

expression was significantly increased in tumours compared to adjacent normal tissue (figure 1A). Mice treated with CD5-2 + anti-PD1 antibody had significantly smaller tumours (50% reduction) compared to mice treated with either agent alone, controls, or untreated mice (figure 1B). Histologically, tumours in the CD5-2 + anti-PD1 group exhibited a more favourable immune infiltrate (significantly higher CD3+ and CD8+ T-cells and lower Ly6G+ neutrophils) compared to tumours in other groups (figure 1C). Tumours in CD5-2-treated mice had less leaky vasculature (as measured by Dextran beads extravasation) and less tumour hypoxia (carbonic anhydrase IX staining) compared to non-CD5-2-treated mice (figure 1D).

Conclusions In the DEN model, CD5-2 normalised tumour vasculature and reduced tumour hypoxia. CD5-2 plus anti-PD1 antibody reduced tumour size possibly by altering immune infiltrate to being immunosupportive. The combination of vascular normalisation by targeting VE-Cadherin and immunotherapy is a promising novel approach to treat HCC.

IDDF2020-ABS-0213 CXCR2 BLOCKADE DISRUPTS TUMOR TRAFFICKING OF MDSC TO POTENTIATE IMMUNOTHERAPY EFFICACY

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Background The heterogeneity and diverse pathogenic conditions of HCC construct an immunosuppressive tumor micro-environment (TME) which may lead to low immune checkpoint blockade (ICB) therapeutic responsiveness. Therefore, alleviating immunosuppression to potentiate ICB anti-cancer immunity is in urgent need. Myeloid-derived suppressor cells (MDSCs) with potent T cell suppressive property are correlated with poor prognosis and unsatisfactory ICB response in HCC. In this study, we aimed to study the potential efficacy and functional mechanisms of targeting C-X-C motif chemokine receptor 2 (CXCR2) chemotaxis pathway to block MDSC tumor infiltration, enhancing ICB efficacy using pre-clinical orthotopic HCC mouse models.

Methods CXCR2-chemotaxis pathway activation in MDSCs was determined by multi-color flow cytometry in tumor and paired non-tumor liver specimens from HCC patients, as well as healthy blood samples. Therapeutic efficacy of CXCR2 blockade was conducted in an orthotopic mouse model using AZD5069 (100 or 150 mg/kg) which is a CXCR2 antagonist currently undergoing clinical trials and in combination with anti-PD-L1 antibody (10F.9G2). Tumorigenic monitor, immune profiling and survival analysis were performed. Mechanistic study was determined using lentivirus-based gene knockdown in human-blood cell models.

Results The result showed that both monocytic (M-MDSC) and polymorphonuclear (PMN-MDSC) populations are elevated in HCC liver tissue compared to healthy donor (HD) control. CXCR2 was widely expressed in immune cells, in particular for MDSC, while its ligand interleukin-8 (IL-8) was expressed in the majority of tumor cells, as well as CD45⁺ leukocytes in HCC. Notably, the blockade of CXCR2 chemotaxis pathway significantly inhibits MDSC trafficking into tumor microenvironment in HCC orthotopic mouse model.

Furthermore, co-blockade of CXCR2 and PD-L1 remarkably reduced tumor weight when compared to a single treatment, in which intratumoral CXCR2⁺PD-L1⁺ MDSC was positively associated with tumor burden.

Conclusions Our data demonstrated the intricate link between IL-8/CXCR2 axis and MDSC trafficking to TME, providing insight into the immunosuppression mechanism in HCC. Targeting IL-8/CXCR2 chemotaxis pathway may potentiate ICB responsiveness, serving as a novel potential therapeutic option for effectively combined immunotherapy in liver cancer.

Clinical gastroenterology

IDDF2020-ABS-0033 THE EFFECT OF IMMUNOMODULATORS AND OTHER FACTORS ON THE PERSISTENCE OF BIOLOGICAL AGENTS FOR CROHN'S DISEASE AND ULCERATIVE COLITIS: DATA FROM THE AUSTRALIAN POPULATION-BASED REGISTRY

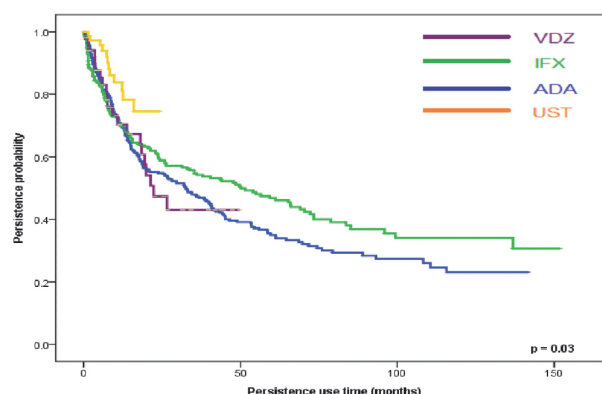
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Background Treatment persistence (duration of medication use) provides real-world evidence on therapeutic effectiveness, tolerability and prescriber and patient preferences. Biological agent persistence in Crohn's disease (CD) and ulcerative colitis (UC) was compared from the national population-based registry with no hierarchical prescribing order. We hypothesized immunotherapy co-therapy would increase persistence through decreased immunogenicity.

Methods A randomly selected ten percent subgroup of the prospectively collected population-based registry from the Australian Pharmaceutical Benefits Scheme between June 2005-June 2019 was analysed. Treatment persistence of adalimumab (ADA), infliximab (IFX), vedolizumab (VDZ) and ustekinumab (UST) was compared.

Results 2499 patients were included consisting of 3713 lines of therapy (2864 CD, 849 UC) which equated to 7470 person-years of follow-up. In CD, UST had the highest overall persistence rate (median persistence rate >74.6% where 24.6 months is the maximum follow up time recorded), followed by VDZ, IFX and ADA (p=0.03) (figure 1). In UC, VDZ had



Abstract IDDF2020-ABS-0033 Figure 1 Persistence Kaplan meier graphs- Luminal crohn's disease persistence