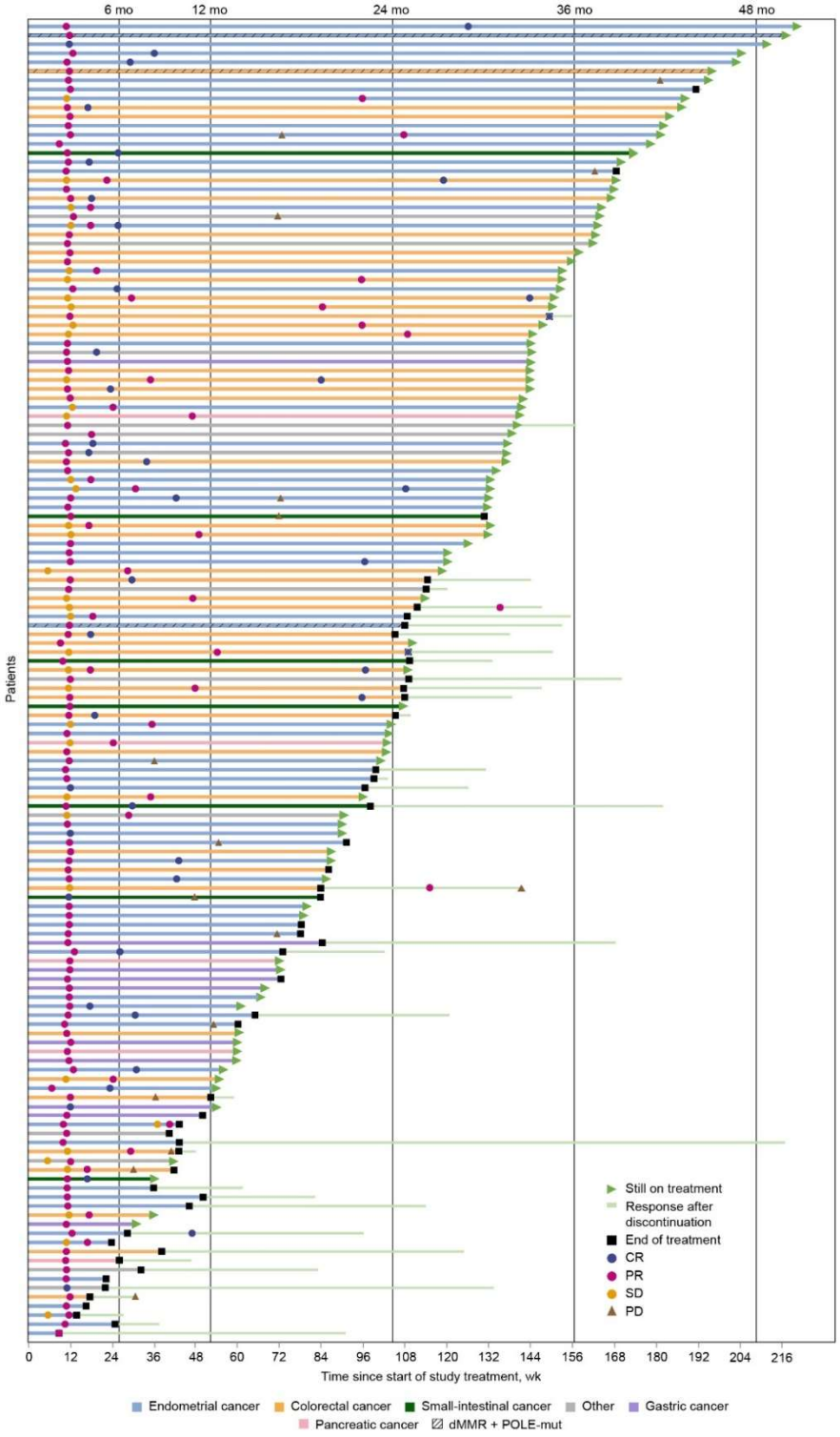
*Safety analyses*

Safety analyses included incidence of treatment-emergent adverse events, immune-related adverse events of interest, and serious adverse events occurring while patients

were on treatment or up to 90 days after the end of treatment. Any changes in clinical laboratory parameters (hematology, chemistry, thyroid function, coagulation, urinalysis) and Common Terminology Criteria for Adverse Events v4.03–graded laboratory toxicities, vital signs, Eastern Cooperative Oncology Group performance status, electrocardiogram parameters, physical examinations, and usage of concomitant medications were recorded.

No formal hypothesis-testing analysis of adverse event incidence rates was performed. Additional information can be found in the protocol.

## eFigure 1. Duration of Treatment for Responders With dMMR Solid Tumors




Abbreviations: CR, complete response; dMMR, mismatch repair deficient; PD, progressive disease; POLE-mut, polymerase epsilon mutation; PR, partial response; SD, stable disease.

**eTable 1. Antitumor Activity Analysis**

| Characteristic | dMMR solid tumors N = 327[a] | dMMR or MSI-H or POLE N = 347[b] |
|---|---|---|
| Median follow-up time, mo | 27.7 | 29.1 |
| Confirmed responses, n | 144 | 153 |
| ORR, % (95% CI) | 44.0 (38.6-49.6) | 44.1 (38.8-49.5) |
| CR, n (%) | 43 (13.1) | 46 (13.3) |
| PR, n (%) | 101 (30.9) | 107 (30.8) |
| SD, n (%) | 47 (14.4) | 50 (14.4) |
| PD, n (%) | 114 (34.9) | 119 (34.3) |
| NE, n (%) | 22 (6.8) | 25 (7.2) |
| Disease control rate, % (95% CI) | 58.4 (52.9-63.8) | 58.5 (53.1-63.7) |
| Response ongoing, n (%) | 123 (85.4) | 131 (85.6) |
| Duration of response, median (range), mo | NR (1.18+ to 47.21+) | NR (1.18+ to 47.21+) |
| Patients with duration of response ≥12 mo, n (%) | 104 (72.2) | 110 (71.9) |
| Probability of remaining in response, % (95% CI) | | |
| 6 mo | 95.7 (90.6-98.0) | 95.9 (91.0-98.1) |
| 12 mo | 92.4 (86.4-95.9) | 92.8 (87.0-96.1) |
| 24 mo | 84.7 (76.7-90.2) | 84.5 (76.6-89.9) |

Abbreviations: BICR, blinded independent central review; CR, complete response; CRC, colorectal cancer; dMMR, mismatch repair deficient; EC, endometrial cancer; MMRp, mismatch repair proficient; MMRunk, mismatch repair status unknown; MSI-H, microsatellite instability–high; NE, not evaluable; NR, not reached; ORR, objective response rate; PD, progressive disease; POLE, polymerase epsilon; PR, partial response; SD, stable disease.

[a] This number included 141 patients with endometrial cancer, 105 patients with CRC, and 81 patients with other tumor types. Overall, 347 patients in the whole population had measurable disease at baseline by BICR and ≥6 months of follow-up and were included in the efficacy population.

[b] Includes 186 patients with dMMR non-EC solid tumors, 141 patients with dMMR EC tumors, 15 patients with MMRunk/MSI-H non-EC solid tumors, 3 patients with MMRp/MSI-H non-EC solid tumors, and 2 patients with MMRunk/MSI-H EC.

**eTable 2. Progression-Free Survival**

| Variable | dMMR solid tumors N = 327 | dMMR or MSI-H or POLE-mut N = 347 |
|---|---|---|
| Median follow-up time, mo | 27.7 | 29.1 |
| PFS events observed, n (%) | 188 (57.5) | 197 (56.8) |
| Median PFS, % (95% CI), mo | 6.9 (4.2-13.6) | 7.0 (4.2-13.8) |
| Estimated probability of PFS, % (95% CI) | | |
| 6 mo | 50.5 (44.9-55.9) | 50.9 (45.4-56.1) |
| 12 mo | 45.8 (40.2-51.2) | 46.4 (40.9-51.6) |
| 24 mo | 40.6 (35.0-46.1) | 41.0 (35.5-46.3) |
| 36 mo | 39.7 (33.9-45.3) | 40.0 (34.4-45.6) |

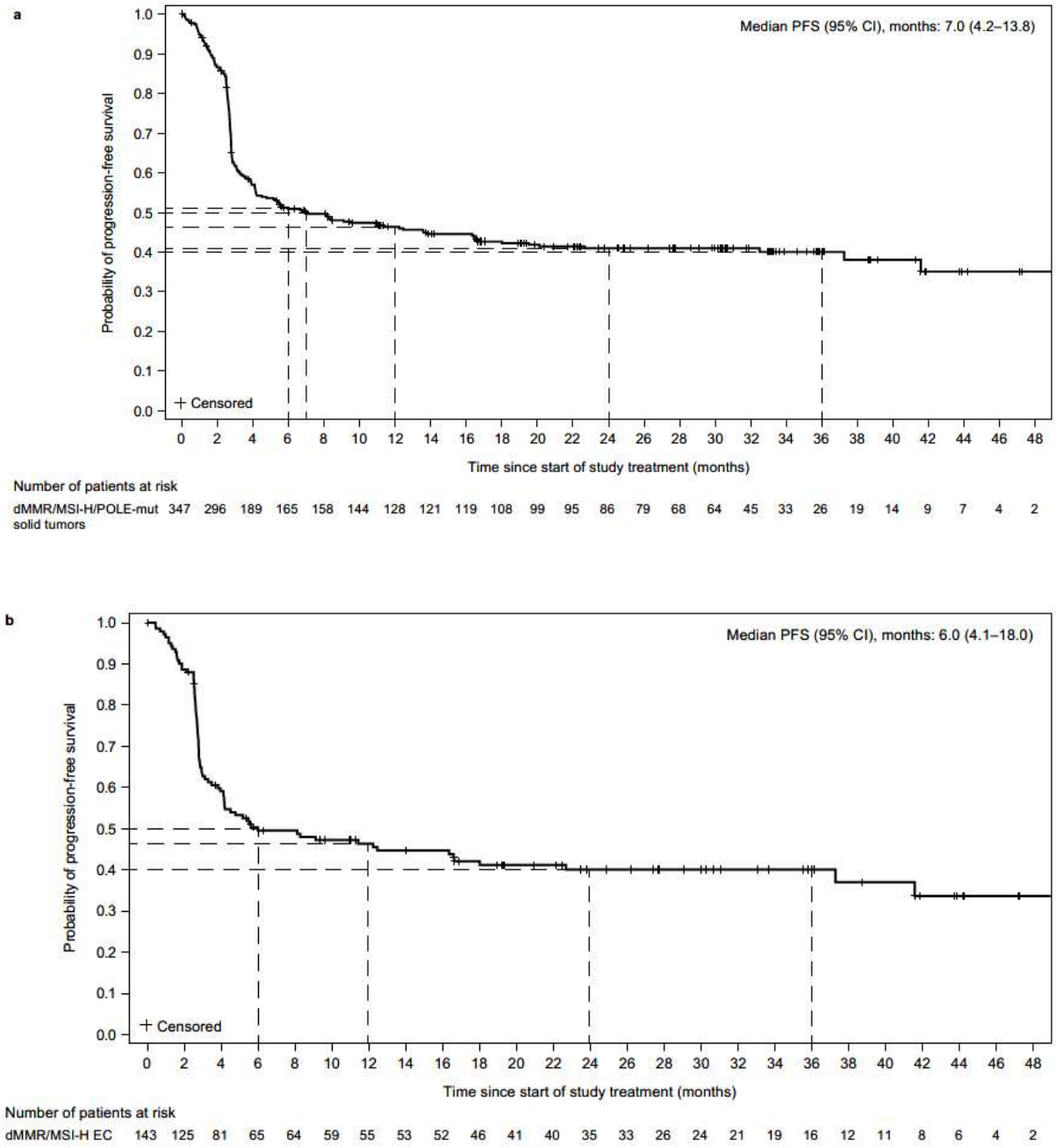
Abbreviations: dMMR, mismatch repair deficient; MSI-H, microsatellite instability–high; POLE-mut, polymerase epsilon mutation; PFS, progression-free survival.

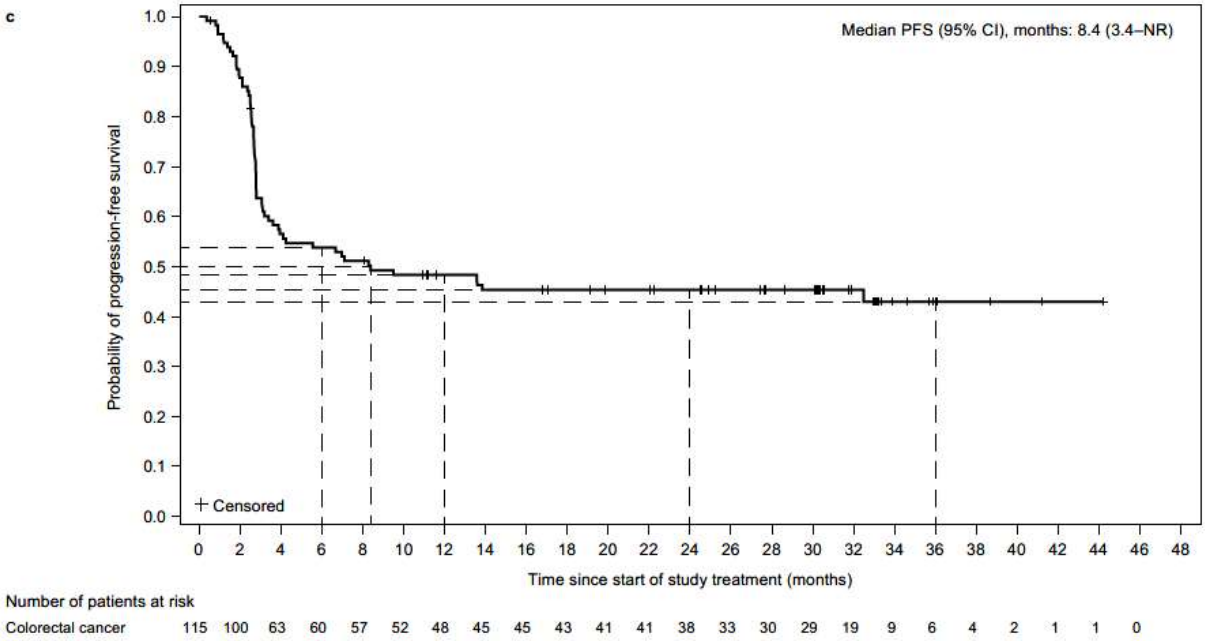
**eTable 3. Overall Survival**

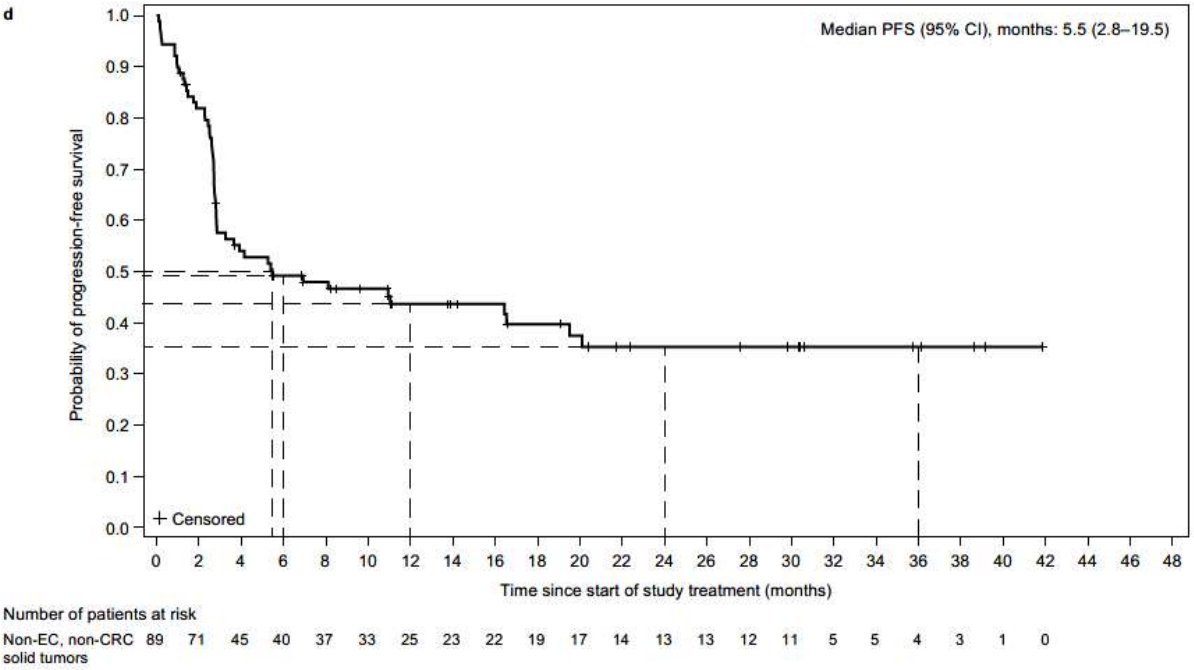
| Variable | dMMR solid tumors N = 341 | dMMR or MSI-H or POLE-mut N = 363 |
|---|---|---|
| Median follow-up time, mo | 27.7 | 29.1 |
| OS events observed, n (%) | 132 (38.7) | 140 (38.6) |
| Median OS, % (95% CI), mo | NR (31.6-NR) | NR (39.9-NR) |
| Estimated probability of OS, % (95% CI) | | |
| 6 mo | 82.6 (78.0-86.2) | 82.5 (78.1-86.1) |
| 12 mo | 70.6 (65.3-75.3) | 70.7 (65.5-75.2) |
| 24 mo | 58.4 (52.5-63.9) | 58.5 (52.7-63.8) |
| 36 mo | 55.9 (49.7-61.7) | 56.1 (50.1-61.6) |

Abbreviations: dMMR, mismatch repair deficient; MSI-H, microsatellite instability–high; NR, not reached; OS, overall survival; POLE-mut, polymerase epsilon mutation.

## eFigure 2. Progression-Free Survival by Tumor Type

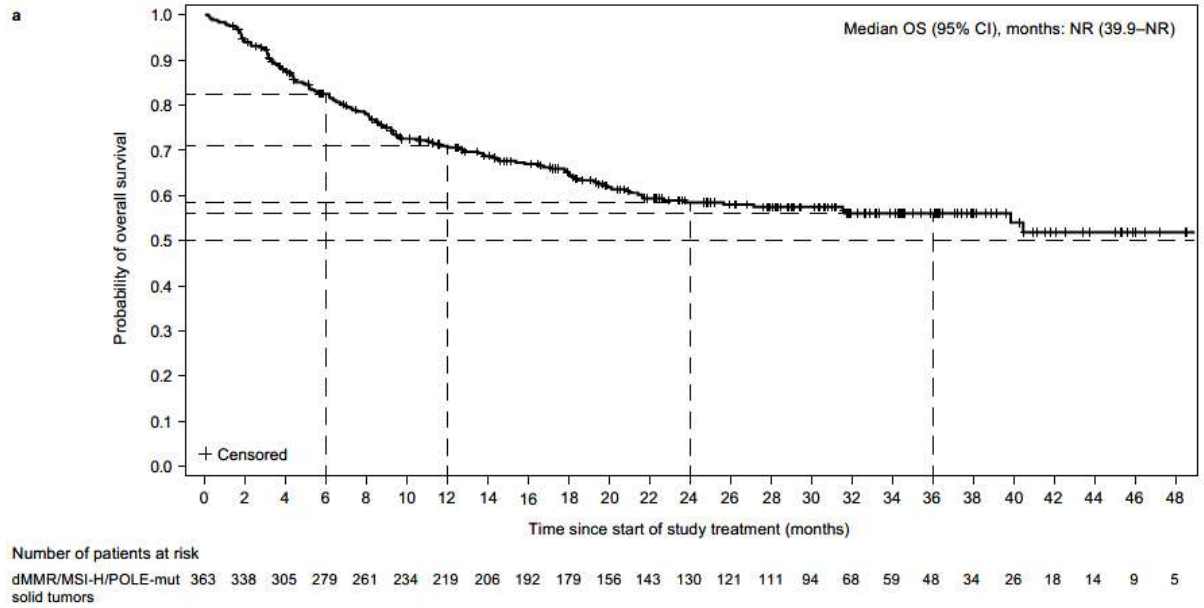


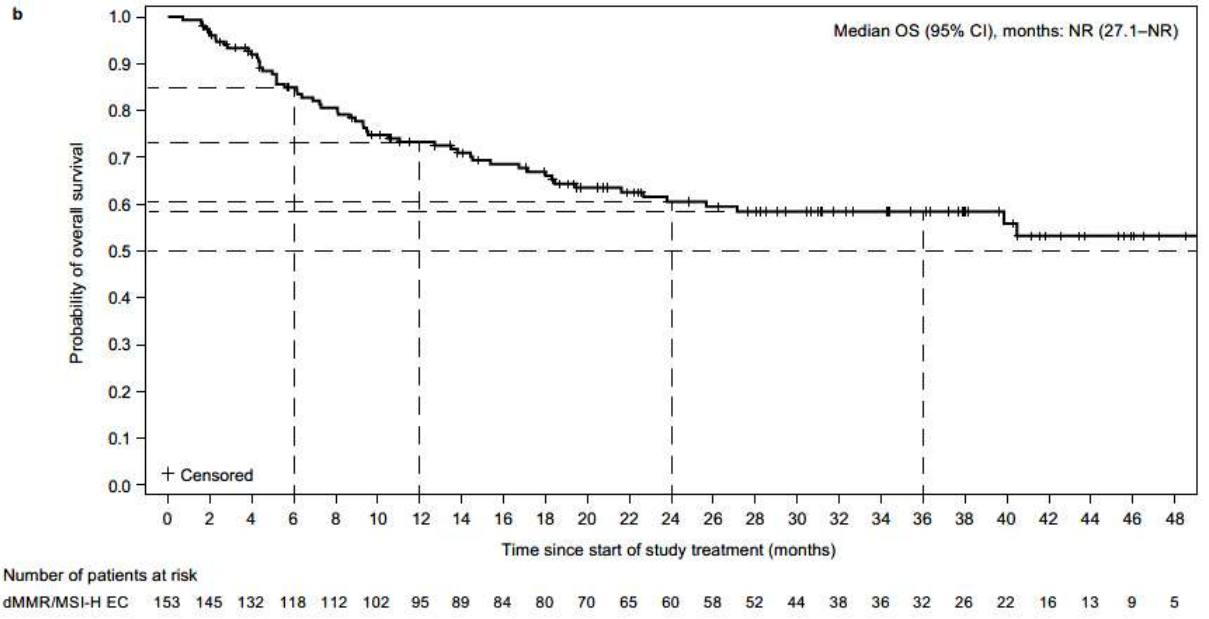


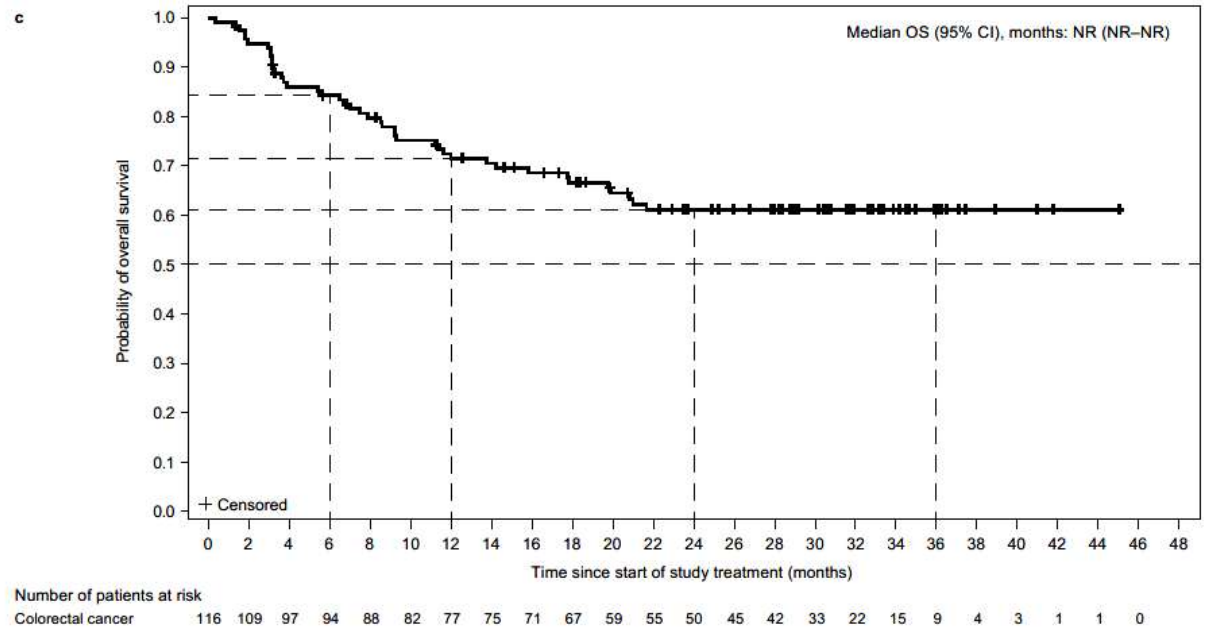



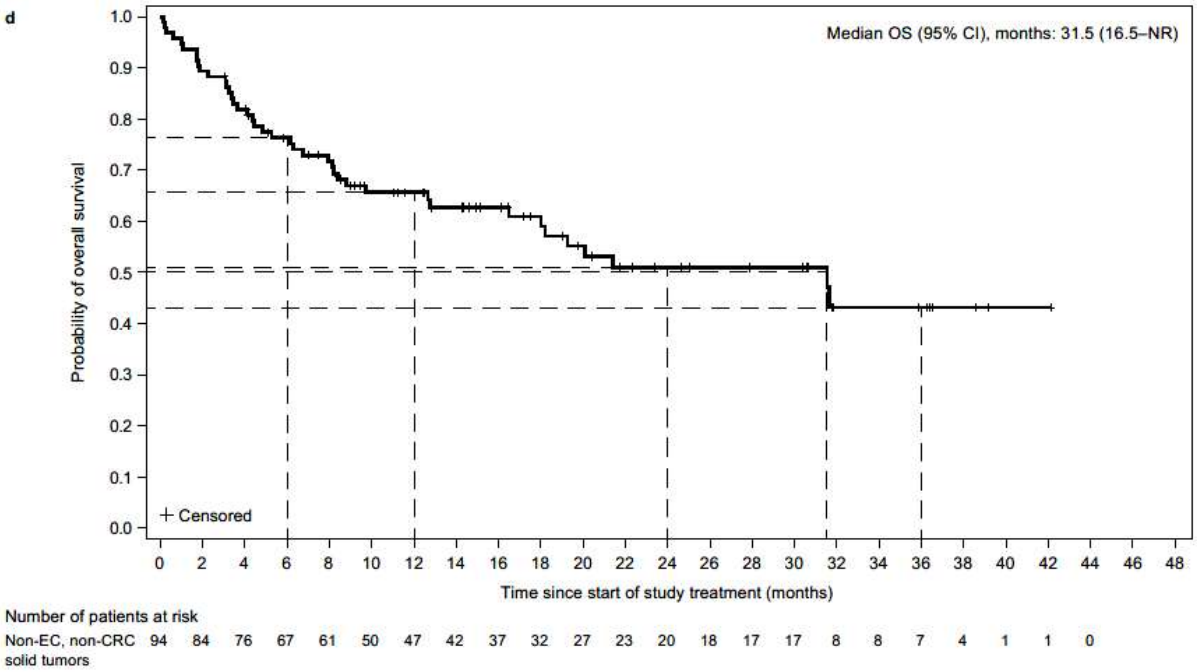

Progression-free survival for (A) all dMMR/MSI-H or POLE-mut solid tumors, (B) dMMR/MSI-H endometrial cancer, (C) dMMR/MSI-H or POLE-mut colorectal cancer, and (D) all other dMMR/MSI-H or POLE-mut tumors.[a]
Abbreviations: dMMR, mismatch repair deficient; EC, endometrial cancer; MSI-H, microsatellite instability–high; NR, not reached; POLE-mut, polymerase epsilon mutation; PFS, progression-free survival.
[a] Includes adrenal cortical carcinoma, biliary neoplasm, brain cancer, breast cancer, cancer of unknown primary origin, esophageal cancer, gastric cancer, malignant neoplasm of the female genitals, mesothelioma, ovarian cancer, pancreatic cancer, prostate cancer, renal cell carcinoma, sarcoma, small-intestinal cancer, and thymic tumor.

## eFigure 3. Overall Survival by Tumor Type






Overall survival for (A) all dMMR/MSI-H or POLE-mut solid tumors, (B) dMMR/MSI-H endometrial cancer, (C) dMMR/MSI-H or POLE-mut colorectal cancer, and (C) all other dMMR/MSI-H or POLE-mut tumors.
Abbreviations: dMMR, mismatch repair deficient; EC, endometrial cancer; MSI-H, microsatellite instability–high; NR, not reached; OS, overall survival; POLE-mut, polymerase epsilon mutation.
[a]Includes adrenal cortical carcinoma, biliary neoplasm, brain cancer, breast cancer, cancer of unknown primary origin, esophageal cancer, gastric cancer, malignant neoplasm of the female genitals, mesothelioma, ovarian cancer, pancreatic cancer, prostate cancer, renal cell carcinoma, sarcoma, small-intestinal cancer, and thymic tumor.

**eAppendix 2. Post Hoc Analysis of PFS by BOR**

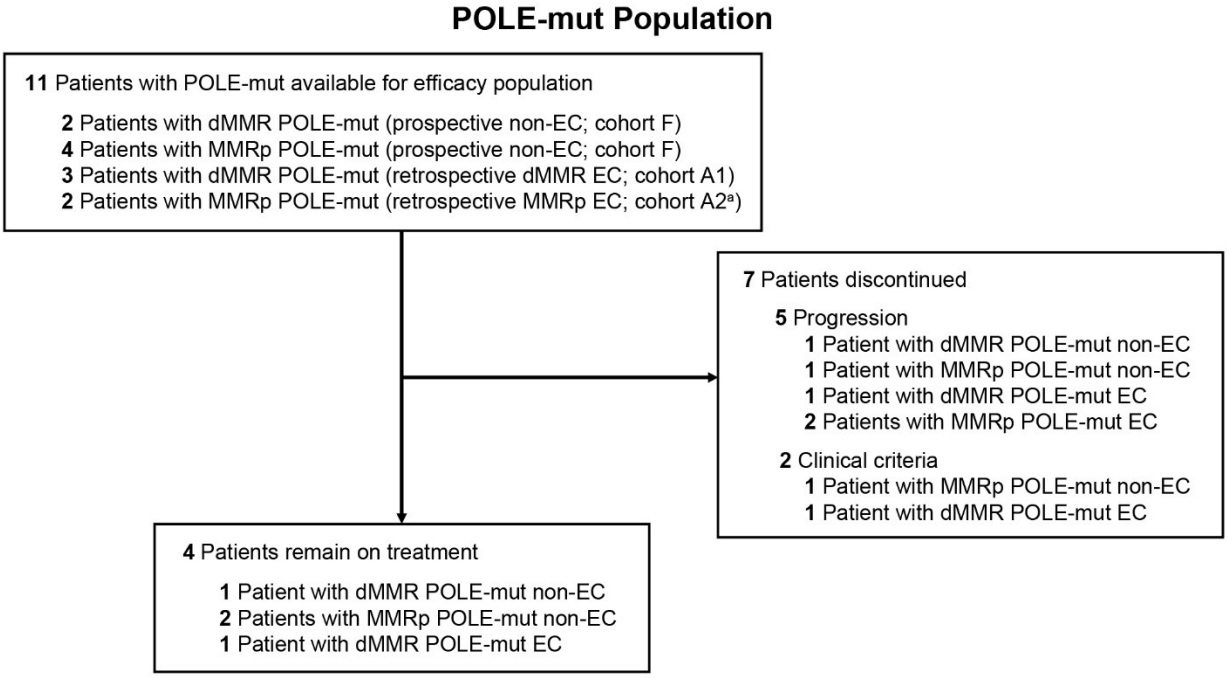
A post hoc analysis was completed to determine PFS per BOR. For patients in the full efficacy population (n = 347), patients with a BOR of CR (n = 46) or PR (n = 107) had a median progression-free survival (mPFS) of not reached; the majority of these patients, 93.5% of those with CR and 83.2% of those with PR, had not experienced a progression event at the time of data cut (eTable 4). For patients with a BOR of stable disease (SD; n = 50), the mPFS was 5.5 months, with 76.0% of patients experiencing a progression event (eTable 4). The probability of PFS at 6, 12, 24, and 36 months was 100%, 97.7%, 92.3%, and 92.3%, respectively, for patients with a BOR of CR; 99.1%, 94.1%, 83.1%, and 80.1%, respectively, for patients with a BOR of PR; and 39.9%, 19.6%, 9.8%, and not reached, respectively, for patients with a BOR of SD (eTable 4).

**eTable 4. Progression-Free Survival by Best Overall Response per BICR in the Overall Efficacy Population**

| | Overall efficacy population N = 347 | | | | |
|---|---|---|---|---|---|
| | **Complete response N = 46** | **Partial response N = 107** | **Stable disease N = 50** | **Progressive disease N = 119** | **Not evaluable N = 25** |
| Progression events, n (%) | 3 (6.5) | 18 (16.8) | 38 (76.0) | 119 (100) | 19 (76.0) |
| Censored, n (%) | 43 (93.5) | 89 (83.2) | 12 (24.0) | 0 | 6 (24.0) |
| mPFS (95% CI), mo | NR (NR-NR) | NR (41.6-NR) | 5.5 (4.2-6.9) | 2.6 (2.5-2.7) | 1.7 (1.2-3.1) |
| Probability of remaining progression free, (95% CI), mo | | | | | |
| 6 mo | 100 | 99.1 (93.5-99.9) | 39.9 (25.7-53.8) | 0 | 0 |
| 12 mo | 97.7 (84.9-99.7) | 94.1 (87.3-97.3) | 19.6 (9.1-32.9) | 0 | 0 |
| 24 mo | 92.3 (77.9-97.5) | 83.1 (73.4-89.5) | 9.8 (2.7-22.3) | 0 | 0 |
| 36 mo | 92.3 (77.9-97.5) | 80.1 (68.5-87.8) | NR (NR-NR) | 0 | 0 |

Abbreviations: BICR, blinded independent central review; mPFS, median progression-free survival; NR, not reached.

## eFigure 4. Enrollment and Outcomes for Patients With POLE-Altered Tumors




Abbreviations: dMMR, mismatch repair deficient; EC, endometrial cancer; MMRp, mismatch repair proficient; MSS, microsatellite stable; POLE-mut, polymerase epsilon mutation.
[a] Cohort A2 is the MMRp/MSS EC cohort from the GARNET trial. Patients from cohort A2 are not included in Table 1. These 2 patients from cohort A2 are included in the POLE-mut population for a post hoc analysis of all patients with POLE-mut included in the GARNET trial.

**eTable 5. Demographics and Baseline Characteristics of Patients With POLE Alterations**

| Characteristic | POLE-mut N = 11 |
|---|---|
| Age, median (range), y | 64 (29-74) |
| Sex, n (%) | |
| Female | 7 (63.6) |
| Male | 4 (36.4) |
| Biomarkers, n (%) | |
| dMMR | 5 (45.5) |
| MMRp | 6 (54.5) |
| Race, n (%) | |
| White | 9 (81.8) |
| Black | 0 |
| Asian | 0 |
| American Indian or Alaska Native | 0 |
| Native Hawaiian or other Pacific Islander | 0 |
| Other/unknown/not reported | 2 (18.2) |
| Ethnicity, n (%) | |
| Hispanic or Latino | 0 |
| Not Hispanic or Latino | 9 (81.8) |
| Unknown/not reported | 2 (18.2) |
| ECOG performance status, n (%) | |
| 0 | 5 (45.5) |
| 1 | 6 (54.5) |
| Prior lines of therapy, n (%)[a] | |
| 1 | 3 (27.3) |
| 2 | 8 (72.7) |
| ≥ 3 | 0 |
| Prior therapy type, n (%) | |
| Surgery | 8 (72.7) |
| Radiotherapy | 5 (45.5) |
| Tumor types, n (%) | |
| Biliary neoplasm | 1 (9.1) |
| Colorectal cancer | 4 (36.4) |
| Endometrial cancer | 5 (45.5) |
| Esophageal cancer | 1 (9.1) |

Abbreviations: dMMR, mismatch repair deficient; ECOG, Eastern Cooperative Oncology Group; MMRp, mismatch repair proficient; MMRunk, mismatch repair status unknown; POLE-mut, polymerase epsilon mutation.

[a] Includes lines of therapy in the adjuvant setting.

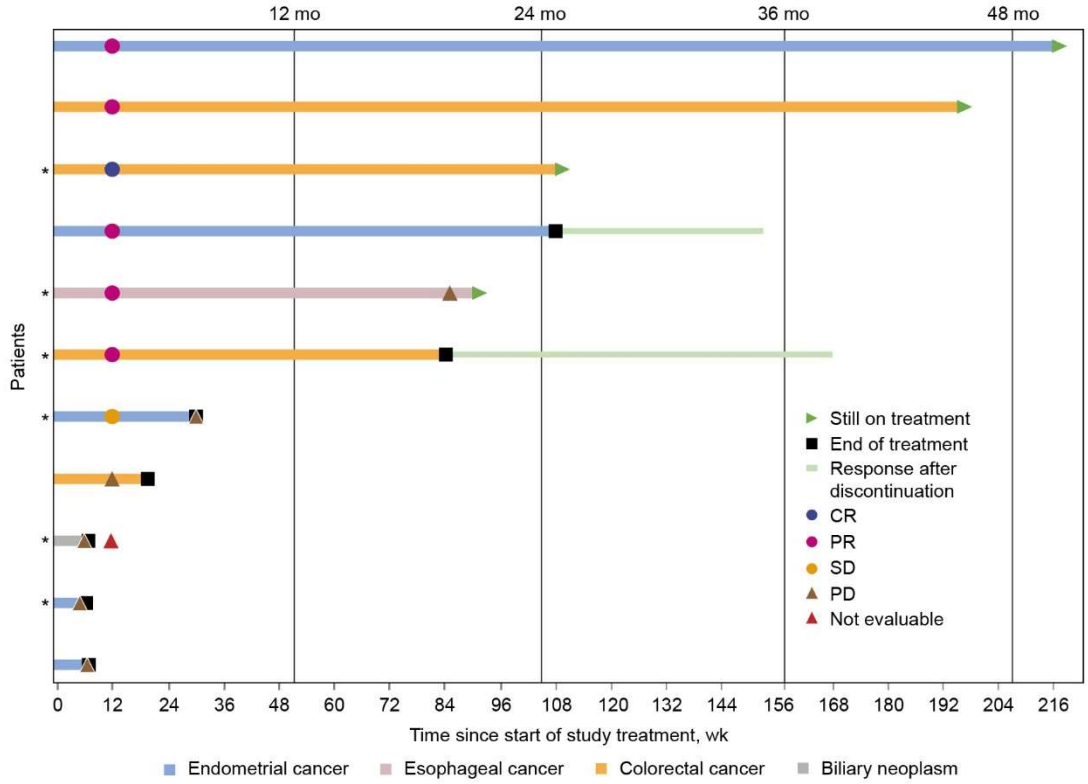
**eTable 6. POLE-Altered Antitumor Activity Analysis by BICR**

| Characteristic | POLE-mut solid tumors N = 11[a] |
|---|---|
| Median follow-up time, mo | 38.7 |
| Confirmed responses, n | 6 |
| ORR, % (95% CI) | 54.5 (23.4-83.3) |
| CR, n (%) | 1 (9.1) |
| PR, n (%) | 5 (45.5) |
| SD, n (%) | 1 (9.1) |
| PD, n (%) | 4 (36.4) |
| Disease control rate, % (95% CI) | 63.6 (30.8-89.1) |
| Response ongoing, n (%) | 5 (83.3) |
| Duration of response, median (range), mo | NR (16.9-44.4+) |
| Patients with duration of response ≥6 mo, n (%) | 6 (100) |
| Median PFS (95% CI), mo | 19.5 (1.2-NR) |
| Median OS (95% CI), mo | NR (1.8-NR) |

Abbreviations: BICR, blinded independent central review; CR, complete response; dMMR, mismatch repair deficient; EC, endometrial cancer; MMRp, mismatch repair proficient; NR, not reached; ORR, objective response rate; OS, overall survival; PD, progressive disease; POLE-mut, polymerase epsilon mutation; PFS, progression-free survival; PR, partial response; SD, stable disease.

[a] Includes 2 patients with dMMR POLE-mut non-EC (prospective), 4 patients with MMRp POLE-mut non-EC (prospective), 3 patients with dMMR POLE-mut EC (retrospective), and 2 patients with MMRp POLE-mut EC (retrospective).

## eFigure 5. Duration of Treatment for Patients With POLE-Altered Solid Tumors

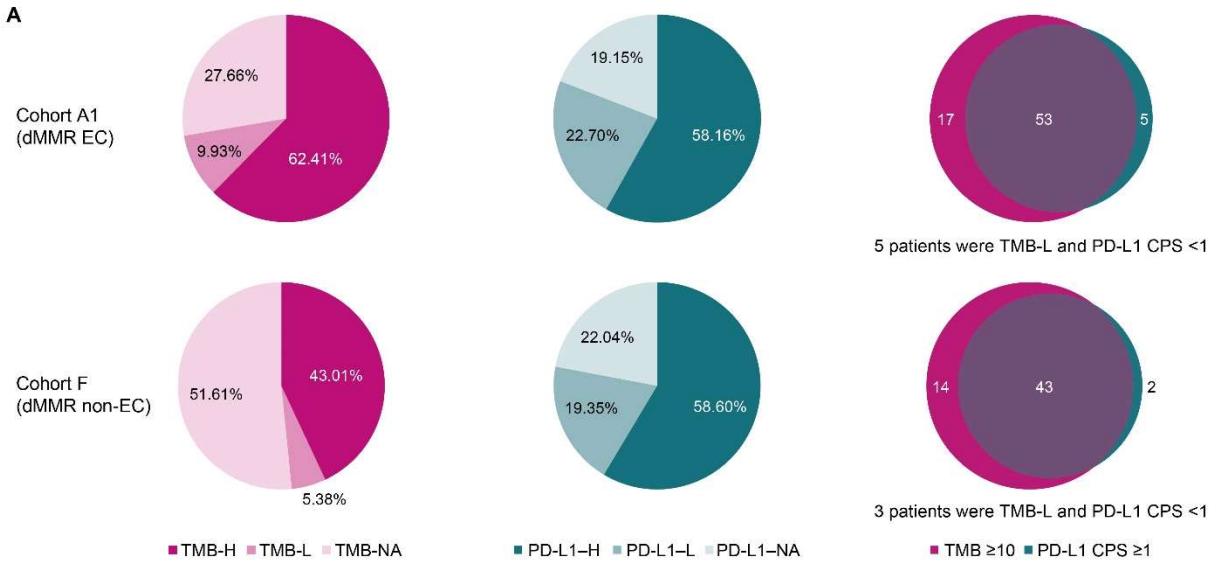



Abbreviations: CR, complete response; PD, progressive disease; POLE-mut, polymerase epsilon mutation; PR, partial response; SD, stable disease.

**eAppendix 3. Exploratory Analysis of Biomarkers**

An exploratory analysis of the biomarkers TMB and PD-L1 was performed for 141 patients with dMMR EC and for 186 patients with dMMR non-EC solid tumors (eFigure 6). TMB-high and PD-L1–high were common in dMMR solid tumors. In cohort A1, for dMMR EC, 62.41% were classified as TMB-high, 9.93% classified as TMB-low, and 27.66% as TMB not available; 58.16% were classified as PD-L1–high, 22.70% classified as PD-L1–low, and 19.15% classified as PD-L1 not available. In cohort F, for dMMR non-EC solid tumors, 43.01% were classified as TMB-high, 5.38% classified as TMB-low, and 51.61% as TMB not available; 58.60% were classified as PD-L1–high, 19.35% classified as PD-L1–low, and 22.04% classified as PD-L1 not available (eFigure 6). The majority of TMB-high tumors were also PD-L1–high (eFigure 6). Most patients had a combined positive score (CPS) ≥1 (191/327 patients with dMMR solid tumors; 82/141 with EC, and 109/186 with non-EC solid tumors; eFigure 6 and 7), and most tumors had a TMB score of >10 mutations/Mb on the FMI test (eFigure 7). ORR by CPS or TMB was also calculated as a continuous variable (eFigure 8 and 9). In both cohorts, a CPS score of ≥1 corresponded with an increased response rate that leveled out, compared with the response rate of CPS scores <1 (eFigure 8). ORR also increased with increasing TMB score until reaching approximately 10 mutations/Mb in the EC cohort, and slightly higher (approximately 13-15 mutations/Mb) in the non-EC cohort (eFigure 9). When looking at ORR by biomarker status, in a combined analysis of patients with dMMR solid tumors, those with TMB-high/PD-L1–high tumors had a higher ORR (60.4%) than that seen in patients with TMB-low/PD-L1–low (25.0%), TMB-high/PD-L1–low (32.3%), or TMB-low/PD-L1–high (42.9%; eTable 7).

## eFigure 6. Prevalence of TMB and PD-L1 in GARNET Cohorts A1 and F




**B**

Cohort A1
(dMMR EC)

| | PD-L1–H | PD-L1–L | PD-L1–NA |
|---|---|---|---|
| **TMB-H** | 53 | 17 | 18 |
| **TMB-L** | 5 | 5 | 4 |
| **TMB-NA** | 24 | 10 | 5 |

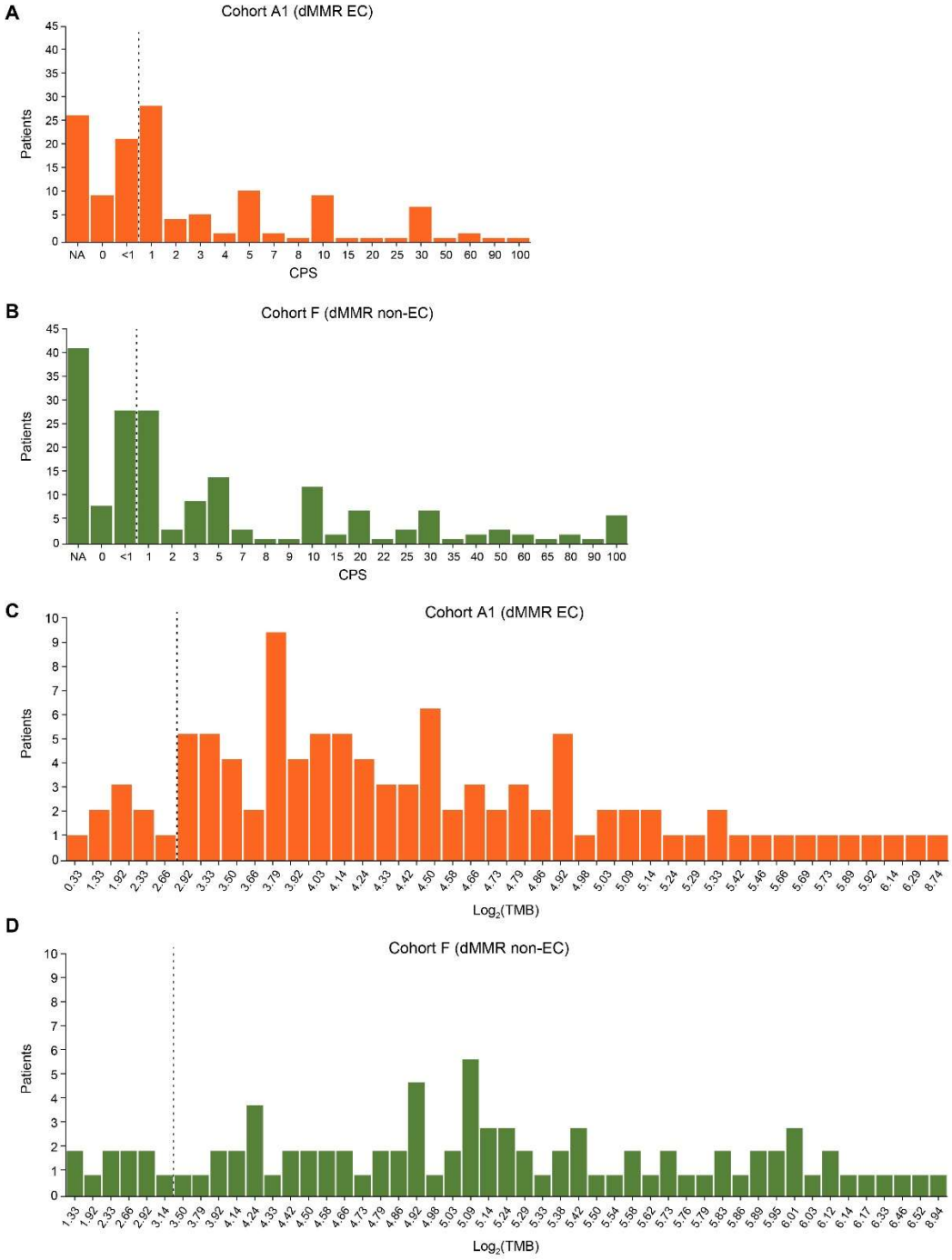
**C**

Cohort F
(dMMR non-EC)

| | PD-L1–H | PD-L1–L | PD-L1–NA |
|---|---|---|---|
| **TMB-H** | 43 | 14 | 23 |
| **TMB-L** | 2 | 3 | 5 |
| **TMB-NA** | 64 | 19 | 13 |

Prevalence of TMB and PD-L1 in GARNET cohorts A1 and F: (A) prevalence of TMB-H and PD-L1–H in both cohorts, (B) TMB and PD-L1 in dMMR EC (cohort A1), and (C) TMB and PD-L1 in dMMR non-EC (cohort F). Venn diagrams are restricted to only patients with a known CPS and TMB.
Abbreviations: CPS, combined positive score; dMMR, mismatch repair deficient; EC, endometrial cancer; H, high; L, low; NA, not applicable; PD-L1, programmed death ligand 1; TMB, tumor mutational burden.

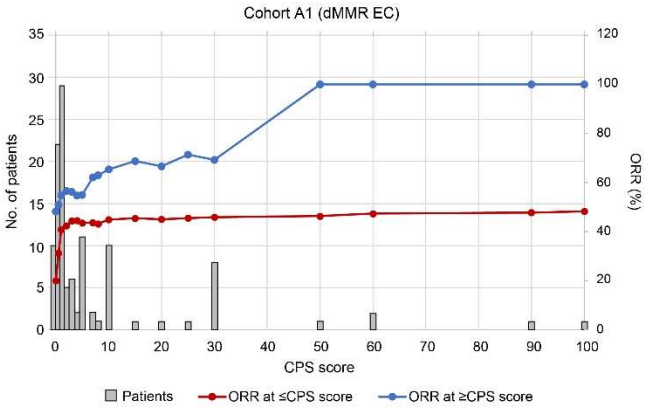
## eFigure 7. CPS and TMB Distribution by Cohort




CPS and TMB distribution by cohort: (A) CPS distribution in cohort A1, (B) CPS distribution in cohort F, (C) TMB distribution in cohort A1, and (D) TMB distribution in cohort F.
Patients with “NA” CPS scores are not included.
Dashed lines in panels (A) and (B) are located at CPS score of 1. All patients to the right of the dashed line have CPS scores of ≥1. Dashed lines in panels (C) and (D) are located at TMB scores of 10 mutations/Mb. All patients to the right of the dashed lines have TMB scores of ≥10 mutations/Mb.
Abbreviations: CPS, combined positive score; dMMR, mismatch repair deficient; EC, endometrial cancer; NA, not applicable; TMB, tumor mutational burden.

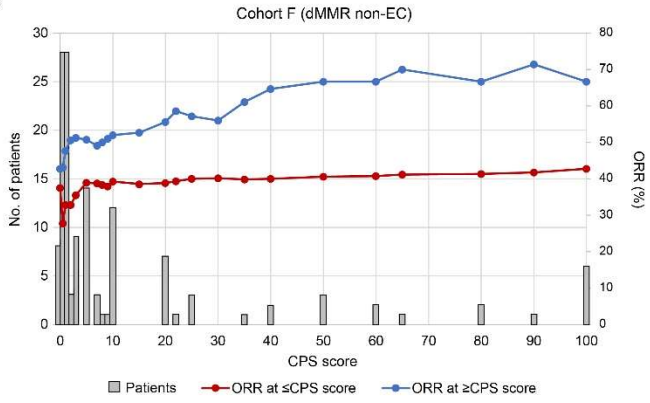
## eFigure 8. ORR by CPS as Continuous Variable

A




| CPS score | Patients | Responders | ORR (%) at ≤CPS score | ORR (%) at ≥CPS score |
|---|---|---|---|---|
| 0 | 10 | 2 | 20.00 | 48.25 |
| <1 | 22 | 8 | 31.25 | 50.96 |
| 1 | 29 | 15 | 40.98 | 54.88 |
| 2 | 5 | 3 | 42.42 | 56.60 |
| 3 | 6 | 4 | 44.44 | 56.25 |
| 4 | 2 | 1 | 44.59 | 54.76 |
| 5 | 11 | 4 | 43.53 | 55.00 |
| 7 | 2 | 1 | 43.68 | 62.07 |
| 8 | 1 | 0 | 43.18 | 62.96 |
| 10 | 10 | 6 | 44.90 | 65.38 |
| 15 | 1 | 1 | 45.45 | 68.75 |
| 20 | 1 | 0 | 45.00 | 66.67 |
| 25 | 1 | 1 | 45.54 | 71.43 |
| 30 | 8 | 4 | 45.87 | 69.23 |
| 50 | 1 | 1 | 46.36 | 100.00 |
| 60 | 2 | 2 | 47.32 | 100.00 |
| 90 | 1 | 1 | 47.79 | 100.00 |
| 100 | 1 | 1 | 48.25 | 100.00 |

B

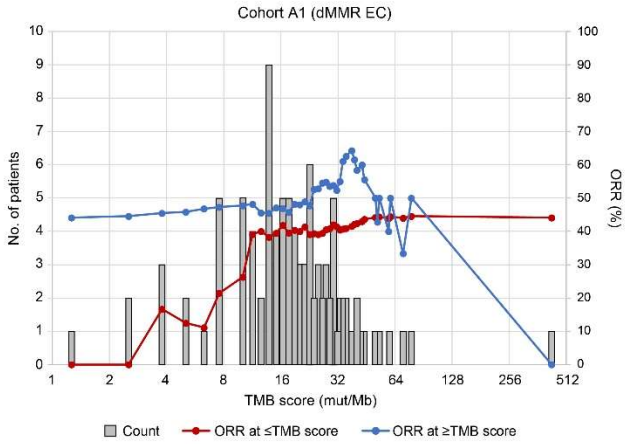



| CPS score | Patients | Responders | ORR (%) at ≤CPS score | ORR (%) at ≥CPS score |
|---|---|---|---|---|
| 0 | 8 | 3 | 37.50 | 42.76 |
| <1 | 28 | 7 | 27.78 | 43.07 |
| 1 | 28 | 11 | 32.81 | 47.71 |
| 2 | 3 | 1 | 32.84 | 50.62 |
| 3 | 9 | 5 | 35.53 | 51.28 |
| 5 | 14 | 8 | 38.89 | 50.72 |
| 7 | 3 | 1 | 38.71 | 49.09 |
| 8 | 1 | 0 | 38.30 | 50.00 |
| 9 | 1 | 0 | 37.89 | 50.98 |
| 10 | 12 | 6 | 39.25 | 52.00 |
| 15 | 2 | 0 | 38.53 | 52.63 |
| 20 | 7 | 3 | 38.79 | 55.56 |
| 22 | 1 | 1 | 39.32 | 58.62 |
| 25 | 3 | 2 | 40.00 | 57.14 |
| 30 | 7 | 3 | 40.16 | 56.00 |
| 35 | 1 | 0 | 39.84 | 61.11 |
| 40 | 2 | 1 | 40.00 | 64.71 |
| 50 | 3 | 2 | 40.60 | 66.67 |
| 60 | 2 | 1 | 40.74 | 66.67 |
| 65 | 1 | 1 | 41.18 | 70.00 |
| 80 | 2 | 1 | 41.30 | 66.67 |
| 90 | 1 | 1 | 41.73 | 71.43 |
| 100 | 6 | 4 | 42.76 | 66.67 |

ORR by CPS as continuous variable in (A) cohort A1 and (B) cohort F.
Abbreviations: CPS, combined positive score; dMMR, mismatch repair deficient; EC, endometrial cancer; ORR, objective response rate.

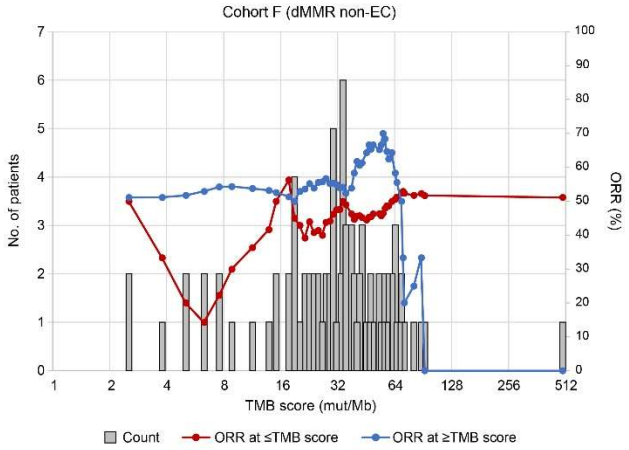
## eFigure 9. ORR by TMB as Continuous Variable

A




| TMB score | Patients | Responders | ORR (%) at ≤TMB score | ORR (%) at ≥TMB score |
|---|---|---|---|---|
| 1.26 | 1 | 0 | 0.00 | 44.12 |
| 2.52 | 2 | 0 | 0.00 | 44.55 |
| 3.78 | 3 | 1 | 16.67 | 45.45 |
| 5.04 | 2 | 0 | 12.50 | 45.83 |
| 6.3 | 1 | 0 | 11.11 | 46.81 |
| 7.57 | 5 | 2 | 21.43 | 47.31 |
| 10.09 | 5 | 2 | 26.32 | 47.73 |
| 11.35 | 4 | 4 | 39.13 | 48.19 |
| 12.61 | 2 | 1 | 40.00 | 45.57 |
| 13.87 | 9 | 3 | 38.24 | 45.45 |
| 15.13 | 4 | 2 | 39.47 | 47.06 |
| 16.39 | 5 | 3 | 41.86 | 46.88 |
| 17.65 | 5 | 1 | 39.58 | 45.76 |
| 18.91 | 4 | 2 | 40.38 | 48.15 |
| 20.17 | 3 | 1 | 40.00 | 48.00 |
| 21.43 | 3 | 2 | 41.38 | 48.94 |
| 22.7 | 6 | 1 | 39.06 | 47.73 |
| 23.96 | 2 | 1 | 39.39 | 52.63 |
| 25.22 | 3 | 1 | 39.13 | 52.78 |
| 26.48 | 2 | 1 | 39.44 | 54.55 |
| 27.74 | 3 | 2 | 40.54 | 54.84 |
| 29 | 2 | 1 | 40.79 | 53.57 |
| 30.26 | 5 | 3 | 41.98 | 53.85 |
| 31.52 | 1 | 0 | 41.46 | 52.38 |
| 32.78 | 2 | 0 | 40.48 | 55.00 |
| 34.04 | 2 | 1 | 40.70 | 61.11 |
| 35.3 | 2 | 1 | 40.91 | 62.50 |
| 37.83 | 1 | 1 | 41.57 | 64.29 |
| 39.09 | 1 | 1 | 42.22 | 61.54 |
| 40.35 | 2 | 1 | 42.39 | 58.33 |
| 42.87 | 1 | 1 | 43.01 | 60.00 |
| 44.13 | 1 | 1 | 43.62 | 55.56 |
| 50.43 | 1 | 1 | 44.21 | 50.00 |
| 51.69 | 1 | 0 | 43.75 | 42.86 |
| 52.96 | 1 | 1 | 44.33 | 50.00 |
| 59.26 | 1 | 0 | 43.88 | 40.00 |
| 60.52 | 1 | 1 | 44.44 | 50.00 |
| 70.61 | 1 | 0 | 44.00 | 33.33 |
| 78.17 | 1 | 1 | 44.55 | 50.00 |
| 428.69 | 1 | 0 | 44.12 | 0.00 |

B




| TMB score | Patients | Responders | ORR (%) at ≤TMB score | ORR (%) at ≥TMB score |
|---|---|---|---|---|
| 2.52 | 2 | 1 | 50.00 | 51.11 |
| 3.78 | 1 | 0 | 33.33 | 51.14 |
| 5.04 | 2 | 0 | 20.00 | 51.72 |
| 6.3 | 2 | 0 | 14.29 | 52.94 |
| 7.57 | 2 | 1 | 22.22 | 54.22 |
| 8.83 | 1 | 1 | 30.00 | 54.32 |
| 11.35 | 1 | 1 | 36.36 | 53.75 |
| 13.87 | 1 | 1 | 41.67 | 53.16 |
| 15.13 | 2 | 2 | 50.00 | 52.56 |
| 17.65 | 2 | 2 | 56.25 | 51.32 |
| 18.91 | 4 | 0 | 45.00 | 50.00 |
| 20.17 | 1 | 0 | 42.86 | 52.86 |
| 21.43 | 2 | 0 | 39.13 | 53.62 |
| 22.7 | 2 | 2 | 44.00 | 55.22 |
| 23.96 | 2 | 0 | 40.74 | 53.85 |
| 25.22 | 2 | 1 | 41.38 | 55.56 |
| 26.48 | 1 | 0 | 40.00 | 55.74 |
| 27.74 | 2 | 2 | 43.75 | 56.67 |
| 29 | 2 | 1 | 44.12 | 55.17 |
| 30.26 | 5 | 3 | 46.15 | 55.36 |
| 31.52 | 1 | 1 | 47.50 | 54.90 |
| 32.78 | 2 | 1 | 47.62 | 54.00 |
| 34.04 | 6 | 4 | 50.00 | 54.17 |
| 35.3 | 3 | 1 | 49.02 | 52.38 |
| 37.83 | 3 | 0 | 46.30 | 53.85 |
| 39.09 | 2 | 0 | 44.64 | 58.33 |
| 40.35 | 1 | 1 | 45.61 | 61.76 |
| 41.61 | 2 | 1 | 45.76 | 60.61 |
| 42.87 | 3 | 1 | 45.16 | 61.29 |
| 45.39 | 1 | 0 | 44.44 | 64.29 |
| 46.65 | 1 | 1 | 45.31 | 66.67 |
| 47.91 | 2 | 1 | 45.45 | 65.38 |
| 49.17 | 1 | 1 | 46.27 | 66.67 |
| 52.96 | 2 | 1 | 46.38 | 65.22 |
| 54.22 | 1 | 0 | 45.71 | 66.67 |
| 55.48 | 1 | 1 | 46.48 | 70.00 |
| 56.74 | 2 | 2 | 47.95 | 68.42 |
| 58 | 1 | 1 | 48.65 | 64.71 |
| 59.26 | 2 | 1 | 48.68 | 62.50 |
| 61.78 | 2 | 2 | 50.00 | 64.29 |
| 64.3 | 3 | 2 | 50.62 | 58.33 |
| 65.56 | 1 | 1 | 51.22 | 55.56 |
| 69.35 | 2 | 2 | 52.38 | 50.00 |
| 70.61 | 1 | 1 | 52.94 | 33.33 |
| 71.87 | 1 | 0 | 52.33 | 20.00 |
| 80.69 | 1 | 1 | 51.72 | 25.00 |
| 88.26 | 1 | 1 | 52.27 | 33.33 |
| 92.04 | 1 | 0 | 51.69 | 0.00 |
| 491.73 | 1 | 0 | 51.11 | 0.00 |

ORR by TMB as continuous variable in (A) cohort A1 and (B) cohort F.
Abbreviations: dMMR, mismatch repair deficient; EC, endometrial cancer; mut, mutations; ORR, objective response rate; TMB, tumor mutational burden.

**eTable 7. Antitumor Activity Results by TMB and PD-L1 Status for dMMR EC and Non-EC Solid Tumors[a]**

| ORR by BICR per RECIST v1.1, n/N (%, 95% CI)[a] | dMMR solid tumors N = 327 | dMMR EC N = 141 | dMMR non-EC N = 186 |
|---|---|---|---|
| Overall cohort for all patients with dMMR status | 144/327 (44.0, 38.6-49.6) | 64/141 (45.4, 37.0-54.0) | 80/186 (43.0, 35.8-50.5) |
| Overall ORR for patients with both known TMB status and known CPS | 73/142 (51.4, 42.9-59.9) | 40/80 (50.0, 38.6-61.4) | 33/62 (53.2, 40.1-66) |
| TMB-low/PD-L1–low (L/L) | 2/8 (25.0, 3.2-65.1) | 1/5 (20.0, 0.5-71.6) | 1/3 (33.3, 0.8-90.6) |
| TMB-low/PD-L1–high (L/H) | 3/7 (42.9, 9.9-81.6) | 2/5 (40.0, 5.3-85.3) | 1/2 (50.0, 1.3-98.7) |
| TMB-high/PD-L1–low (H/L) | 10/31 (32.3, 16.7-51.4) | 5/17 (29.4, 10.3-56.0) | 5/14 (35.7, 12.8-64.9) |
| TMB-high/PD-L1–high (H/H) | 58/96 (60.4, 49.9-70.3) | 32/53 (60.4, 46.0-73.5) | 26/43 (60.5, 44.4-75.0) |

Abbreviations: BICR, blinded independent central review; CPS, combined positive score; dMMR, mismatch repair deficient; EC, endometrial cancer; H, high; L, low; ORR, objective response rate; PD-L1, programmed death ligand 1; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; TMB, tumor mutational burden.

[a] Only those patients with both known TMB status and known CPS were included in ORR calculations.