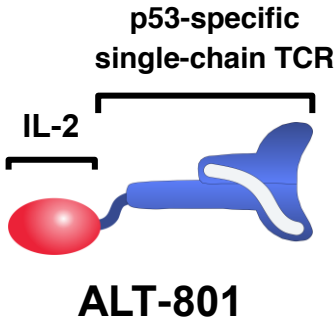
ALT-801 (Tumor-targeted IL-2 immunotherapeutic)

FACT SHEET

ALT-801 is an investigational agent and has not been approved by regulatory agencies



ALT-801

Background: ALT-801 is an innovative immunotherapeutic fusion protein consisting of interleukin-2 (IL-2), an approved cytokine for treatment of metastatic melanoma and renal cell carcinoma, linked to a single-chain T-cell receptor domain (STAR™). Through this fusion, ALT-801 changes the functional activity of the IL-2 domain. As shown in comparative pharmacokinetic, biodistribution, pharmacodynamic, tolerability and efficacy studies in experimental animal models, ALT-801 exhibits more potent immunostimulatory and antitumor activities against solid and hematological malignancies than IL-2. Thus, ALT-801 is expected to provide greater efficacy, lower toxicity, more convenient treatment regimens and a better quality of life for patients with cancer.

The STAR™ targeting domain of ALT-801 was developed through Altor's STAR™ technology platform to recognize cancer cells that overexpress the tumor-associated antigen, p53. The p53 protein is mutated and overexpressed in roughly 50% of all human cancers and typically correlates with poor prognosis, making it an ideal target for a targeted therapeutic. However, p53 cannot be used as a target for antibody-based therapies because it is an intracellular protein not displayed on the cell surface. The soluble STAR™ domain of ALT-801 was generated from a high affinity TCR that binds to a peptide antigen derived from p53 and displayed in the context of HLA-A*0201 (Zhu, et al. 2006). When fused to IL-2, this STAR™ domain promotes targeting of immunostimulatory activity to the site of p53-overexpressing tumor cells, thereby localizing immune effector cytotoxic activities to the tumor microenvironment. This fusion protein also binds to and activates immune cells differently than IL-2 and has a longer *in vivo* half-life with extended localization in immune organs when compared to IL-2. Together, these properties provide ALT-801 with significantly greater antitumor activity than IL-2 against both p53-overexpressing and non-target-bearing tumors in various animal efficacy models (Card, et al.2004; Belmont, et al. 2006; Wen, et al. 2008).

Clinical Development of ALT-801: ALT-801 is the first TCR-based therapeutic to enter clinical trials and has been administered to over 100 patients with various cancer indications.

A $3 MM NCI-SBIR Bridge grant has been awarded to Altor to help fund the Phase 2 ALT-801 clinical trials and Altor was named as a "Success Story" by the Small Business Innovative Research program of NIH/NCI (NCI-SBIR Success Stories).

Phase	Investigational Therapy	Trial Number	Trial Description
I	ALT-801	NCT00496860	Phase I Study of ALT-801 in Patients With Progressive Metastatic Malignancies*
I	ALT-801 + cisplatin	NCT01029873	A Phase 1 Study of ALT-801 With Cisplatin in Patients With Metastatic Melanoma
II	ALT-801 + cisplatin + gemcitabine	NCT01326871	A Study of ALT-801 in Combination With Cisplatin and Gemcitabine in Muscle Invasive or Metastatic Urothelial Cancer
I	ALT-801 + gemcitabine +BCG	NCT01625260	A Study of ALT-801 in Patients With Bacillus Calmette-Guerin (BCG) Failure Non-Muscle Invasive Bladder Cancer

*Fishman MN, et al. Clin Cancer Res. 2011 Dec 15;17(24):7765-75.

Publications:

1. Phase I trial of ALT-801, an interleukin-2/T-cell receptor fusion protein targeting p53 (aa264-272)/HLA-A*0201 complex, in patients with advanced malignancies. Fishman MN, Thompson JA, Pennock GK, Gonzalez R, Diez LM, Daud AI, Weber JS, Huang BY, Tang S, Rhode PR, Wong HC. Clin Cancer Res. 2011 Dec 15;17(24):7765-75.
2. Targeting activity of a TCR/IL-2 fusion protein against established tumors. Wen J, Zhu X, Liu B, You L, Kong L, Lee HI, Han KP, Wong JL, Rhode PR, Wong HC. Cancer Immunol Immunother. 2008 Dec;57(12):1781-94.
3. Potent antitumor activity of a tumor-specific soluble TCR/IL-2 fusion protein. Belmont HJ, Price-Schiavi S, Liu B, Card KF, Lee HI, Han KP, Wen J, Tang S, Zhu X, Merrill J, Chavillaz PA, Wong JL, Rhode PR, Wong HC. Clin Immunol. 2006 Oct;121(1):29-39.
4. Visualization of p53(264-272)/HLA-A*0201 complexes naturally presented on tumor cell surface by a multimeric soluble single-chain T cell receptor. Zhu X, Belmont HJ, Price-Schiavi S, Liu B, Lee HI, Fernandez M, Wong RL, Builes J, Rhode PR, Wong HC. J Immunol. 2006 Mar 1;176(5):3223-32.
5. A soluble single-chain T-cell receptor IL-2 fusion protein retains MHC-restricted peptide specificity and IL-2 bioactivity. Card KF, Price-Schiavi SA, Liu B, Thomson E, Nieves E, Belmont H, Builes J, Jiao JA, Hernandez J, Weidanz J, Sherman L, Francis JL, Amirkhosravi A, Wong HC. Cancer Immunol Immunother. 2004 Apr;53(4):345-57.

More detailed documentation on ALT-801 may be provided under a confidentiality agreement.

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