Post hoc analysis of pembrolizumab efficacy in potentially platinum-ineligible patients with advanced urothelial carcinoma enrolled in KEYNOTE-052 and LEAP-011

Background

- Platinum-based chemotherapy is a recommended first-line therapy for advanced urothelial carcinoma (UC), but many patients are ineligible because of medical comorbidities.
- There is no standard definition of platinum ineligibility, so treatment decisions are currently made based on clinical judgment.

KEYNOTE-052 (NCT02335424) was a phase 2 trial of first-line pembrolizumab monotherapy in patients with advanced UC who were ineligible for platinum-based chemotherapy, which included patients who were potentially ineligible for any platinum-based chemotherapy:
- After a median follow-up of 5.3 months, the objective response rate (ORR) was 29.5% (95% CI, 24.3-34.8).
- Median overall survival (OS) was 11.3 months (95% CI, 9.7-13.5), and median duration of response (DOR) was 33.4 months (range, 1.4-107.5).

Based on the results of KEYNOTE-052, first-line pembrolizumab monotherapy is now a standard-of-care option for platinum-ineligible patients with advanced UC in the United States and for platinum-ineligible patients with PD-L1 combined positive score (CPS) ≥150 in Europe.

LEAP-011 (NCT03858100) is a phase 3 randomized trial of first-line pembrolizumab plus lenvatinib versus pembrolizumab plus placebo in patients with advanced UC who were considered potentially ineligible for platinum-based chemotherapy:
- The benefit-to-risk ratio for pembrolizumab plus lenvatinib was not considered positive, and enrollment was stopped based on the recommendation of an external data monitoring committee.
- ORR was 28.9% (95% CI, 23.3-35.1) and DOR was 19.3 months (range, 1.4-21.9) in the pembrolizumab + placebo arm.
- Median OS was 12.9 months (95% CI, 9.8-16.7).

Objective

To evaluate the efficacy of pembrolizumab monotherapy in UC based on the definition of platinum ineligibility.

Methods

This post hoc analysis of KEYNOTE-052 and LEAP-011 included an extensive search of the literature to identify criteria commonly used by clinicians for identifying patients who may be intolerant to or at a higher risk of toxicity with platinum-based chemotherapy (potentially platinum ineligible):
- Eastern Cooperative Oncology Group performance status ≥2
- Renal dysfunction (defined as glomerular filtration rate <60 mL/min)
- Visceral disease
- Age ≥80 years
- Subgroups of patients with combinations of these criteria were evaluated:
  - ECOC PS 2
  - ECOC PS 2 + age ≥80 years
  - ECOC PS 2 + renal dysfunction
  - ECOC PS 2 + visceral disease
  - Age ≥80 years + renal dysfunction
  - Visceral disease + age ≥80 years
  - Visceral disease + renal dysfunction
- Patients from KEYNOTE-052 and from the pembrolizumab + placebo arm of LEAP-011 were pooled for this analysis.

Results

- This pooled analysis included patients treated with pembrolizumab monotherapy from KEYNOTE-052 (N = 285) and pembrolizumab plus placebo from LEAP-011 (N = 242) who met at least 1 of the potential criteria for platinum ineligibility:
  - Median time from enrolment to database cutoff was 56.3 months (range, 51.2-65.3) in KEYNOTE-052
  - Median time from randomization to death or database cutoff was 72.0 months (range, 62.2-105.6) in the pembrolizumab + placebo arm of LEAP-011

Efficacy

- ORR, DCR, and best response by platinum eligibility criteria:

Conclusions

- In this post hoc exploratory analysis, durable and effective responses to pembrolizumab monotherapy were observed regardless of the criteria used to define platinum ineligibility.
- Median OS was generally consistent among subgroups and was similar to the overall patient population in each study.

References


Acknowledgments

Contact information

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Table 1. DOR by platinum eligibility criteria

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<th>Age ≥80 years</th>
<th>Renal dysfunction</th>
<th>Visceral disease</th>
<th>Age ≥80 years + renal dysfunction</th>
<th>Visceral disease + age ≥80 years</th>
<th>Visceral disease + renal dysfunction</th>
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Table 2. OS and PFS by platinum eligibility criteria

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<td>12.9 months</td>
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Table 3. Treatment-related AE summary by platinum eligibility criteria

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Figure 1. Study design of (A) KEYNOTE-052 and (B) LEAP-011

Figure 2. ORR, DCR, and best response by platinum eligibility criteria

Figure 3. Kaplan-Meier estimates of (A) OS and (B) PFS for patients with ECOC PS 2

Figure 4. Kaplan-Meier estimates of (A) OS and (B) PFS for patients with ECOC PS 2 and visceral disease

Figure 5. Kaplan-Meier estimates of (A) OS and (B) PFS for patients with visceral disease and renal dysfunction

Figure 6. Kaplan-Meier estimates of (A) OS and (B) PFS for patients with renal dysfunction

Figure 7. Kaplan-Meier estimates of (A) OS and (B) PFS for patients with age ≥80 years

Figure 8. Kaplan-Meier estimates of (A) OS and (B) PFS for patients with renal dysfunction

Figure 9. Kaplan-Meier estimates of (A) OS and (B) PFS for patients with age ≥80 years

Figure 10. Kaplan-Meier estimates of (A) OS and (B) PFS for patients with age ≥80 years

Figure 11. Kaplan-Meier estimates of (A) OS and (B) PFS for patients with renal dysfunction