698 SAFETY AND TOLERABILITY OF MAGROLIMAB IN COMBINATION WITH TAXANES IN PATIENTS WITH SOLID TUMORS

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Background Magrolimab is a monoclonal antibody that blocks the macrophage inhibitory immune checkpoint CD47, which is present on tumor cells. Overexpression of prophagocytic signals makes cells more susceptible to CD47 blockade. Taxanes are known to enhance expression of prophagocytic signals on tumor cells and therefore may synergize with magrolimab. These Phase 2 studies (ELEVATE TNBC: NCT04958785; ELEVATE Lung&UC: NCT04827576) are evaluating safety, tolerability, and recommended Phase 2 dose (RP2D) of magrolimab in combination with taxanes in locally advanced/metastatic triple-negative breast cancer (mTNBC), locally advanced/metastatic non-small cell/small cell lung cancers (mNSCLC/mSCLC), and locally advanced/metastatic urothelial cancer (mUC) (figure 1). We report data from 2 safety run-ins (SRIs) from these studies.

Methods Patients with mTNBC in SRI1 received magrolimab and nanoparticle albumin-bound-paclitaxel or paclitaxel. Patients with mNSCLC/mSCLC or mUC in SRI2 received magrolimab+docetaxel. Magrolimab was started as a 1 mg/kg priming dose, followed by 30 mg/kg weekly (7 weeks in SRI1; 5 weeks in SRI2), and then a maintenance dose of 30 mg/kg Q2W for SRI1 and 60 mg/kg Q3W for SRI2. Chemotherapy was given per standard of care. Safety was assessed in patients who received ≥1 dose of any study drug. Dose-limiting toxicities (DLTs) were assessed in patients who experienced a DLT during the DLT evaluation period or did not experience a DLT and completed ≥3 (SRI1) or ≥2 (SRI2) magrolimab doses and ≥2 (SRI1) or ≥1 (SRI2) taxane 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 assessed.

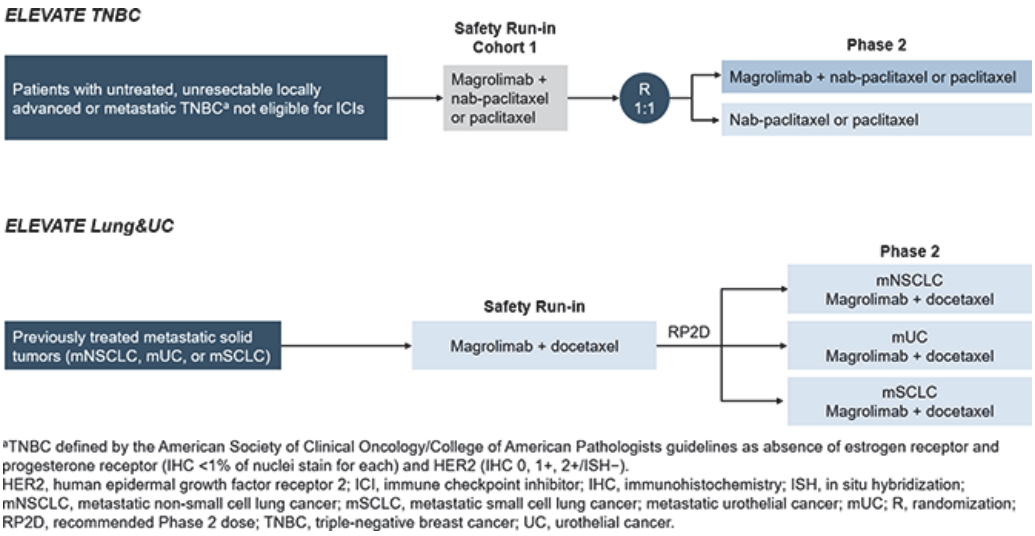
Results Six patients from each SRI were considered DLT-evaluable. The safety analysis population consisted of 8 and 9 patients in SRI1 and SRI2, respectively. No DLTs were observed during the DLT assessment period. Treatment-emergent adverse events (TEAEs) were observed in 8/8 (SRI1) and 9/9 (SRI2) patients (table 1). The most common TEAEs in SRI1 were anemia, vomiting, and headache (5/8 each); in SRI2, fatigue (5/9) and hyponatremia (3/9) were the most common. In SRI2, 2/9 patients experienced TEAEs resulting in discontinuation of magrolimab (fatal gastrointestinal bleed [deemed unrelated to treatment] and grade 3 neuritis). No additional deaths were reported.

Conclusions The observed safety profile was as expected based on the known toxicity profiles of the individual agents, and magrolimab appears tolerable in these combinations. No DLTs, magrolimab-related deaths, or unexpected safety signals were observed across indications. Magrolimab RP2D was determined at the initial dose level tested.

Trial Registration NCT04827576, NCT04958785

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 698 Figure 1 ELEVATE TNBC and ELEVATE Lung&UC Study Design.

Abstract 698 Table 1 TEAEs occurring in ≥2 patients in either of the SRI cohorts.

TEAE	SRI1 (N=8)[a]		SRI2 (N=9)[b]	
	All grades, n	Grade ≥3, n	All grades, n	Grade ≥3, n
Fatigue	3	0	5	2
Anemia	5	2	2	1
Headache	5	0	2	0
Vomiting	5	1	2	0
Pyrexia	4	0	2	0
Nausea	3	1	2	0
Hyponatremia	0	0	3	1
Alopecia	2	0	2	0
Diarrhea	2	1	2	1
COVID-19	2	1	0	0
Infusion-related reaction	2	0	0	0
Constipation	0	0	2	0
Neutrophil count decreased	0	0	2	2
WBC count decreased	0	0	2	2

[a]Eight patients were evaluable for safety; 6 patients were evaluable for DLTs.
[b]Nine patients were evaluable for safety; 6 patients were evaluable for DLTs.
COVID-19, coronavirus disease 2019; DLT, dose-limiting toxicity; SRI, safety run-in; TEAE, treatment-emergent adverse events; WBC, white blood cell.

http://dx.doi.org/10.1136/jitc-2023-SITC2023.0698