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Phase Ia/Ib study of RS-0139, a novel tumor-targeted delivery of docetaxel, in patients with recurrent, locally advanced, or metastatic non-small cell lung cancer (NSCLC)

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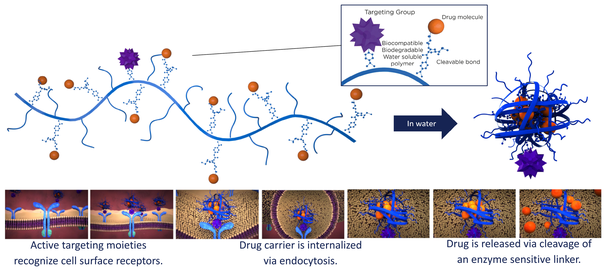
BACKGROUND

- Docetaxel (DTX) is an anti-microtubule agent registered for multiple indications and is usually administered 3-weekly (Q3W) at doses ranging from 60 to 100 mg/m^2.
- Important limitations of docetaxel include acute hypersensitivity reactions, neutropenia, neuropathy, fatigue, nausea, vomiting, and nail toxicity.
- RS-0139 was developed as a DTX-releasing, tumor-targeted prodrug. The active molecule (DTX) is covalently bound to a polymer backbone, together with a targeting peptide, which shows a high affinity to $\alpha_v\beta_3$, $\alpha_v\beta_5$, and $\alpha_v\beta_6$ integrin receptors highly expressed on the tumor cell surface. Once RS-0139 is uptaken by the cell, the covalent bond is cleaved to release DTX in the cytoplasm.

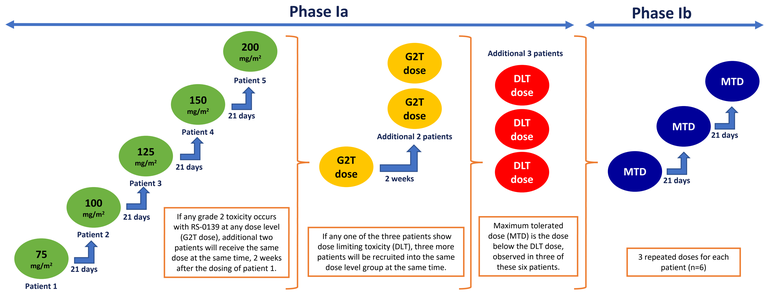


- In preclinical studies, the enzymatically cleavable covalent conjugation of DTX enabled sustained release inside the tumor, reducing adverse effects due to limited circulating free DTX. Hence, RS-0139 showed superior tolerability to DTX in healthy mice, rats, and rabbits. Besides, the dosing frequency decreased owing to the increased half-life, which is related to the release rate from the carrier platform. Preclinical data strongly support the clinical translation of this novel nanomedicine to treat solid tumors.

METHODS

- This is a Phase Ia/Ib open-label, multicenter, dose-escalation, and expansion study to evaluate the safety and tolerability of RS-0139 monotherapy in non-small cell lung cancer (NSCLC).
- To determine the maximum tolerated dose, a dose-escalation protocol consisting of an accelerated titration design was developed. Each step will increase until the recommended phase Ib dose is reached. In case of grade 2 toxicity, the protocol will be switched to the standard 3+3 design.
- Phase Ib will be initiated following the decision of the recommended dose for RS-0139 upon evaluating all available safety and pharmacokinetic (PK) data, and 6 more participants will receive 3 cycles every 21 days.
- All protocols and procedures are approved by and conducted under the supervision of Koc University Ethics Committee for Clinical Trials (2020.360.IRB1.142).

STUDY DESIGN



OBJECTIVES

- The primary objective of this study is to determine the maximum tolerated dose of RS-0139 monotherapy in recurrent, locally advanced or metastatic NSCLC patients who are not responding to existing treatments.

Secondary Objectives:

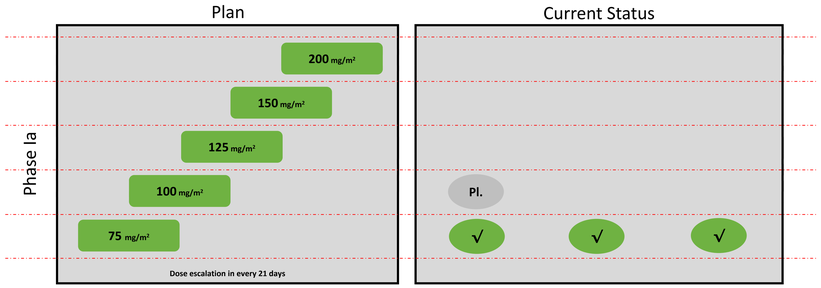
- To assess the safety and tolerability of the study drug
- To assess the pharmacokinetics and the toxicity of the study drug

KEY ELIGIBILITY CRITERIA

- Patients of both sexes aged between 18 and 75 years.
- Patients with stage IIIB or IV NSCLC and measurable disease by Response Evaluation Criteria in Solid Tumors and availability of at least one measurable tumor focus under RECIST v.1.1 criteria.
- Patients with NSCLC progressed after standard therapy options consisting of chemotherapy and/or immunotherapy.
- Patients who completed the previous treatments 21 days before the first dose of the study drug.
- Patients who have at least three months of life expectancy.
- Patients with ECOG performance score 0-1.
- Patients who have earlier biopsy material confirming the expression of integrin αvβ6 (Phase Ib only).

CURRENT STATUS

- The study is open for enrollment in 2 sites in Turkey. 16 patients will be enrolled in total.



- This trial is registered under the NCT Number: NCT04261413
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- The presenter has no conflicts of interest to declare

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