675 **SAFETY AND TOLERABILITY OF MAGROLIMAB COMBINATION THERAPY IN PATIENTS WITH RECURRENT OR METASTATIC HEAD AND NECK SQUAMOUS CELL CARCINOMA (RM-HNSCC)**

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Background Novel combination therapies are needed to improve outcomes in RM-HNSCC. Magrolimab is a monoclonal antibody that blocks CD47, a 'don't eat me' signal overexpressed on cancer cells. Magrolimab induces macrophage-mediated phagocytosis of tumor cells and may synergize with chemotherapy agents through enhancement of phagocytic signals. The Phase 2 ELEVATE HNSCC multicenter, open-label study (NCT04854499) is evaluating magrolimab-containing regimens in patients with RM-HNSCC (figure 1). Here, we report data from 2 safety run-ins (SRI1 and SRI2) designed to assess safety/tolerability and recommended Phase 2 dose (RP2D) of magrolimab in combination with standard of care.

Methods Patients in SRI1 with previously untreated RM-HNSCC received magrolimab+pembrolizumab+platinum+5-fluorouracil; patients in SRI2 with locally advanced or RM-HNSCC (1–2 lines of prior systemic therapy) received magrolimab+docetaxel. Magrolimab was first administered as a 1 mg/kg priming dose, followed by weekly 30 mg/kg doses for two 21-day cycles and then a maintenance dose of 60 mg/kg Q3W. Pembrolizumab and chemotherapy were given per standard of care. Primary endpoints of the SRI were incidence of adverse events (AEs) and dose-limiting toxicities (DLTs). Safety was assessed in patients who received ≥1 dose of study drug. The incidence of DLTs was assessed using patients who experienced a DLT during the DLT evaluation period or who completed ≥2 magrolimab and ≥1 combination agent doses. To select an RP2D, ≤2 of 6 DLT-evaluable patients could experience a DLT, or the magrolimab dose would be de-escalated and a new cohort would be assessed.

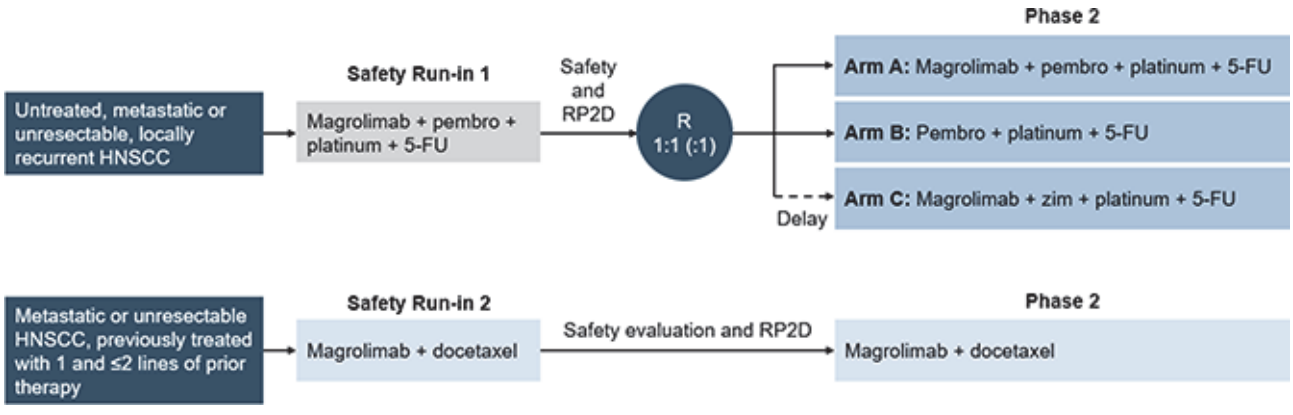
Results At least 6 patients from each SRI were considered DLT-evaluable. The safety analysis population consisted of 6 patients in SRI1 and 7 patients in SRI2. No DLTs were reported. Treatment-emergent AEs (TEAEs) occurred in 6/6 (SRI1) and 7/7 (SRI2) patients (table 1). The most common TEAEs observed in each SRI were fatigue (SRI1) and anemia (SRI2). TEAEs leading to magrolimab discontinuation occurred in 1/6 patients in SRI1 (fatigue) and 1/7 patients in SRI2 (oral cavity fistula unrelated to study drug). In SRI1, no deaths were reported; 3 deaths were reported as unrelated to study treatment and occurred after the DLT evaluation period in SRI2: oral cavity fistula, pneumonia, and disease progression (during long-term follow-up).

Conclusions The observed safety profile was as expected based on the known toxicity profiles of the individual agents. Magrolimab appears tolerable in these combinations. No DLTs or treatment-related deaths occurred. Magrolimab RP2D was declared at the initial dose level tested in both SRIs.

Trial Registration NCT04854499

Ethics Approval The protocol and proposed informed consent form were reviewed and approved by all relevant Institutional Review Boards, Independent Ethics Committees and/or Research Ethics Boards prior to study commencement. There is no number provided as we did not receive one. Participants gave informed consent to participate in the study before taking part.

Consent The protocol and proposed informed consent form were reviewed and approved by all relevant Institutional Review Boards, Independent Ethics Committees and/or Research Ethics Boards prior to study commencement. There is no number provided as we did not receive one. Participants gave informed consent to participate in the study before taking part.



Abstract 675 Figure 1 ELEVATE HNSCC cohort overview. 5-FU. 5-fluorouracil; HNSCC, head and neck squamous cell carcinoma; R, ranomization; RP2D, recommended Phase 2 dose; pembro, pembrolizumab; zim, zimberelimab

Abstract 675 Table 1 TEAEs occurring in ≥2 patients in either SRI.

TEAEs	SRI1 (n=6)[a]		SRI2 (n=7)[b]	
	All grades, n	Grade ≥3, n	All grades, n	Grade ≥3, n
Fatigue	5	3	4	2
Diarrhea	4	1	1	0
Nausea	4	0	3	0
Platelet count decreased	4	1	2	0
Stomatitis	4	2	2	0
White blood cell count decreased	4	3	2	2
Anemia	3	2	5	4
Decreased appetite	3	1	3	0
Hypophosphatemia	3	0	0	0
Peripheral neuropathy	3	0	0	0
Pyrexia	3	0	1	0
Maculopapular rash	3	0	0	0
Blood thyroid stimulating hormone increased	2	0	0	0
Dehydration	2	1	1	0
Hiccups	2	1	0	0
Hyperglycemia	2	1	0	0
Hyponatremia	2	0	1	0
Absolute neutrophil count decreased	2	1	3	3
Oral dysesthesia	2	0	0	0
Headache	1	0	2	0
Febrile neutropenia	1	1	3	3
Hypotension	0	0	2	1

[a]Six patients were evaluable for safety and DLTs.
[b]Seven patients were evaluable for safety; 6 patients were evaluable for DLTs.
DLT, dose-limiting toxicity; SRI, safety run-in; TEAE, treatment-emergent adverse event.

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