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Development of a Novel Immunotherapeutics with Tumor-associated Macrophage(TAM) Suppression Mechanism

Senelix Co. Ltd.

Senelix

ONCOLOGY | **Lead**

Product Type	Monoclonal Antibody
Indication	Non-small cell lung cancer (NSCLC) and other refractory solid tumors
Target	Chitinase-3 Like-Protein-1 (CHI3L1, YKL-40)
MoA(Mechanism of Action)	▶ CHI3L1 is soluble ligand secreted by a variety of cells, including macrophage, cancer-associated fibroblast (CAF) and cancer cell. Cancer patients have higher levels of CHI3L1 in their serum and tumor tissue compared to healthy individuals. ▶ IL13Rα2 is known to be CHI3L1's primary receptor, however CHI3L1 also binds to Galectin-3, CD44, TMEM219, VEGFR, and p53. CHI3L1 promotes the M2-polarization of macrophage (TAM), the expression of immune checkpoints such as PD-(L)1, CTLA4, LAG3 and TIM3, and angiogenesis in the tumor microenvironment (TME). ▶ As an innovative immuno-oncology treatment candidate, the anti-CHI3L1 antibody has abilities to suppress tumor-associated macrophage (TAM), immune checkpoint proteins (PD-1/PD-L1 axis modulation), and angiogenesis in the TME. Through the combination with immune checkpoint inhibitors as well as conventional chemo agents, the new MoA of anti-CHI3L1 antibody offers a novel approach to significantly improve treatment effectiveness for refractory cancers.
Competitiveness	▶ PD-(L)1 inhibitors only have a 10~30% response rate in non-small cell lung cancer (NSCLC), while many other carcinomas still do not respond to ICIs (eg, pancreatic, prostate, ovarian cancers and GBM). ▶ Therefore, novel immuno-therapeutics that target innate immunity, such as tumor-associated macrophages (TAM), are very appealing. Furthermore, the anti-CHI3L1 antibody inhibits the immune checkpoint system and angiogenesis. This combination of actions gives the anti-CHI3L1 antibody a unique competitive advantage. ▶ As innate immunity modulators, several pipelines that inhibit the CD47-SIRPα axis are actively being developed, but clinical trials have been negative, due to side effects such as erythrocytopenia and low efficacy. CD40 agonists are being developed, but due to their severe side effects, their administration route is limited to intratumoral injection. ▶ As a result, despite the enormous need for novel treatments that could modify innate immunity or TAM, there aren't many clear competitors either on the market or in development.
Development Stage	Lead
Route of Administration	Intravenous injection

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