head and neck cancer

CLINICAL ACTIVITY AND SAFETY OF MEDI4736, AN ANTI-PD-L1 ANTIBODY, IN PATIENTS WITH HEAD AND NECK CANCER

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Aim: Squamous cell carcinoma of the head and neck (SCCHN) is associated with tobacco use, human papillomavirus (HPV) infection, and PD-L1 expression. An ongoing Phase I, multicenter, open-label study (NCT01693562) is evaluating the safety and efficacy of MEDI4736, a human IgG1 mAb, engineered to prevent ADCC activity, that blocks PD-L1 binding to PD-1 and CD-80.

Methods: MEDI4736 is administered IV every 2 weeks (q2w) at a dose of 10 mg/kg in a recurrent/metastatic SCCHN expansion cohort. Retreatment is permitted upon progression after 12 months of therapy. Smoking history, HPV status and prior treatments are collected at baseline. PD-L1 expression within the tumor is assessed by immunohistochemistry. Response is assessed by RECIST v1.1.

Results: As of 14 Apr, 2014, 50 pts with SCCHN; mean age 58 y (range 24–96); 86% male, 63% current/prior smokers, with median 3 prior treatments (1–11), received median 3 doses (1–12) of MEDI4736 10 mg/kg q2w. Treatment-related adverse events (TRAE) were observed in 39% of pts; most frequently nausea (6%), diarrhea, dizziness, and rash (4% each). Dyspnea, syncope, raised gamma-glutamyltransferase (GGT) and sepsis (each 5%) were the most common grade ≥3 AEs; only raised GGT (n = 1) was considered treatment-related. No TRAEs led to study discontinuation and no pts had pneumonitis or colitis. Median time of follow up was 8 wks at data cutoff. In all, 29 SCCHN pts were evaluable for efficacy (first assessment at 6 weeks), with 7 having radiographic shrinkage in target tumor lesions ranging from 7% to 76%. Five of the 7 pts have been followed for at least 12 wks (6–24 wks) and none have evidence of objective progression. Four pts have a partial response (confirmed + unconfirmed).

Further assessment of clinical activity and its potential relationship to clinical attributes (HPV status, smoking history, prior therapies), and biomarkers, including PD-L1 expression, are ongoing.

Conclusions: Preliminary clinical activity in pts with SCCHN has been observed with manageable safety profile consistent with previous reports for MEDI4736. These data support continued clinical development of MEDI4736 in SCCHN.

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