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Health-Related Quality of Life With Pembrolizumab Monotherapy in Patients With Previously Treated Advanced Microsatellite Instability High (MSI-H)/Mismatch Repair Deficient (dMMR) Endometrial Cancer: Results From KEYNOTE-158

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Background

- Symptoms associated with endometrial cancer and treatment, including pain, fatigue, anxiety, distress, and depression, result in decreased health-related quality of life (HRQoL)[1]
- Approximately 25%–31% of patients with endometrial cancer have high levels of microsatellite instability (MSI-H) and mismatch repair deficiency (dMMR)[2,3]
- KEYNOTE-158 (NCT02628067) is a nonrandomized, open-label, multicohort, phase 2 study of the anti–PD-1 antibody pembrolizumab across multiple types of advanced (unresectable and/or metastatic) rare cancers that progressed on prior therapy
  - In an initial analysis of patients with MSI-H/dMMR endometrial cancer from cohorts D and K of KEYNOTE-158 (n = 49), ORR was 57% and median duration of response was not reached[4]
- We present HRQoL data, an exploratory endpoint, from patients with previously treated advanced MSI-H/dMMR endometrial cancer from an updated analysis of the KEYNOTE-158 study, including a larger number of patients with longer follow-up

Objectives

- Prespecified exploratory objectives related to HRQoL included change from baseline to week 9 in all patients and by best overall response for
  - European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire–Core 30 (QLQ-C30) global health status (GHS)/QoL
  - QLQ-C30 functional and symptom scales/items
  - EuroQol EQ-5D-3L visual analogue scale (VAS)

Methods

Study Design, Patients, and Treatment

- KEYNOTE-158 is an open-label, multicohort, nonrandomized, phase 2 study
  - Patients from cohort D had advanced endometrial cancer regardless of MSI-H status, excluding sarcomas and mesenchymal tumors
  - Patients from cohort K had any MSI-H/dMMR advanced solid tumor except colorectal
- Patients received pembrolizumab 200 mg every 3 weeks (Q3W) for 35 cycles

Assessments

- The EORTC QLQ-C30 and EQ-5D-3L were administered at baseline, every cycle for the first 4 cycles, then every 3 cycles until 9 months, then every 4 cycles during study treatment until disease progression, at the treatment discontinuation visit, and at the 30-day safety follow-up visit
  - EQ-5D-3L questionnaire was administered first, followed by EORTC QLQ-C30
  - Questionnaires were administered before treatment administration, adverse event evaluation, and tumor imaging

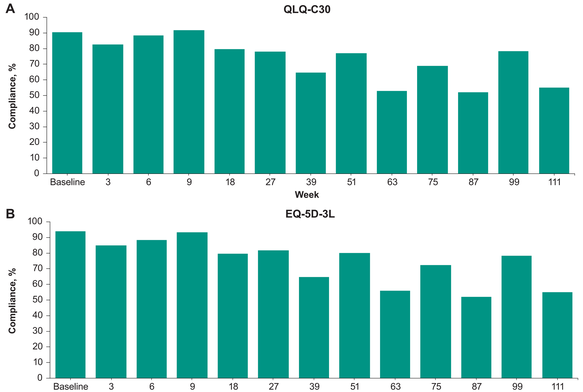
Statistical Analysis

- HRQoL was analyzed in all patients who completed ≥1 patient-reported outcomes (PRO) assessment and received ≥1 dose of study treatment; changes from baseline were analyzed in patients who also had both a baseline and post-baseline PRO assessment
- Changes from baseline in the EORTC QLQ-C30 GHS/QoL and EQ-5D-3L VAS scores were summarized overtime through final PRO assessment at week 111

Results

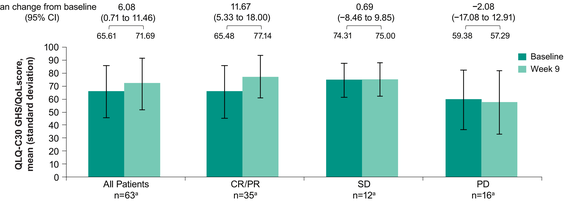
- As of the data cutoff date (October 5, 2020), 90 patients were enrolled
  - 76 patients completed ≥1 QLQ-C30 questionnaire
  - 79 patients completed ≥1 EQ-5D-3L questionnaire

Figure 1. Compliance Rates for (A) EORTC QLQ-C30 and (B) EQ-5D-3L Assessments[a]



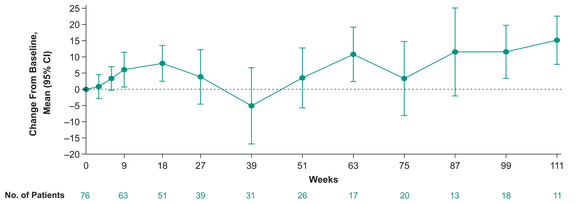
[a]Compliance rate was defined as the proportion of patients who completed the PRO questionnaire among those who were expected to complete the questionnaire at each time point, excluding those missing by design.

Figure 2. Change From Baseline to Week 9 in EORTC QLQ-C30 GHS/QoL



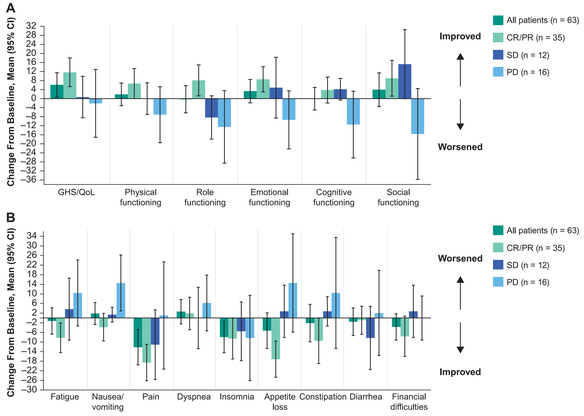
[a]Number of patients with nonmissing change from baseline at the specific time point.

Figure 3. Mean Change From Baseline in EORTC QLQ-C30 GHS/QoL by Study Visit Over Time



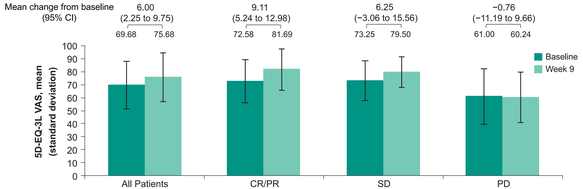
Two patients experienced a sudden decrease in EORTC QLQ-C30 GHS/QoL at week 39: changes from baseline were –100 (patient died ~3 months later) and –75.

Figure 4. Change From Baseline to Week 9 in (A) EORTC QLQ-C30 GHS/QoL and Functional Scales and (B) Symptom Scales



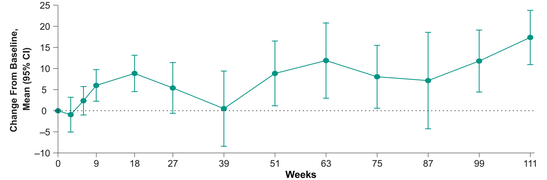
For GHS/QoL score and functional scales, a higher score indicates better health or function. For symptom scales, a higher score denotes worse symptoms. n is the number of subjects in the analysis population in each group.

Figure 5. Change From Baseline to Week 9 in EQ-5D-3L VAS



[a]Number of patients with nonmissing change from baseline at the specific time point.

Figure 6. Mean Change From Baseline in EQ-5D-3L VAS by Study Visit Over Time



Conclusions

- Pembrolizumab maintained or improved HRQoL in patients with previously treated, advanced MSI-H/dMMR endometrial cancer enrolled in the KEYNOTE-158 study
  - Mean scores for QLQ-C30 GHS/QoL and all functional and symptom scales were maintained or improved from baseline to week 9 in the overall population, with greater improvements observed among patients with best overall response of CR or PR
  - QLQ-C30 GHS/QoL scores and functional and symptom scales were not improved from baseline in patients with best overall response of SD or PD
  - Mean EQ-5D-3L VAS scores improved from baseline to week 9 in the overall population and in patients with CR/PR, but not in patients with SD or PD
- These results highlight the importance of disease control as a key factor in improving HRQoL in patients with previously treated, advanced MSI-H/dMMR endometrial cancer and demonstrate the need for efficacious agents with manageable safety profiles, such as pembrolizumab
- Taken together with the durable and clinically meaningful responses from efficacy analyses, these data provide further support for the use of pembrolizumab in patients with previously treated, advanced MSI-H/dMMR endometrial cancer
- Efficacy analyses from patients in KEYNOTE-158 with previously treated, advanced MSI-H/dMMR endometrial cancer are also being presented at ESMO Congress 2021 (abstract #3122; FPN#795P)

Disclosures

David M. O'Malley reports personal fees from consulting and/or advisory board membership from AstraZeneca, Tesaro/GSK, BBI, Immunogen, Ambry, Janssen/J&J, AbbVie, Regeneron, Amgen, Novocure, Genentech/Roche, GOG Foundation, Iovance Biotherapeutics, Inc, Myriad Genetics, Eisai, Agenus, Tarveda, Merck & Co., Inc., Kenilworth, NJ, USA, SeaGen, Novartis, Mersana, Clovis, Rubis, Elevar. Research funding (all funding to institution): AstraZeneca, Tesaro/GSK, Immunogen, Janssen/J&J, AbbVie, Regeneron, Amgen, Novocure, Genentech/Roche, VentiRx, Array Biopharma, EMD Serono, Ergomed, Ajinomoto Inc., Ludwig Cancer Research, Stemcentrx, Inc, CERULEAN PHARMA, GOG Foundation, NCI, Bristol Myers Squibb Co, Serono Inc, Yale University, New Mexico Cancer Care Alliance, INC Research, Inc, inVentiv Health Clinical, Iovance Biotherapeutics, Inc, PRA Intl, Eisai, Agenus, Merck & Co., Inc., Kenilworth, NJ, USA, GenMab, SeaGen, Mersana, Clovis.

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