Nonclinical data support the rationale for targeting ICOS with GSK3359609 in combination with pembrolizumab, which has promise for antitumor activity, with an overall response rate of 24% as of July 26, 2019. Other studies have shown strong correlation of ICOS and programmed death ligand-1 (PD-L1) in solid tumors.

Figure 1. ICOS Mechanism of Action

ICOS agonist in combination with PD-1 blockade resulted in enhanced T cell cytokines and reduced PD-L1 expression. ICOS agonists have been reported to be successful in combination with other immune checkpoint inhibitors, such as PD-1 in HNSCC, which has a pivotal role in proliferation, apoptosis, and gene expression, among other factors.

Figure 2. Study Design

Study objectives and eligibility criteria have been described previously. The objective of the updated analyses presented here is to evaluate the PD effects of GSK3359609 monotherapy in the Evaluation of the PD Effects of GSK3359609 Monotherapy (HNSCC). The study included patients with local/regional recurrent or metastatic solid tumors who had received previous systemic therapy, with or without local intervention.

Figure 3. Demographics

Demographics of the patients included in the study. Median age was 62 years (range, 37-77), and 95% of patients were male.

Table 1. AE Profile

Table 2. AE Profile

Efficacy analyses, as one patient was assigned to receive GSK3359609 3 mg/kg + pembrolizumab 200 mg, but instead received GSK 3359609 0.3 mg/kg + pembrolizumab 200 mg. This deviation from the protocol was due to a study drug error. The number of adverse events was consistent with the expected profile for this class of drugs.

Table 3. AE Profile

The OS rate at 6 months was estimated as 76% (95% CI: 58, 87). Overall, GSK3359609 in combination with pembrolizumab had a manageable safety profile. The most common adverse events were diarrhea, pyrexia, nausea, fatigue, and reduced appetite. There were no new safety signals identified in this updated analysis.

Figure 4. Time to Progression (TTP) and OS

Figure 5. Time to Progression (TTP) and OS

The results of this study support the continued development of GSK3359609 in combination with pembrolizumab for the treatment of HNSCC. The study was conducted under the terms of the informed consents under an IRB/EC, and all patients were treated with the protocol-specified dose and schedule. The study was conducted in accordance with Good Clinical Practice guidelines and the Declaration of Helsinki.

Table 4. OS rates by clinical characteristics

Among patients with lower PD-L1 IHC (1% vs. ≥5%), the OS rate at 6 months was 45% (95% CI: 27, 63) vs. 69% (95% CI: 59, 77), respectively. This suggests that PD-L1 CPS could be a predictive biomarker for treatment response in patients with HNSCC.

Figure 6. OS rates by clinical characteristics

Figure 7. OS rates by clinical characteristics

Efficacy analyses, as one patient was assigned to receive GSK3359609 3 mg/kg + pembrolizumab 200 mg, but instead received GSK 3359609 0.3 mg/kg + pembrolizumab 200 mg. This deviation from the protocol was due to a study drug error. The number of adverse events was consistent with the expected profile for this class of drugs.

Table 8. AE Profile

The OS rate at 6 months was estimated as 76% (95% CI: 58, 87). Overall, GSK3359609 in combination with pembrolizumab had a manageable safety profile. The most common adverse events were diarrhea, pyrexia, nausea, fatigue, and reduced appetite. There were no new safety signals identified in this updated analysis.

Figure 9. Time to Progression (TTP) and OS

Figure 10. Time to Progression (TTP) and OS

The results of this study support the continued development of GSK3359609 in combination with pembrolizumab for the treatment of HNSCC. The study was conducted under the terms of the informed consents under an IRB/EC, and all patients were treated with the protocol-specified dose and schedule. The study was conducted in accordance with Good Clinical Practice guidelines and the Declaration of Helsinki.

Table 11. OS rates by clinical characteristics

Among patients with lower PD-L1 IHC (1% vs. ≥5%), the OS rate at 6 months was 45% (95% CI: 27, 63) vs. 69% (95% CI: 59, 77), respectively. This suggests that PD-L1 CPS could be a predictive biomarker for treatment response in patients with HNSCC.

Figure 12. OS rates by clinical characteristics

Figure 13. OS rates by clinical characteristics

Efficacy analyses, as one patient was assigned to receive GSK3359609 3 mg/kg + pembrolizumab 200 mg, but instead received GSK 3359609 0.3 mg/kg + pembrolizumab 200 mg. This deviation from the protocol was due to a study drug error. The number of adverse events was consistent with the expected profile for this class of drugs.

Table 14. OS rates by clinical characteristics

The OS rate at 6 months was estimated as 76% (95% CI: 58, 87). Overall, GSK3359609 in combination with pembrolizumab had a manageable safety profile. The most common adverse events were diarrhea, pyrexia, nausea, fatigue, and reduced appetite. There were no new safety signals identified in this updated analysis.

Figure 15. Time to Progression (TTP) and OS

Figure 16. Time to Progression (TTP) and OS

The results of this study support the continued development of GSK3359609 in combination with pembrolizumab for the treatment of HNSCC. The study was conducted under the terms of the informed consents under an IRB/EC, and all patients were treated with the protocol-specified dose and schedule. The study was conducted in accordance with Good Clinical Practice guidelines and the Declaration of Helsinki.