Immunology

Abstract 2724: YIV906 (PHY906) enhanced the antitumor activity of immune checkpoint blockade therapy: Anti-PD1 against liver cancer

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Abstract

Immune checkpoint blockade therapy has recently been recognized as a breakthrough in cancer treatment. Recently, FDA has approved Nivolumab (anti-PD1) for the treatment of hepatocellular carcinoma (HCC) patients previously treated with sorafenib. However, the percentage of patients with a complete response was only 1.9% that is much lower than Nivolumab used for treating melanoma. Diarrhea, nausea and fatigue are common side effects for HCC patients who received Nivolumab. YIV906(PHY906) is inspired by the Huang Qin Tang, which was first described in Chinese texts 1800 years ago for the treatment of numerous gastrointestinal symptoms. Consistent preparations of PHY906 can be manufactured apart 10 years. Our clinical results suggest that YIV906 has potential to increase the therapeutic index of capecitabine or sorafenib for HCC patient by improving quality of life and prolonging life. In animal studies, YIV906 can increase the anti-tumor activity of a broad spectrum of chemotherapies through multiple mechanism of actions. We believe that YIV906 could have potential to improve the efficacy of Nivolumab, either by increasing its anti-tumor activity or decreasing its side effects. Here, we studied the effect of YIV906 on the anti-tumor activity of anti-PD1 using BDF1 mice bearing with Hepa 1-6 tumors. Results indicated that YIV906 alone had only

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Volume 78, Issue 13
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Table of Contents

moderate effects on the Hepa 1-6 tumor growth. Anti-PD1 alone could stabilize 80% tumor growth and caused 20% tumor shrinkage following 8-day injection. YIV906 plus anti-PD1 made all tumors disappear following 7-day treatment and no tumor rebound was found for one month. When YIV906 and different dosages of anti-PD1 (70ug or 200ug per animal) were used, YIV906 plus anti-PD1 (70ug) had an stronger anti-tumor effect than anti-PD1 (200ug) alone. The above results suggested that YIV906 could reduce the usage of anti-PD1 by 3-fold while having better antitumor effects than anti-PD1 alone. qRT-PCR results recovered that many genes related to M1-like macrophages and T cell activation were strongly up-regulated in the tumor tissues following YIV906 plus anti-PD1 treatment. More macrophages were found in tumor tissues associated with an upregulation of MCP1 protein following YIV906 plus anti-PD1 treatment. Biostatical analysis, based on the mRNA expression of M1 and M2-like macrophage signature genes, suggested the tumor microenvironment was favorable for M1 status following YIV906 plus anti-PD1 treatment. In addition, YIV906 could decrease LPS-induced PD1 protein of macrophages in culture. In conclusion, YIV906 might enhance the anti-tumor activity of anti-PD1 by changing the tumor microenvironment favorable to M1-like macrophages. Our results provide supportive information to initialize HCC clinical trial with YIV906 plus Nivolumab. This work was supported by grant (PO1CA154295-01A1) from NCI, USA. Dr. Y.-C. C is a fellow of NFCR, USA.

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Previous

Back to top

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Alerts
Feedback

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Online First
Current Issue
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