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Safety and efficacy of MEDI0457 plus durvalumab in patients (pts) with human papillomavirus-associated recurrent/metastatic head and neck squamous cell carcinoma (HPV+ R/M HNSCC)

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Background

Immunotherapy targeting programmed death protein 1 (PD-1) or its ligand (PD-L1) offers clinical benefit in HNSCC, but combination treatments are needed to improve outcomes. Here we report initial safety and efficacy of the anti-PD-L1 durvalumab plus MEDI0457, a DNA immunotherapeutic vaccine expressing HPV 16/18 E6/E7 proteins and IL-12, in pts with HPV+ R/M HNSCC.

Methods

This phase Ib/IIa, open-label, multicenter study (NCT03162224) enrolled pts with incurable, histologically/cytologically confirmed R/M HPV+ HNSCC, who had ≥1 prior platinum-containing regimen or other approved therapy if platinum-ineligible. MEDI0457 at a dose of 7 mg IM (weeks 1, 3, 7, then Q8W after week 12) and durvalumab 1500 mg IV Q4W were given until disease progression or unacceptable toxicity. Primary objectives included safety and efficacy by objective response rate (ORR; RECIST v1.1). Exploratory endpoints included induction of antibodies and HPV-specific T cells peripherally. Tumor-infiltrating T cells were measured.

Results

In July 2017 to Aug 2019, 35 pts were enrolled. Most were male (97.1%) with oropharyngeal primary (82.9%); 31.4% had PD-L1 ≥25%. At the interim data cutoff (DCO; 22 Nov 2019), therapy was ongoing in 13 pts (37.1%) and 27 were response-evaluable. Treatment-related adverse events (TRAEs) occurred in 77.1% of pts, mostly of Grade 1–2 severity. Fatigue (37.1%) and injection site pain (34.3%) were most common. Five pts (14.3%) had Grade 3 TRAEs and 1 pt (2.9%) had 3 serious Grade 3 TRAEs (AST and ALT increased and myocarditis causing discontinuation). No pts had Grade 4/5 TRAEs. ORR was 22.2% with 3 complete responses (all ongoing at DCO) and 3 partial responses (2 ongoing at DCO). Peripheral HPV-specific T cells and tumoral CD8+ T cells were increased.Table: 916MO

	1 prior line of platinum tx for R/M HNSCC (non-refractory) n=12	1 prior line of platinum tx for R/M HNSCC (refractory) n=6	≥2 prior lines of platinum tx for R/M HNSCC n=9	TotalN=27
Best overall response, n				
CR	3	0	0	3
PR	1	0	2	3
SD	2	1	3	6
PD	5	4	4	13
NE	1	1	0	2
ORR (CR or PR), %	33.3	0.0	22.2	22.2

Conclusions

MEDI0457 plus durvalumab was well tolerated and showed clinical benefit. The study is active but not recruiting.

Clinical trial identification

NCT03162224.

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Legal entity responsible for the study

AstraZeneca.

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Disclosure

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