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Chimeric antigen receptor modified T-cell redirected to EGFR in patients with metastatic and advanced pancreatic adenocarcinoma and biliary tract cancers

Statement of the Problem: Limited effective treatment opinions and dismal prognosis in metastatic pancreatic adenocarcinoma (mPA) and biliary tract cancers (BTCs) require developing novel therapeutic approaches.

Methodology & Theoretical Orientation: Epidermal growth factor receptor (EGFR) is a well-known candidate therapeutic target due to its frequent overexpression in epithelium-derived tumors. The purpose of this study is to further expand our clinical trial (NCT01869166) of EGFR-specific chimeric antigen receptor-engineered autologous T-cell (CAR T-EGFR)-based therapeutic modality to mPA and mBTCs to evaluate its feasibility and efficacy. Patients were enrolled when >50% EGFR+ ratio was observed in tumor specimens by immunohistochemical staining. CAR copy number in peripheral blood was serially measured to determine the therapeutic cycles.

Findings: A total 34 of patients including 12 mPA and 22 mBTCs received 1 to 3-cycle cell infusions (Range from 0.6 to 4.1×106/kg, median dose is 2.3×106/kg) within 6 months. The acute toxicities included infusion-associated febrile syndrome (Grade 1/2 in 34 cases) and pulmonary edema/pleural effusion (Grade 3 in 4 cases). The common toxicities occurred 1 week after cell infusions included febrile syndrome (Grade 1/2 in 11 cases) accompanied with the elevation of serum cytokine such as IL6 and/or TNFα and CRP and mucosal/cutaneous damages (Grade 1/2 in 19 cases). Of 31 patients who were treated by nab-paclitaxel/cyclophosphamide conditioned cell infusions, 5 obtained 8-16 weeks PR and 5 had 4-12 week SD in mPA patients and 1 obtained a 22-month ongoing CR and 10 had 6-56 week SD in BTCs patients. 3 BTC patients were treated by cell infusion alone given their tolerance and relatively small disease burden, 1 obtained a 20-month ongoing CR, 1 had 8.5-month PR and 1 had 9-month SD.

Conclusion & Significance: This trial further indicated the controllable safety and efficacy of EGFR-targeted CAR T therapy, providing basis for further optimal combination strategy.

Biography

Weidong Han has obtained his PhD degree in Clinical Hematology from Chinese PLA Postgraduate Medical School and worked in Department of Molecule & Immunology of Chinese PLA General Hospital. In 2003, he did Postdoctoral work at the University College London. In 2006, he was promoted to Professor of Molecular and Cellular Biology. Presently, he is the Director of Department of Molecular and Cellular Biology, Director of Clinical Translational Ward, the General Hospital of PLA. Since 2001, he focused on mechanism research involved in cancer-treatment resistance and clinical translation of cell therapy. He has published over 100 articles.

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