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First-in-class small molecule Icaritin Induced Immunomodulatory Efficacy in Advanced HBV-Related Hepatocellular Carcinoma:Immunodynamic Biomarkers and Overall Survival

Advanced HBV-related HCC with poor prognosis is often associated with chronic inflammation, immune tolerance and marked heterogeneity. IL-6/JAK/STAT3 signal pathways play multiple regulatory roles in modulating inflammation and immunity in cancers. Polarisation of myeloid-derived suppressor cells (MDSCs) is involved in HBV-related immunosuppression and $CD8^+$ T-cell activation via ERK/IL-6/STAT3. Icaritin is a small molecule that has displayed anticancer activities via IL-6/JAK/STAT3 pathways in tumour cells and immune cells including $CD8^+$ T cells, MDSCs, neutrophils and macrophages. This study aimed to confirm icaritin immunomodulation in advanced HBV-related HCC patients with poor prognosis. Immunomodulation of MDSCs was evaluated in BALB/c mice in vivo. Immunomodulation of serum cytokines and panel of immune checkpoint proteins were assessed in HBV-related, histologically confirmed HCC patients. Poor prognostic characteristics included HBV-infection, bulky tumours, Child-Pugh B classification and metastasis. Clinical endpoints included safety, tumour response and overall survival (OS). Icaritin treatment-induced dynamics of serum cytokines IL-6, IL-8, IL-10 and TNF-α and soluble immune checkpoint proteins TIM3, LAG3, CD28, CD80, and CTLA-4 were assessed. No grade III/IV treatment-related adverse events were observed. Time-to-progression was significantly associated with the prognostic factors. Improved survival was observed in the advanced HCC patients with dynamic changes of cytokines, immune checkpoint proteins and immune cells. Median OS (329-565 days) was significantly correlated with baseline $HBsAg^+$, cytokines, tumour neo-antigens and *Stenotrophomonas maltophilia* infection. Composite biomarker scores of high-level AFP and Th1/Th2 cytokines associated with favourable survivals warrant further clinical development of icaritin as an alternate immune-modulatory regimen to treat advanced HCC patients with poor prognosis.

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Keywords: icaritin anticancer immunomodulation, dynamic biomarkers, survival, HBV-related advanced HCC

Biography:

Dr. Bin Ye graduated from Weizmann Institute, Israel in 1998, followed his Post.Doc training in Harvard Medical School, was promoted as Assistant Professor in Brigham Women's Hospital/Dana-Farber Cancer Center in 2008 with several competitive Cancer Research awards. He has contributed more than >40 original research papers and 7 patents Since 2011, Dr. Ye acted as senior Investigator and led China Biomarker Development (BMD) outsourcing at Novartis in early phase global trials. Dr. Ye jointed in Shenogen Pharma lead biomarker informatics and Translation Medicine in first-in-class icaritin development program from phase I to III and focus on immune therapy.

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