A Phase 2, Multi-Arm Study of Anti-CD47 Antibody, Magrolimab, in Combination With Docetaxel in Patients With Locally Advanced or Metastatic Solid Tumors (ELEVATE Lung & Urothelial Cancer)

TPS9142

ELEVATE LUNG AND UROTHELIAL CANCER

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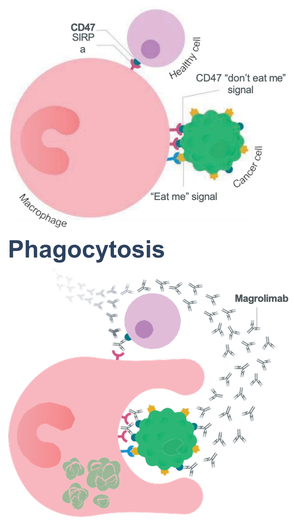
Background

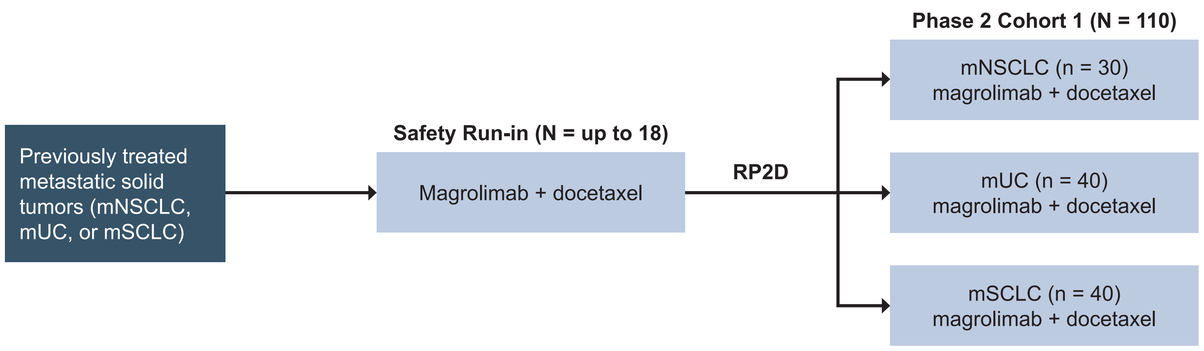
- Novel combination therapies are needed to extend the survival of patients with solid tumors whose disease has progressed on standard chemotherapy and/or immune checkpoint inhibitors[1-3]
- Magrolimab is a first-in-class monoclonal antibody that blocks the macrophage inhibitory immune checkpoint cluster of differentiation 47 (CD47), a "do not eat me" signal overexpressed on tumor cells[4]
- Magrolimab binding to CD47 leads to phagocytosis of cancer cells, enhances antitumor efficacy through stimulation of both innate and adaptive immune responses, and has shown clinical activity in hematologic malignancies[4-8]
- Chemotherapeutic agents, including taxanes, enhance prophagocytic signals on tumor cells, leading to potential synergistic antitumor activity when combined with magrolimab[9]
- This Phase 2 study (NCT04827576) is evaluating the safety, tolerability, and efficacy of magrolimab with docetaxel in metastatic non-small cell lung cancer (mNSCLC), metastatic urothelial cancer (mUC), and metastatic small cell lung cancer (mSCLC)

Magrolimab Mechanism of Action[8]



CD47, cluster of differentiation 47; SIRPa, signal-regulatory protein alpha.

Study Design



mNSCLC, metastatic non-small cell lung cancer; mSCLC, metastatic small cell lung cancer; mUC, metastatic urothelial cancer; RP2D, recommended phase 2 dose.

Patient Eligibility

Key Inclusion Criteria	Key Exclusion Criteria
Safety Run-in Cohort 1 — Metastatic advanced solid tumors that have had at least 1 prior line of systemic anticancer therapy (mNSCLC and mSCLC) or 2 prior lines of systemic anticancer therapy (mUC) in a locally advanced/metastatic setting and not more than 3 prior lines of systemic anticancer therapy **Cohort 1a (mNSCLC)** — Prior PBC and/or ICI therapy — At least 1 prior line of systemic anticancer therapy and not more than 2 prior lines of systemic anticancer therapy — Patients who were treated for EGFR, ROS1, ALK, NTRK, or MET exon 14 genomic alterations are excluded **Cohort 1b (mUC)** — Prior PBC and/or ICI therapy — At least 2 prior lines of systemic anticancer therapy and not more than 3 prior lines of systemic anticancer therapy **Cohort 1c (mSCLC)** — Prior treatment with PBC with or without ICI — At least 1 prior line of systemic anticancer therapy in a locally advanced/metastatic setting and not more than 2 prior lines of systemic anticancer therapy	**All Patients** — Prior treatment with CD47- or SIRPα-targeting agents — Treatment with a taxane within 12 months or patients refractory to prior taxane treatment — History of hemolytic anemia, autoimmune thrombocytopenia, or Evans syndrome in the last 3 months — Significant medical diseases or conditions, including but not limited to myocardial infarction within the past 6 months, unstable angina, uncontrolled diabetes mellitus, significant active infections, and congestive heart failure — Second malignancy, except treated basal cell or localized squamous skin carcinomas, localized prostate cancer, or those for which patients are not on active anticancer therapy and have been in complete remission for >2 years — Prior anticancer therapy, including but not limited to chemotherapy, immunotherapy, or investigational agents within 4 weeks prior to magrolimab

Note: Other protocol-defined inclusion/exclusion criteria may apply.
ALK, anaplastic lymphoma kinase; CD47, cluster of differentiation 47; EGFR, epidermal growth factor receptor; ICI, immune checkpoint inhibitor; MET, mesenchymal-epithelial transition factor; NTRK, neurotrophic tyrosine receptor kinase; PBC, platinum-based chemotherapy; ROS1, c-ros oncogene 1; SIRPα, signal regulatory protein alpha..

Objectives

Primary
- Determine safety, tolerability, recommended phase 2 dose (RP2D) of magrolimab and docetaxel (Safety Run-in Cohort 1, Phase 2 Cohorts)
- Determine efficacy of magrolimab and docetaxel: investigator assessed overall response rate (ORR) (Phase 2 Cohorts)

Secondary
- Investigator-assessed progression-free survival (PFS) (Phase 2 Cohorts)
- Duration of response (DOR), overall survival (OS) (Phase 2 Cohorts)
- Pharmacokinetics (PK) and immunogenicity (Safety Run-in and Phase 2 Cohorts)

Exploratory
- Evaluate PD, pharmacodynamics, mechanism of action (MoA), therapeutic response of biomarkers
- Explore biomarkers that may predict response to therapy

DOR, duration of response; ORR, objective response rate; OS, overall survival; PD, pharmacodynamics; PFS, progression-free survival; PK, pharmacokinetics; RP2D, recommended phase 2 dose.

Endpoints

Primary Endpoints
- Adverse events
- ORR* (Phase 2)

Secondary Endpoints
Phase 2:
- PFS
- DOR
- OS

Run-in and Phase 2:
- PK
- Antidrug antibodies

Exploratory Endpoints
- Change in PK, MoA, or response biomarkers on treatment
- Correlation between clinical response and biomarkers

*Based on investigator-assessed Response Evaluation Criteria in Solid Tumors 1.1 criteria.

Statistical Considerations

Sample Size Calculation: Sample sizes of 30 patients in the mNSCLC cohort (provides 81% power, 1-sided alpha 0.2) and 40 patients each for mUC (provides 79% power, 1-sided alpha 0.2) and mSCLC (provides 84% power, 1-sided alpha 0.15) were calculated using a chi-squared test

Primary Efficacy Endpoint Analyses: PFS will be analyzed using the Kaplan–Meier method; ORR with 95% confidence interval will be estimated based on the Clopper–Pearson method

Dosing

- Up to 6 patients will be enrolled into the Safety Run-in Cohort 1 at a starting dose level
- If >2 patients experience at least 1 dose-limiting toxicity (DLT) during Cycle 1, dose de-escalation will occur Up to another 6 patients will then be enrolled and evaluated at a lower dose level in the same manner
- If ≤2 of 6 patients evaluable for DLTs experience a DLT in Cycle 1, enrollment into the Phase 2 Cohort 1 will begin at this dose level as the RP2D

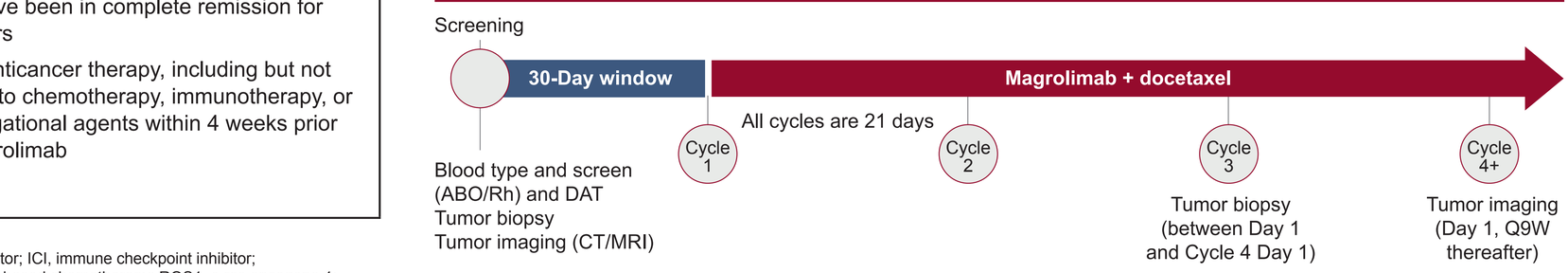
Safety Run-in

Drug	Dose Level	Cycle 1	Cycle 2	Cycle 3+
Magrolimab	Starting dose 30 mg/kg	1 mg/kg IV on Day 1 30 mg/kg IV on Days 8, 15	30 mg/kg IV on Days 1, 8, 15	45 mg/kg IV on Day 1
	De-escalation Level - 1 20 mg/kg	1 mg/kg IV on Day 1 20 mg/kg IV on Days 8, 15	20 mg/kg IV on Days 1, 8, 15	30 mg/kg IV on Day 1
	De-escalation Level - 2 15 mg/kg	1 mg/kg IV on Day 1 15 mg/kg IV on Days 8, 15	15 mg/kg IV on Days 1, 8, 15	20 mg/kg IV on Day 1
Docetaxel	75 mg/m² IV	75 mg/m² IV on Day 1	75 mg/m² IV on Day 1	75 mg/m² IV on Day 1

IV, intravenous.

- Magrolimab is administered intravenously, with an initial priming dose to mitigate on-target anemia, followed by 30 mg/kg during Cycle 1 (cycles are 21 days) in the safety run-in cohort to identify any DLTs and determine a RP2D
- De-escalation may occur for DLTs per protocol
- In Phase 2, following the priming dose on Day 1, magrolimab RP2D will be administered on Days 8 and 15 of Cycle 1; Days 1, 8, and 15 of Cycle 2; and Day 1 for Cycles 3 and beyond

Key Assessments and Timing



CT, computed tomography; DAT, direct antiglobulin test; MRI, magnetic resonance imagining; Q9W, every 9 weeks; Rh, rhesus factor.

Enrollment: The study opened to accrual in August 2021 and is currently recruiting participants. Planned enrollment is approximately 116 patients. Additional information at https://clinicaltrials.gov/ct2/show/NCT04854499.

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