National Cancer Center (NCC) Japan, NCC Seed Acceleration Program（NCC SAP）

Establishment of a startup aiming to commercialize the anticancer drug, RK-582

 # S1-225102

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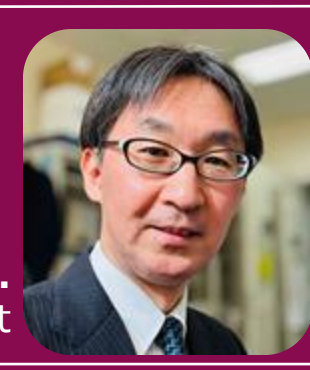


Vision

- We aim to develop a new drug for unresectable advanced and recurrent colorectal cancer.
- The response rates of current later-line treatments are only around 1–4%. Our originally developed tankyrase inhibitor, RK-582, will become an alternative therapy by inducing the degradation of β-catenin, a crucial but undruggable target molecule in colorectal cancer.
- Since β-catenin also contributes to immune evasion, this drug is expected to enhance the efficacy of immune checkpoint inhibitors (ICIs) and overcome the drug resistance. In such cases, the target cancer types may expand further.

Marketability

- Despite the relatively broad range of treatment options available for colorectal cancer, their therapeutic efficacy remains limited. Notably, none of the existing treatments effectively target β-catenin, a key oncogenic driver of the disease.
- On a global scale, including Japan, the United States, Europe, and China, the annual incidence is estimated at approximately 120,000 cases. Furthermore, the potential for combination therapies is expected to significantly expand the market.
- Regarding competitors, ST Pharm has recently completed a first-in-human (FIH) clinical trial for basroparib (STP1002).

Innovation

- Facilitates the degradation of β-catenin, a target that has long been considered undruggable.
- As predictive biomarkers, short APC mutations and β-catenin accumulation have been identified.
- Compared to CBP/β-catenin inhibitors, this drug candidate not only induces β-catenin degradation but is also expected to exert antitumor effects through the inhibition of pathways such as the YAP signaling pathway.

Partnering

【Expected partners】
Pharmaceuticals・CMO/CDMO/CRO/SMO・Venture capitals

【Expectation】Support for startup, Design/execution of clinical trials, including Phase II mono/Phase Ib/II combination, Manufacturing of investigational drugs, Regulatory affairs

Research Outline

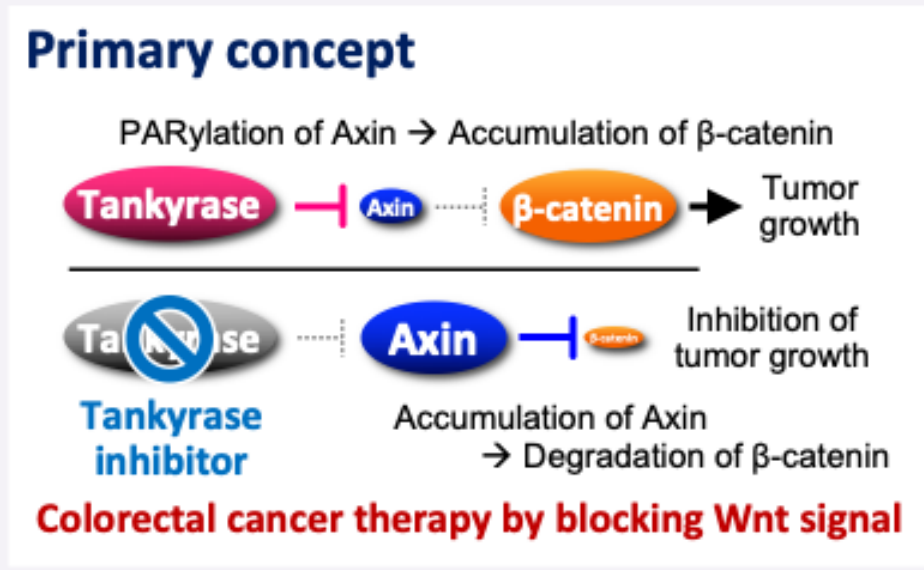
Key Words: #Small molecule, #Biomarker, #Immune response, #Genetic mutation, #Project Management

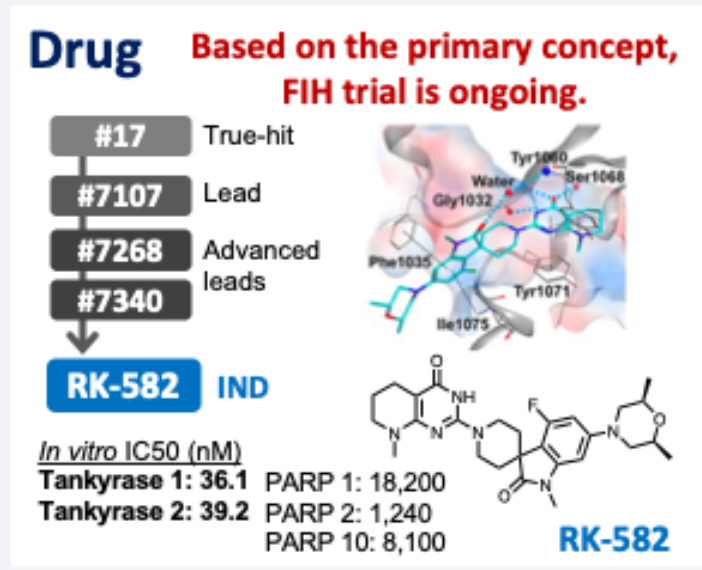
【Research plan】

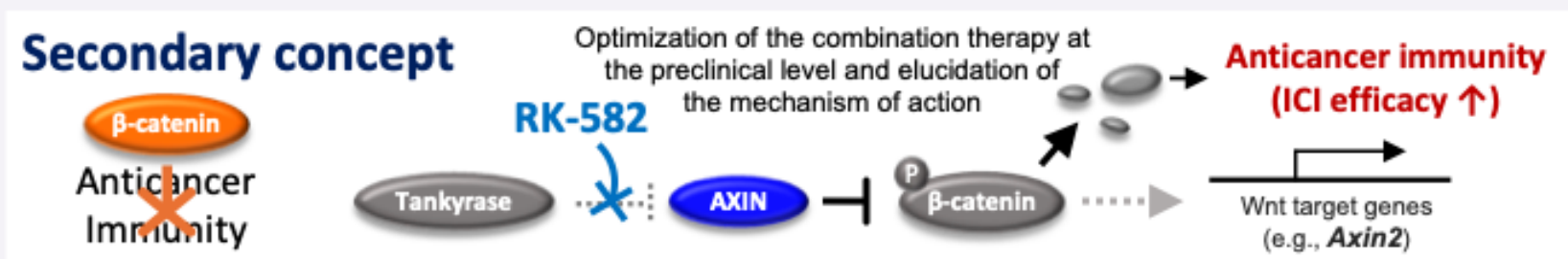
- We have demonstrated the synergistic antitumor effect of RK-582 in combination with an ICI in a mouse model. This study aims to optimize the combination therapy protocol at the preclinical level and further elucidate its mechanism of action.
- Based on the results of the ongoing FIH trial, we will conduct an independent validation of the predictive biomarkers and formulate a clinical trial plan for a Phase II monotherapy study.
- Combination of RK-582 with ICIs or small-molecule drugs.

【Business plan】

- A startup will be established, securing an exclusive license agreement and initiating activities for alliances with pharmaceutical companies.
- Funding will be raised from VCs for a Phase II clinical trial.
- Phase Ib/II combination therapy trial will be designed based on preclinical findings to maximize therapeutic potential.







【References】Chen, Mashima et al. (2024) Brit J Cancer 130: 151-162; Shirai et al. (2020) J Med Chem 63: 4183-4204; Seimiya et al. (2005) Cancer Cell 7: 25-37

【Patents】JP6923138B2, US11414429, EP3480198B1, AU2017288755B2, CN110023315, KR10-2373624, IN406335, CA3029305, NZ749946