Cost-Effectiveness of Pembrolizumab (Keytruda®) Version 4 in Patients with Advanced Melanoma in the United States

Abstract

Objective: To evaluate the cost-effectiveness of pembrolizumab version 4 in improving the health outcomes of patients with advanced melanoma who are previously untreated with ipilimumab from the U.S. Medicare perspective.

Methods: A partitioned survival model was developed, which partitioned the overall survival (OS) time into progression-free survival (PFS) and post-progression (post-PD) period. Time horizon for the study was 20 years. Costs and health outcomes were discounted at a rate of 3% per year. Clinical trial data were obtained from an interim analysis (cut-off date March 5, 2015) of a randomized phase 3 PFS study KEYNOTE-006, comparing pembrolizumab and ipilimumab, and cost data from public sources were used to populate the model. The model used Kaplan-Meier estimates of PFS and OS from the trial with extrapolation based on parametric functions and literature data. Cost data include drug acquisition, treatment administration, adverse event management, and clinical management of advanced melanoma. Incremental cost-effectiveness ratios (ICER) were calculated as cost per quality-adjusted life year (QALY) gained. Sensitivity analyses were performed to test the robustness of the results.

Results: Pembrolizumab is projected to increase the life expectancy for patients with advanced melanoma by 1.42 years, corresponding to a gain of 1.26 QALYs over ipilimumab. The model developed shows that pembrolizumab can increase the average patient direct cost of treatment with $4,316 per 100,000. The discounted ICER was $71,417/QALY over a 20-year time horizon and is $370,000/QALY at the threshold. The base-case result is cost-effective. When input parameters were varied in a one-way sensitivity analysis, the results showed that the model is cost-effective in all scenarios. Probabilistic sensitivity analysis was performed to generate a cost-effectiveness plane. The ICER is cost-effective in 99% of the simulations.

Conclusions: Compared with ipilimumab, pembrolizumab improves QALYs and is cost-effective for the treatment of patients with advanced melanoma in the Medicare perspective.

Methods (cont’d)

• A piecewise modeling approach was used for pembrolizumab:
  - KN005 KM estimates were used as long as reliable data were available (Week 60).
  - Hazard rates from external long-term IP data survival in the literature were used to generate survival curve from Week 60 to Week 520.
  - Hazard rates from ipilimumab survival registry data and US general population mortality data were used to generate the survival curve for Week 520 and beyond.

• Drug acquisition costs were based on US list prices:
  - Pembrolizumab: $4,316 per 100 mg vial
  - Ipilimumab: $6,659.07 per 4 mg vial
  - Average number of vials per dose for pembrolizumab was calculated based on the weight using pembrolizumab at the US usage algorithm
  - Drug administration costs per dose were estimated from Medicare hospital outpatient prospective payment system for 2015.
  - Health states were aligned with how cost data were reported in the literature, by on- or off-treatment period.

• Treatment duration is modeled according to the KN005 protocol where pembrolizumab was administered for 180 weeks (2 years) in both arms. All patients stayed on treatment until disease progression or death-related cost.
• Data from a 1-year re-induction treatment if applicable.
• The patients on ipilimumab were treated for a maximum of 1 year.

Figure 2. Modeled overall survival

Figure 3. tornado diagram

Figure 4. Cost-effectiveness acceptability curve

Results

• The mean survival over 20 years for US advanced melanoma patients was estimated to be 5.91 and 4.93 years for patients treated with pembrolizumab and ipi, respectively. Pembrolizumab improved the mean survival by 1.42 years.
• Pembrolizumab was also associated with an average QALY gain of 0.96 over ipi. The incremental cost per QALY gained with pembrolizumab vs ipi was $71,417.

Table 1. Utility values, pre- or post-progression

Table 2. Utility values by time to death

Table 3. Drug administration costs

Figure 4. Cost-effectiveness acceptability curves

Conclusion

• Pembrolizumab improves the QALYs and is a cost-effective therapeutic option compared to ipilimumab in advanced melanoma patients in the United States

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References

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ISPOR 21st Annual International Meeting May 21-25, 2016 Washington Hilton Washington, DC, USA