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Gynecologic Oncology 196 (2025) 28–35

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

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HIGHLIGHTS

- We evaluated cemiplimab + peltopepimut-S vaccine therapy in 113 patients with recurrent HPV16+ cervical cancer
- The ORR with cemiplimab + peltopepimut-S was 16.8 %
- Higher PD-L1 was correlated with higher ORR: PD-L1 ≥ 1 % (24.1 %) and PD-L1 ≥ 20 % (33.3 %) versus PD-L1 < 1 % (15.8 %)
- The safety profile of combination therapy was generally similar to that of cemiplimab monotherapy
- The treatment showed potential benefit in HPV16+ cervical cancer, particularly in patients with higher PD-L1 expression

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https://doi.org/10.1016/j.ygyno.2025.03.019

ARTICLE INFO

Article history:
Received 23 December 2024
Received in revised form 10 March 2025
Accepted 12 March 2025
Available online 27 March 2025

Keywords:
Cemiplimab
Recurrent/metastatic
Cervical cancer
Peltopepimut-S vaccine
HPV16

ABSTRACT

Objective. To estimate the clinical benefit of cemiplimab+peltopepimut-S vaccine after disease progression on first-line chemotherapy.

Methods. This global phase 2 open-label study (NCT04646005) recruited patients with recurrent HPV16+ cervical cancer who had previously experienced disease progression after first-line chemotherapy. Patients received a total of 3 doses of peltopepimut-S vaccine on days 1, 29, and 50 and cemiplimab 350 mg every 3 weeks until disease progression or other reason for early discontinuation. Primary endpoint was objective response rate (ORR) per RECIST version 1.1; secondary endpoints were duration of response (DOR), overall survival (OS), progression-free survival (PFS), and safety.

Results. Of 113 patients enrolled between June 28, 2021 and May 22, 2023, 80.5 % were white, with a median age of 49.0 years, and 58.4 % had an ECOG PS of 0. Median duration of follow-up was 4.9 months. ORR (95 % CI) per investigator assessment was 16.8 % (9.9–23.7). ORR of patients with squamous cell carcinoma by PD-L1 expression in tumor cells was 15.8 % for patients with PD-L1 < 1 % and 24.1 % for patients with PD-L1 ≥ 1 %. Median (95 % CI) DOR was 5.6 (3.5–not estimable) months. Median (95 % CI) OS and PFS were 13.3 (10.8–16.3) months and 3.0 (1.7–4.0) months, respectively. Treatment-emergent adverse events (TEAEs) occurred in 92.9 % of patients, the most common being injection-site reaction (38.9 %) and anemia (25.7 %). Six (5.3 %) patients died from a TEAE.

Conclusion. Cemiplimab+peltopepimut-S vaccine provides similar benefits to cemiplimab monotherapy; patients with higher PD-L1 expression in tumor cells may be more likely to benefit from treatment.

1. Introduction

Cervical cancer is the fourth most common type of cancer and the second-leading cause of death in developing countries [1]. Although survival for patients with cervical cancer has improved [2], outcomes remain especially poor in those with advanced-stage or recurrent disease [3]. Conventional cytotoxic chemotherapy has limited efficacy in patients who experience disease progression following first-line platinum-based chemotherapy [4–6]. Estimated overall survival (OS) at 5 years is approximately 65 % and 17 % for locally advanced and metastatic disease, respectively [7].

Recent developments in targeted therapies, such as immune checkpoint inhibitors (ICIs), have provided new therapeutic opportunities for patients [3]. ICIs as monotherapy or in combination with chemotherapy have emerged as novel treatments that could have durable responses, with an impact on OS. In particular, investigation of programmed cell death-ligand 1 (PD-L1) expression in patients with cervical cancer suggests a potential programmed cell death-1 (PD-1)/PD-L1 pathway blockade in these patients [8]. Recent studies have shown improved outcomes in patients treated for first-line recurrent or metastatic cervical cancer who received anti–PD-1/PD-L1 therapy in combination with chemotherapy (with or without anti-vascular endothelial growth factor [VEGF] treatment) [9,10]. Studied treatments include pembrolizumab (anti–PD-1) plus chemotherapy with or without bevacizumab (anti-VEGF) and atezolizumab (anti–PD-1) plus chemotherapy and bevacizumab.

Cemiplimab is a fully human hinge-stabilized immunoglobulin G4 ICI targeting the PD-1 receptor [11]. In an international phase 3 randomized study (EMPOWER-Cervical 1; NCT03257267) of patients with recurrent or metastatic cervical cancer after first-line platinum-based chemotherapy, regardless of PD-L1 status, cemiplimab monotherapy resulted in significantly improved OS (12.0 vs 8.5 months; hazard ratio for death 0.69; $P < 0.001$), and a higher objective response rate (ORR; 16.4 % vs 6.3 %) compared with investigator's choice of chemotherapy [12]. Cemiplimab is currently approved as monotherapy (regardless of PD-L1 expression) for the treatment of recurrent or metastatic cervical cancer in Europe, Japan, Canada, Brazil, and South Korea [13–16].

Therapeutic cancer vaccines target the primary causal factor of cervical cancer: persistent high-risk human papillomavirus (HPV) infection [17]. The most predominant high-risk strain, HPV16, is estimated to be responsible for over 50 % of human cervical cancers [18,19]. The peltopepimut-S vaccine consists of 9 overlapping synthetic long peptides derived from the E6 (five 32-mer and four 25-mer E6 peptides) and E7 (three 35-mer E7 peptides) oncogenic proteins of the HPV16 virus [20–22]. Peltopepimut-S in combination with chemotherapy in advanced, metastatic, or recurrent cervical cancer has previously shown tumor regression in 43 % of 72 evaluable patients; moreover, higher levels of vaccine-induced immune responses correlated with longer survival [21]. In 2020, peltopepimut-S received orphan drug designation as a single agent in HPV16-positive cervical cancer [23]; it is currently being studied in HPV16-positive cancers in combination with cemiplimab in several phase 2 clinical trials (NCT04398524, NCT03669718, NCT04646005).

Here, we present the efficacy and safety findings of a phase 2 study of the combination of cemiplimab and peltopepimut-S vaccine in patients with recurrent HPV16-positive cervical cancer with disease progression after first-line chemotherapy (NCT04646005).

2. Methods

2.1. Study design

This was a global, phase 2, open-label, single-group study in patients with recurrent HPV16-positive cervical cancer with disease progression after first-line chemotherapy (NCT04646005).

Patients were recruited from 19 sites in the following countries: Brazil ($n = 5$), the Netherlands ($n = 4$), Belgium ($n = 3$), South Korea ($n = 3$), Italy ($n = 2$), and Spain ($n = 2$). Patients received peltopepimut-S vaccine administered by subcutaneous injection on days 1, 29, and 50 and cemiplimab 350 mg administered intravenously every 3 weeks until disease progression or withdrawal from the study (**Fig. S1**).

Patients withdrawing due to disease progression were followed for 90 days following the last dose of cemiplimab for safety evaluation. Patients who withdrew due to reasons other than progression were followed-up every 4 months until disease progression or commencement of other anti-cancer systemic therapy. Dose modifications were not permitted. Additional details regarding criteria for treatment discontinuation and treatment with cemiplimab beyond disease progression are provided in the **supplementary material**.

This study was conducted in accordance with the ethical principles of the Declaration of Helsinki and the International Conference on Harmonization Good Clinical Practice guidelines. All patients provided written informed consent.

2.2. Patients

This study enrolled adults (≥18 years of age) with histologically confirmed recurrent or metastatic HPV16-positive cervical cancer (determined by an investigational HPV16 polymerase chain reaction assay), with squamous cell carcinoma (SCC) histology or adenocarcinoma/adenosquamous histology who had progressed on first-line platinum-containing chemotherapy in the recurrent or metastatic setting. The number of patients with adenocarcinoma/adenosquamous histology was capped at approximately 20 % of total enrollment to mimic global incidence [24]. Key inclusion criteria were: HPV16 genotype–positive cervical cancer, as determined by a specified central reference laboratory and which progressed after platinum-based chemotherapy; measurable disease as defined by Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1; prior receipt of bevacizumab (if available) and paclitaxel therapy; and Eastern Cooperative Oncology Group performance status (ECOG PS) of 0 or 1.

Patients were excluded from the trial if they had: prior treatment with an anti–PD-1/PD-L1 agent or other systemic immune-modulating agent; major surgery or radiation therapy within 14 days of the first administration of the study drug; received treatment with an approved systemic therapy within 4 weeks of the first dose of the study drug; or had not yet recovered (ie, grade ≤ 1 or baseline) from any acute toxicities except for laboratory changes.

A full description of inclusion and exclusion criteria is provided in the **supplementary material**.

2.3. Study outcomes

The primary endpoint was ORR: complete response (CR) + partial response (PR) until disease progression, measured by RECIST version 1.1 at screening, day 50 of cycle 1, day 43 of cycles 2 to 4, and day 64 from cycle 5 onwards.

Secondary endpoints included duration of response (DOR); progression-free survival (PFS); OS; and incidence and severity during and up to 90 days after the last dose of study treatment of treatment-emergent adverse events (TEAEs), adverse events (AEs) of special interest (more details available in the **supplementary material**), an immune-mediated AE of any grade in a patient previously treated with a phosphoinositide 3-kinase inhibitor, and serious AEs. Exploratory analyses examined the association of clinical efficacy endpoints with baseline PD-L1 expression (measured in tumor cells).

2.4. Statistical analysis

As this was a single-arm, open-label study, no formal statistical hypothesis testing was performed. A total of 105 patients was planned for the study. Sample size justification is described in the **supplementary material**. The data presented in this manuscript are based on the data cut-off for the primary efficacy analysis: May 22, 2023 (date of last observation from the last patient for the primary efficacy endpoint). The full analysis set (FAS) included all enrolled patients who received any study drug. Efficacy, safety, and baseline variables were analyzed or summarized using the FAS. The ORR was defined as the proportion of patients who achieved a best overall response (BOR) of CR or PR. Patients who were not evaluable for BOR were considered non-responders. The ORR, along with the 2-sided 95 % confidence interval (CI) using a normal approximation of the binomial distribution, was summarized.

3. Results

3.1. Demographics and baseline clinical characteristics

Patient demographics, baseline characteristics, and tumor characteristics are summarized in Table 1. A total of 113 female patients were enrolled. Most patients (80.5 %) were white, with a median (range) age of 49.0 (28.0, 78.0) years, and the majority had an ECOG PS of 0 (58.4 %); most patients had squamous disease (85.0 %) as the number of patients with adenocarcinoma/adenosquamous histology was capped at 20 %. The median (interquartile range [IQR]) number of prior lines of anti-cancer systemic therapy was 2.0 (1.0–3.0).

Table 1
Demographics, clinical characteristics, and tumor characteristics at baseline.

	Cemiplimab + peltopepimut-S ($N = 113$)
Age, years	
Median (range)	49.0 (28.0–78.0)
<65, n (%)	98 (86.7)
Female sex, n (%)	113 (100.0)
Race, n (%)	
Asian	14 (12.4)
Black or African American	3 (2.7)
Native Hawaiian/other Pacific Islander	1 (0.9)
White	91 (80.5)
Multiple	2 (1.8)
Not reported	2 (1.8)
Ethnicity n (%)	
Hispanic or Latinx	25 (22.1)
Not Hispanic or Latinx	88 (77.9)
Region of enrollment, n (%)	
Europe	76 (67.3)
Asia	13 (11.5)
South America	24 (21.2)
ECOG PS, n (%)	
0	66 (58.4)
1	47 (41.6)
Histology/cytology, n (%)	
Adenocarcinoma	17 (15.0)
Squamous cell carcinoma	96 (85.0)
PD-L1 expression, n (%)	
<1 %	48 (42.5)[a]
≥1 %	58 (51.3)[a]
Median prior lines of cancer-related systemic therapy, n (IQR)	2 (1.0–3.0)
Number of prior lines, n (%)	
1	29 (25.7)
2	52 (46.0)
≥3	32 (28.3)

Abbreviations: ECOG PS, Eastern Cooperative Oncology Group performance status; IQR, interquartile range; PD-L1, programmed cell death-ligand 1.
[a] PD-L1 expression was not evaluable for 7 patients.

The median (IQR) duration of study follow-up was 4.9 (3.0–7.5) months. The median (IQR) duration of treatment exposure was 10.0 (9.7–10.3) weeks for peltopepimut-S injection and 18.2 (9.0–27.6) weeks for cemiplimab.

Of 113 patients treated with peltopepimut-S plus cemiplimab, 20.4 % ($n = 23$) were still being treated at data cut-off (**Fig. S2**). Ninety patients discontinued treatment: 66.4 % ($n = 75$) due to progressive disease; 7.1 % ($n = 8$) due to death ($n = 4$ of which were due to disease progression); 3.5 % ($n = 4$) because of AEs; and 2.7 % ($n = 3$) due to the patient's decision.

3.2. Response rate

The ORR (95 % CI) per investigator's assessment was 16.8 % (9.9–23.7) (Table 2**;** Fig. 1). All responders had SCC histology.

3.3. Secondary efficacy endpoints

The median (95 % CI) Kaplan–Meier estimated DOR per investigator's assessment was 5.6 (3.5–not evaluable) months (Fig. 2A). The observed DOR ranged from 2.6 to 14.5 months; 31.6 % of patients had a DOR ≥6 months and 5.3 % had a DOR ≥12 months.

Table 2
Best overall tumor response rate per RECIST V1.1 by investigator assessment.

	Cemiplimab + peltopepimut-S ($N = 113$)
Objective response rate (CR + PR), % (95 % CI)[a]	16.8 (9.9–23.7)
Best overall tumor response, n (%)	
CR[b]	3 (2.7)
PR[b]	16 (14.2)
Stable disease[c]	43 (38.1)
NE[d]	11 (9.7)
DCR (CR + PR + stable disease), % (95 % CI)[a]	54.9 (45.7–64.0)
Progression of disease, n (%)	40 (35.4)
Kaplan–Meier estimated duration of response (CR or PR), median (95 % CI), months	5.6 (3.5–NE)

Abbreviations: CI, confidence interval; CR, complete response; DCR, disease control rate; NE, not evaluable; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors.
[a] Wald (normal approximation to binomial distribution) CI.
[b] CR/PR was confirmed by repeated assessments no less than 4 weeks apart.
[c] Stable disease criteria were met at least once after a minimum duration of 42 days after the first dose date.
[d] Includes missing and unknown tumor responses.

The median (95 % CI) OS was 13.3 (10.8–16.3) months (Fig. 2B). The estimated OS probability (95 % CI) was 80.5 % (71.7–86.9) at 6 months and 54.5 % (42.1–65.3) at 12 months.

The median (95 % CI) PFS per investigator's assessment was 3.0 (1.7–4.0) months (Fig. 2C). The estimated PFS probability (95 % CI) was 20.5 % (13.4–28.6) at 6 months and 7.8 % (3.3–15.0) at 12 months.

3.4. Exploratory efficacy

An exploratory analysis of ORR by PD-L1 level (by tumor proportion score) was conducted in the SCC patient subset, as all responders had this histology. The ORR (95 % CI) in patients with SCC and PD-L1 < 1 % was 15.8 % (4.2–27.4) (**Table S1**). The ORR (95 % CI) among patients with SCC and PD-L1 ≥ 1 % was 24.1 % (12.7–35.5) (**Table S1;** Fig. 1). The ORR (95 % CI) among patients with SCC and PD-L1 ≥ 20 % was 33.3 % (11.6–55.1) (**Table S1;** Fig. 1).

The median PFS estimate for patients with PD-L1 < 1 % was 2.3 months (95 % CI, 1.6–3.1) with a probability of event-free survival of 12.8 % (95 % CI, 4.9–24.7) at 6 months. The median PFS estimate

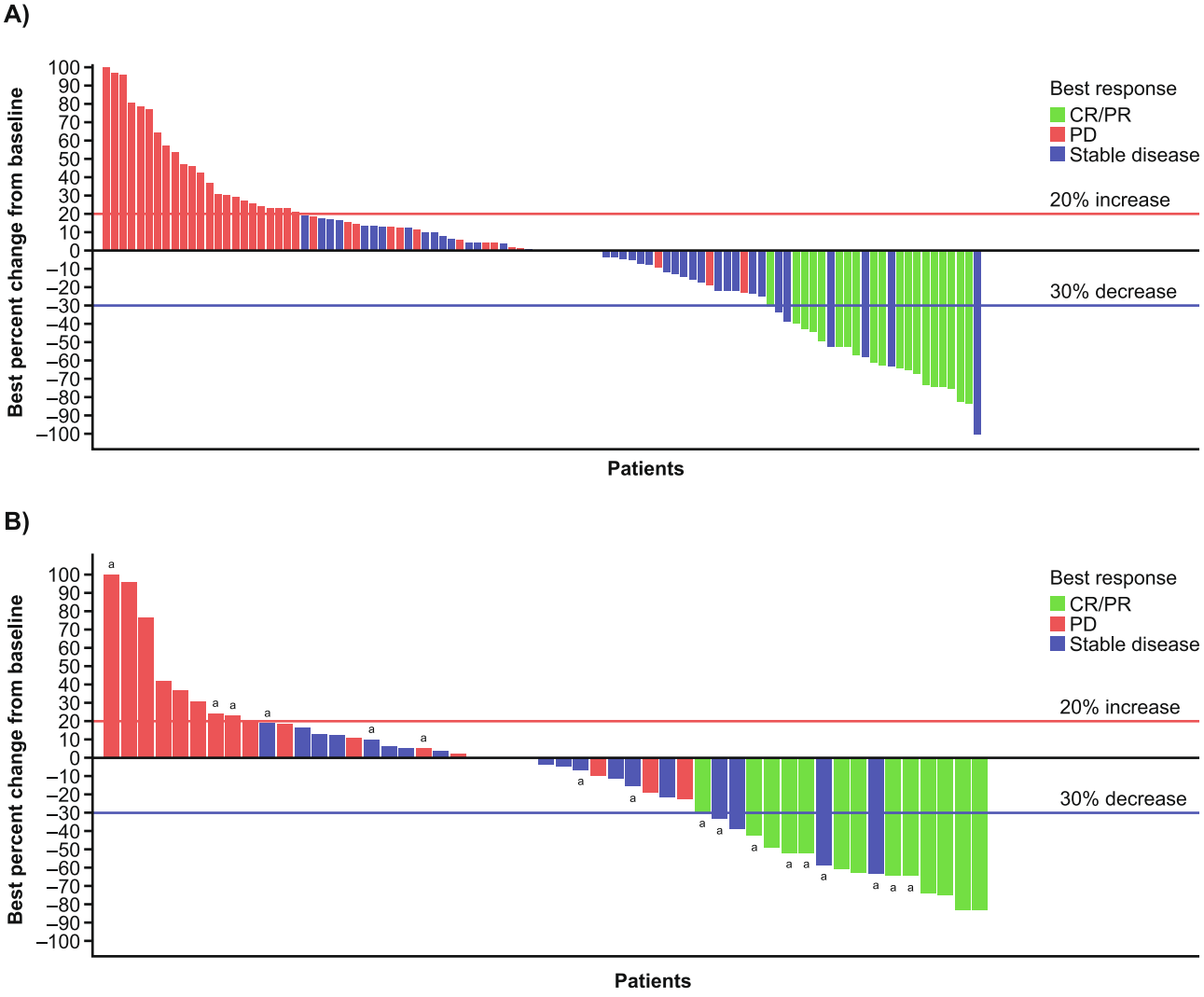

Fig. 1. Waterfall plot of overall response per RECIST version 1.1 criteria by investigator assessment (full analysis set) for (A) all patients and (B) patients with SCC and PD-L1 ≥ 1 % and ≥ 20% in tumor cells.
Abbreviations: CR, complete response; PD, progressive disease; PD-L1, programmed cell death-ligand 1; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SCC, squamous cell carcinoma.
[a]Patients with PD-L1 ≥ 20 % in tumor cells.
Note: some patients experienced a ≥ 30 % decrease in tumor size from baseline but had stable disease according to RECIST version 1.1 criteria due to unconfirmed responses and/or new lesions.

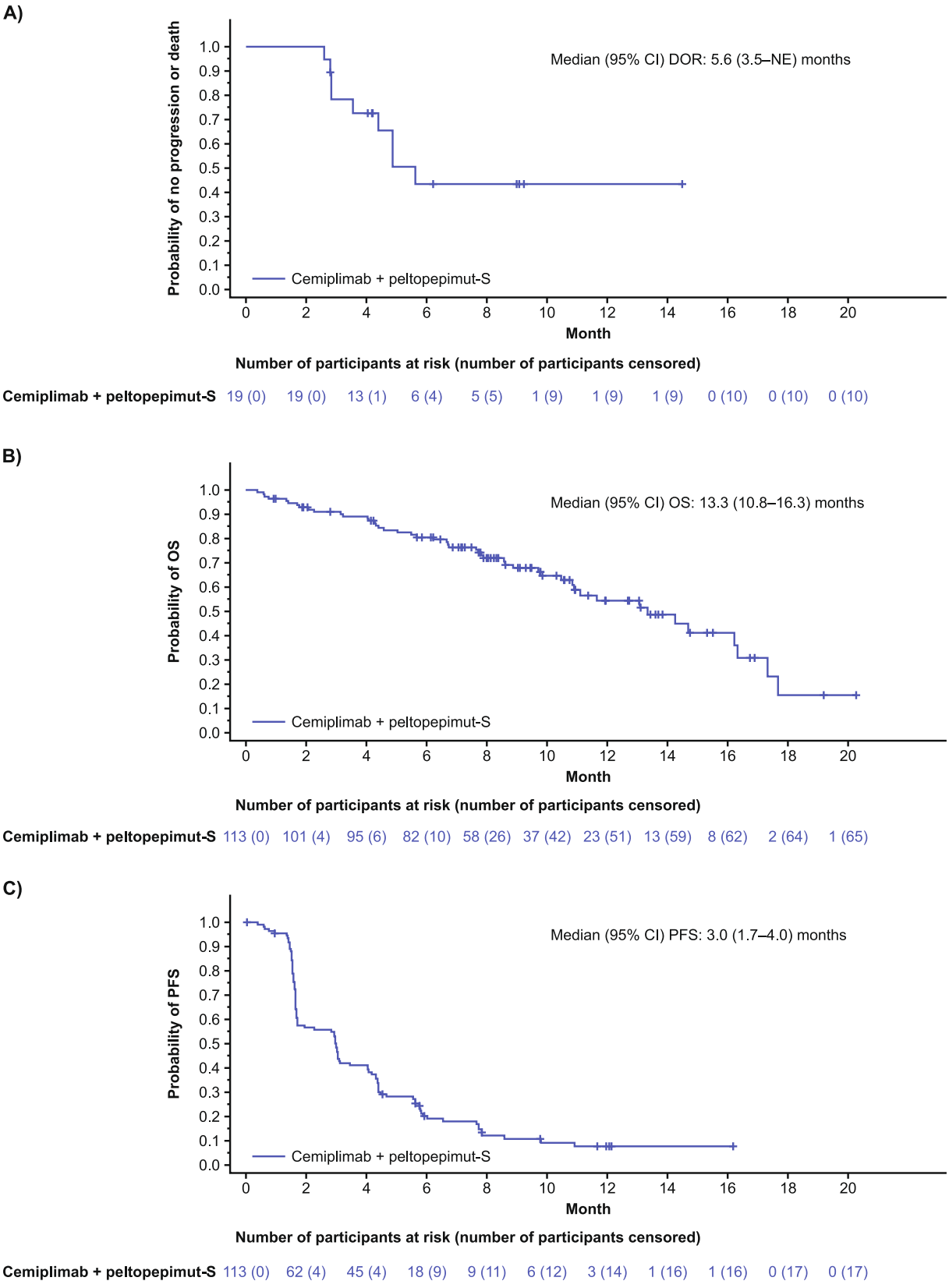

Fig. 2. Kaplan–Meier curves of (A) DOR (patients with confirmed CR or PR), (B) OS[a], and (C) PFS (full analysis set).
[a]Patients were censored at death or study discontinuation; this was an exploratory analysis.
Abbreviations: CI, confidence interval; CR, complete response; DOR, duration of response; NE, not evaluable; OS, overall survival; PFS, progression-free survival; PR, partial response.

for patients with PD-L1 ≥ 1 % was 3.3 months (95 % CI, 2.8–4.4) with a probability of event-free survival of 25.7 % (95 % CI, 15.3–37.4) at 6 months.

Estimated OS by PD-L1 expression in patients with SCC is shown in **Fig. S3**. The Kaplan–Meier estimated median OS in the PD-L1 ≥ 1 % subset was 14.3 months (95 % CI, 10.5–not evaluable [NE]) and in the PD-

Table 3
Summary of safety data.

n (%)	Cemiplimab + peltopepimut-S ($N = 113$)	
	All-cause	Treatment-related
Patients with any TEAE	105 (92.9)	77 (68.1)
Patients with grade ≥ 3 TEAEs	45 (39.8)	11 (9.7)
Patients with serious adverse events	29 (25.7)	4 (3.5)
Patients with TEAEs leading to treatment discontinuation	4 (3.5)	3 (2.7)
Patients with TEAEs resulting in death[a]	6 (5.3)	1 (0.9)
TEAEs that occurred in ≥10 % of patients		
Injection-site reaction	44 (38.9)	44 (38.9)
Anemia	29 (25.7)	3 (2.7)
Nausea	25 (22.1)	11 (9.7)
Pyrexia	22 (19.5)	11 (9.7)
Fatigue	21 (18.6)	12 (10.6)
Vomiting	16 (14.2)	5 (4.4)
Abdominal pain	15 (13.3)	3 (2.7)
Constipation	14 (12.4)	1 (0.9)
Decreased appetite	14 (12.4)	3 (2.7)
Diarrhea	14 (12.4)	8 (7.1)
Asthenia	13 (11.5)	6 (5.3)

Abbreviation: TEAE, treatment-emergent adverse event.
[a] One death occurred after the on-treatment period.

L1 < 1 % subset was 11.7 months (95 % CI, 7.8–16.3). In the PD-L1 ≥ 1 % subset, the estimated probability of survival at 6 months was 83.8 % (95 % CI, 71.2–91.2) and at 12 months was 60.7 % (95 % CI, 43.7–74.0). In the PD-L1 < 1 % subset, the estimated probability of survival at 6 months was 73.7 % (95 % CI, 58.4–84.2) and at 12 months was 49.3 % (95 % CI, 31.0–65.3). The median OS estimate in patients with adenocarcinoma/adenosquamous histology was 13.3 months (95 % CI, 10.9–NE).

3.5. Safety

Table 3 and **Table S2** summarize the safety outcomes for patients with recurrent HPV16-positive cervical cancer who received peltopepimut-S plus cemiplimab. TEAEs occurred in 92.9 % of patients, with the most common being injection-site reaction (44 [38.9 %] patients) and anemia (29 [25.7 %] patients); 39.8 % of patients experienced grade ≥ 3 TEAEs and 25.7 % experienced a serious TEAE (Table 3). TEAEs of any grade that led to treatment discontinuation occurred in 4 patients (3.5 %), while 6 patients (5.3 %) experienced a TEAE of any grade that led to death (Table 3).

Treatment-related TEAEs occurred in 68.1 % of patients, with the most common being injection-site reaction (44 [38.9 %]) and fatigue (12 [10.6 %]); 9.7 % of patients experienced grade ≥ 3 treatment-related TEAEs and 3.5 % experienced a serious treatment-related TEAE (Table 3). Treatment-related TEAEs of any grade that led to treatment discontinuation occurred in 3 patients (2.7 %) (Table 3), while 1 patient (0.9 %) experienced a treatment-related TEAE that led to death (pneumonitis) (Table 3).

A total of 10 (8.8 %) patients reported a TEAE of special interest; 8 (7.1 %) patients experienced grade ≥ 3 TEAEs of special interest, and 3 (2.7 %) experienced serious TEAEs of special interest. The most commonly occurring TEAEs of special interest were increased creatine phosphokinase (3 [2.7 %]), increased alanine aminotransferase (2 [1.8 %]), increased aspartate aminotransferase (2 [1.8 %]), and infusion-related reaction (2 [1.8 %]). A total of 20 patients (17.7 %) died during the treatment period; the most common reason was disease progression or recurrent disease ($n = 13$, 11.5 %); 5 (4.4 %) patients died due to an AE (1 due to respiratory failure, 1 due to dyspnea, 2 due to sepsis, and 1 due to fatal pneumonitis that was potentially related to cemiplimab) and 2 (1.8 %) patients died due to another cause.

4. Discussion

This is the first phase 2 study to evaluate the efficacy and safety of cemiplimab plus peltopepimut-S vaccine in patients with recurrent HPV16-positive cervical cancer with disease progression after first-line chemotherapy, and is one of the first trials of this kind in this patient population. All responders were patients with SCC histology but this could be due to the sample size [8]. In EMPOWER-Cervical 1, similarly, a higher ORR was observed in patients with SCC [12].

The addition of peltopepimut-S 100 μg/peptide to cemiplimab 350 mg every 3 weeks seems comparable to cemiplimab monotherapy (based on cross-study comparison) in this trial. The primary endpoint of ORR (16.8 %) after peltopepimut-S plus cemiplimab combination therapy in the current study was consistent with that observed after cemiplimab monotherapy (ORR of 16.4 %) [12], which may imply that the addition of the vaccine does not provide an additional benefit compared with cemiplimab monotherapy. The estimated median OS was 13.3 months with a 1-year survival probability of 54.5 % after cemiplimab plus peltopepimut-S. This was consistent with OS after cemiplimab monotherapy (median OS of 12.0 months with a 1-year survival probability of approximately 50 %) and is an improvement relative to patients who received chemotherapy alone (median OS of 8.5 months) [12].

The patient subgroup with higher levels of PD-L1 expression in tumor cells may be more likely to benefit from this combination therapy (ORR of 24.1 % among patients with SCC and PD-L1 ≥ 1 %). Patients with SCC and PD-L1 < 1 % demonstrated an ORR of 15.8 %, suggesting that these individuals may still benefit from cemiplimab-containing immunotherapy.

The safety profile of combination therapy with cemiplimab and peltopepimut-S was similar to the established safety profile of cemiplimab monotherapy. There were no new safety findings other than occurrences of mostly grade 1–2 injection-site reactions in 44 (38.9 %) patients.

This study is limited by a lack of randomization and a relatively homogenous study population of predominantly white females of non-Hispanic race. Furthermore, this study excluded patients who had previously received anti–PD-1/L1 therapy or another systemic immune-modulating agent. At the time this study was conducted, anti–PD-1/L1 therapy was not universally used in the first-line setting; however, the treatment landscape has since changed and PD-1/L1 inhibition has shifted to the first-line setting in both locally advanced and recurrent/metastatic disease. The role of combination cemiplimab plus peltopepimut-S vaccine in patients who have previously received immune-modulating therapy is therefore an area of future study. Of note, cemiplimab plus peltopepimut-S vaccine is currently being investigated in an ongoing clinical trial in patients with oropharyngeal cancer who were progressive on anti-PD-1 therapy (NCT04398524), which reported an ORR of 11.5 % [25].

The results of this study suggest that the combination treatment of cemiplimab plus peltopepimut-S vaccine provides similar benefit to that which has been previously observed in patients who received cemiplimab monotherapy. The exploratory analysis suggests that patients with higher levels of PD-L1 expression in tumor cells may be more likely to benefit from the combination therapy, and future studies focusing on this patient subgroup are warranted. As this study is among the first clinical data of ICIs plus a cancer vaccination, further investigations — including in patients with higher PD-L1 expression status — are necessary to expand upon these findings.

Funding

This study was funded by Regeneron Pharmaceuticals, Inc. and ISA Pharmaceuticals.

CRediT authorship contribution statement

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Declaration of competing interest

Domenica Lorusso: honoraria from AstraZeneca, Clovis Oncology, Genmab, GSK, Immunogen, MSD, PharmaMar, Seagen, and Sutro; consulting or advisor role for AstraZeneca, Clovis Oncology, Corcept, Genmab, GSK, Immunogen, MSD, Novartis, Oncoinvent, PharmaMar, Seagen, and Sutro; speakers bureau for AstraZeneca, Clovis Oncology, Genmab, GSK, Immunogen, MSD, PharmaMar, and Seagen; research funding from AstraZeneca, Clovis Oncology, Genmab, GSK, Immunogen, Incyte, MSD, Novartis, PharmaMar, Roche, and Seagen; principal investigator of trials for AstraZeneca, Clovis Oncology, Genmab, GSK, Immunogen, Incyte, MSD, Novartis, PharmaMar, Roche, and Seagen; member of the GCIG Board of Directors and the MITO Board of Directors; and grants for travelling from AstraZeneca, Clovis Oncology, and GSK. **Ana Oaknin:** personal fees for advisory board membership from Agenus, AstraZeneca, Clovis Oncology, Corcept Therapeutics, Daiichi Sankyo, Debiopharm International, Deciphera Pharmaceuticals, Eisai, Exelisis, EMD Serono, F. Hoffmann-La Roche, Genmab, GSK, ImmunoGen, Itheos, Merck Sharp & Dohme de España, SA, Mersana Therapeutics, Myriad Genetics, Novocure, OneXerna Therapeutics, Inc., PharmaMar, Regeneron Pharmaceuticals, Inc., Sattucklabs, Seagen, Sutro Biopharma, and Zentalis; personal fees for travel/accommodation from AstraZeneca, PharmaMar, and Roche; non-remunerated roles at ESMO (member, Officer, Co-Chair of the ESMO Gynaecological Cancers Congress 2023–2025, Chair of the Gynaecological Track ESMO 2019, Scientific Track Member Gynaecological Cancers ESMO 2018, ESMO 2020, ESMO 2022, member of the Gynaecological Cancers Faculty and Subject Editor for the Gynaecological Clinical Practice Guidelines); a non-remunerated role at GCIG (member and Cervix Cancer Chair on behalf of GEICO); and European Society of Gynaecological Oncology (ESGO) Council Member and membership of ASCO, GOG, and SEOM. **Giuliano Santos Borges:** no conflict of interest. **Fernanda Damian:** no conflict of interest. **Nelleke Ottevanger:** no conflict of interest. **Toon Van Gorp:** consulting or advisory role (all payments to institution) for AstraZeneca, Immunogen, Eisai, OncXerna Therapeutics, GSK, MSD/Merck, Seagen, Tubulis GmbH, Incyte, Zentalis, Karyopharm Therapeutics, and BioNTech SE; speakers' bureau (all payments to institution) for GSK, MSD/Merck, and ImmunoGen; research funding (all payments to institution) from Amgen, Roche, and AstraZeneca; and travel, accommodation, and expenses from MSD/Merck, Immunogen, GSK, PharmaMar, and AstraZeneca. **Carlos Eduardo Paiva:** no conflict of interest. **Judith Kroep:** consulting or advisory role (all payments to institution) for AstraZeneca, Eisai, GSK, Immagene, Lilly, and MSD/MERCK; research funding (all payments to institution) from AstraZeneca, Novartis, and Philips/Innosign; and travel and accommodation from Daiichi Sankyo. **Yong-Man Kim:** research funding from MSD, AstraZeneca, Roche, Genmab, Canaria Bio, Seagen, and BeiGene; and a speaker role for Chugai. **Hee Seung Kim:** no conflict of interest. **Jae Kwan Lee:** no conflict of interest. **Hannelore Denys:** consulting or advisory roles for Pfizer, Roche, PharmaMar, AstraZeneca, Eli Lilly and Company, Novartis, Amgen, GSK, MSD, Seagen, Gilead Sciences, and Teva; research funding to institution from Gilead; and travel, accommodation, and expenses from Pfizer, Roche, PharmaMar, Teva, AstraZeneca, Gilead Sciences, MSD Oncology, and GSK. **Roy Lalisang:** no conflict of interest. **Andreia Cristina De Melo:** grants or contracts from Amgen, AstraZeneca, Bristol Myers Squibb, Clovis Oncology, GSK, MSD, Novartis, Pierre Fabre, Regeneron Pharmaceuticals, Inc., and Roche, with payments made to the institution; and payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing, or educational events from Adium, AstraZeneca, Bristol Myers Squibb, Daiichi Sankyo, GSK, MSD, Novartis, and Roche. **Andres Redondo:** consulting or advisory roles for AstraZeneca, GSK, Boehringer Ingelheim, MSD, and Pharma&; speakers bureau for AstraZeneca, GSK, MSD, and Pharma&; and travel, accommodation, and expenses from AstraZeneca. **Anna KL Reyners:** no conflict of interest. **Paulo Mora:** personal fees for advisory boards from AstraZeneca and Knight; travel and accommodation from AstraZeneca; and research funding to institution from AstraZeneca and Regeneron Pharmaceuticals, Inc. **Celine Closset:** no conflict of interest. **Cornelis JM Melief:** employee and beneficiary of stock appreciation rights in ISA Pharmaceuticals. **Leon Hooftman:** employee and stock option holder of ISA Pharmaceuticals. **Shaheda Jamil**, **Lisa Boersma**, **Suk-Young Yoo**, **Matthew G Fury**, **Melissa Mathias**, **Frank Seebach**, and **Israel Lowy:** employees and shareholders of Regeneron Pharmaceuticals, Inc. **Nicoletta Colombo**: consulting or advisory roles with Roche/Genentech, AstraZeneca, Clovis Oncology, MSD Oncology, GSK, Immunogen, Mersana, Eisai, Nuvation Bio, OncXerna, Pieris Pharmaceuticals, and Novocure; speakers' bureau for AstraZeneca, Clovis Oncology, GSK, MSD Oncology, and Eisai; travel, accommodation, and expenses from GSK, AstraZeneca, and Corcept Therapeutics; honoraria from Roche/Genentech, AstraZeneca, GSK, MSD Oncology, Clovis Oncology, Immunogen, Mersana, Eisai, Nuvation Bio, OncXerna, Pieris Pharmaceuticals, and Novocure; research funding from AstraZeneca, Roche, and GSK; and employment of an immediate family member at Sarepta Therapeutics.

Acknowledgements

The authors would like to thank the patients, their families, and all investigators involved in this study. Medical writing support, including assisting authors with the development of the outline and initial draft and incorporation of comments, was provided by Jenna Lee, MSc, and editorial support, including figure preparation, formatting, proofreading, and submission, was provided by Elke Sims, MLangTrans, of Alpha (a division of Prime, Knutsford, UK), supported by Regeneron Pharmaceuticals, Inc. according to Good Publication Practice guidelines

(https://www.acpjournals.org/doi/10.7326/m22-1460). ISA Pharmaceuticals was involved in the study design; Regeneron Pharmaceuticals, Inc., was involved in the study design and collection, analysis, and interpretation of data, as well as data checking of information provided in the manuscript. The authors were responsible for all content and editorial decisions, and received no honoraria related to the development of this publication.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ygyno.2025.03.019.

Data availability

Qualified researchers may request access to study documents (including the clinical study report, blank case report form, and statistical analysis plan) that support the methods and findings reported in this manuscript. Individual anonymized participant data will be considered for sharing: 1) once the product and indication has been approved by major health authorities (eg, FDA, EMA, PMDA, etc.) or development of the product has been discontinued globally for all indications on or after April 2020 and there are no plans for future development; 2) if there is legal authority to share the data; and 3) there is not a reasonable likelihood of participant re-identification. Submit requests to https://vivli.org/.

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