Cancer Research

Clinical Research (Excluding Clinical Trials)

Abstract 2252: YIV-906 (PHY906) enhanced the anti-tumor activity of immune checkpoint blockade therapy (Anti-PD1) against liver cancer by changing the tumor micro-environment associated with M1 macrophages infiltration

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Abstract

YIV-906 (PHY906) is inspired by a traditional 1800-year Chinese herbal formulation, “Huang Qin Tang”, which is commonly used for treating diarrhea. Following chemotherapy and radiation, preclinical and clinical results suggest that YIV-906 has the potential to improve the patient’s quality of life and prolonging survival. Consistent preparations of PHY906 could be manufactured apart 15 years. The effects of YIV-906 were studied on the anti-tumor activity of anti-PD1 using BDF1 mice bearing Hepa 1-6 tumors. Results indicated that anti-PD1 alone had moderate effects on tumor growth however YIV-906 plus anti-PD1 eradicated all tumors in all tumor bearing mice. Further re-implantation of Hepa 1-6 cells did not grow in the “cured” mice, but implanted CMT167 (non-small lung carcinoma) cells or Pan02 (Pancreatic Ductal Adenocarcinoma) cells did grow; suggesting that YIV-906 plus anti-PD1 created a tumor-specific vaccine-like effect. The combination treatment exhibited a highly inflamed tumor microenvironment with more M1-like macrophage expression over M2. In culture YIV-906 could potentiate the action of IFNg (interferon gamma) to polarize bone marrow-derived macrophages (BMDM) into M1 macrophages while inhibiting IL4 action for M2 macrophage polarization. YIV-906 potentiated IFNg action through: 1) stimulating IFNg secretion, 2) phosphorylation of JAK1/2 and STAT1 and 3) increasing IRF1 protein expression. *Scutellaria baicalensis Georgi* (S) and its flavonoids of YIV-906 were responsible for potentiate the IFNg to polarize macrophage into M1. In conclusion, YIV-

906 enhanced the anti-tumor activity of anti-PD1 by enhancing inflammation in the tumor microenvironment and enriching M1-like macrophages. This suggests the potential use of combination YIV-906 and anti-PD1 in cancer treatment. This work was supported by grant (1PO1CA154295-01A1) from National Cancer Institute (NCI), NIH, USA. Dr. Yung-Chi Cheng is a fellow of National Foundation for Cancer Research (NFCR), USA.

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Previous

Back to top

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Table of Contents

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