animal models, knockdown of GM-CSF in pancreatic epithelium or pancreatic mesenchymal stem cells inhibits tumorigenesis, reduces intra-tumor MDSCs and enhances CD8+ T cell accumulation.[6 7 8] Therefore, targeting the GM-CSF receptor alpha (GM-CSFRα) on MDSCs is an attractive strategy to restore anti-tumor immunity. Mavrilimumab is a clinical stage fully human monoclonal antibody that blocks GM-CSFRα. It has demonstrated efficacy and acceptable safety profile in patients with rheumatoid arthritis, and it's currently undergoing investigation in phase II studies in giant cell arteritis and in patients with severe COVID-19 pneumonia and hyperinflammation (NCT03827018, NCT04397497, respectively). The present study investigates its potential as a therapeutic strategy to target MDSCs in the TME as an adjuvant to immunotherapy.

Methods Cancer cell supernatants were collected when cells reached confluency. Human GM-CSF was measured by ELISA. Healthy donor CD14+ monocytes were incubated (± mavrilimumab) with cancer cell supernatants for either 3 or 6 days followed by phenotypic analysis (CD14, CD33, HLA-DR, CD11b, CD206, CD80, PD-L1, Arginase-1) by flow cytometry. On day 3, autologous CD3+ T cells were stimulated with CD3/CD28 and IL-2 and co-cultured with putative MDSCs for 5 days. T-cell proliferation was evaluated by measuring carboxyfluorescein succinimidyl ester (CFSE) dilution in CD4 + and CD8+ T cells by flow cytometry.

Results GM-CSF is expressed in the supernatant of cancer cell lines (HCT116, SW-480, Panc-1, Capan-1). Human monocytes cultured with conditioned medium from colorectal carcinoma (SW-480) or pancreatic adenocarcinoma (Capan-1) show downregulation of HLA-DR, increased expression of PD-L1, Arg-1, CD206, and can suppress T-cell proliferation in-vitro. Similarly, peripheral blood monocytes purified from pancreatic cancer patients suppress T-cell proliferation ex-vivo. Notably, Mavrilimumab inhibits the polarization of healthy donor monocytes to M-MDSCs and restores T-cell proliferation.

Conclusions Targeting of GM-CSFRα with mavrilimumab may alleviate the pro-tumorigenic and immunosuppressive functions of MDSCs in the TME. Future clinical studies should evaluate whether targeting of the GM-CSFRα in combination with immune checkpoint inhibitors is a viable therapeutic option to bolster their efficacy.

Ethics Approval The study was approved by the Institute of Immunology and Immunotherapy, University of Birmingham, UK Ethics Board. Healthy volunteer human material was obtained from commercial sources and approved by Stemexpress Institutional Review Board (IRB).

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474 MULTIPLE COMBINATIONAL STRATEGIES OF IMMUNOTHERAPY FOR ESOPHAGEAL SQUAMOUS CELL CARCINOMA: ONE INSTITUTIONAL EXPERIENCE IN TAIWAN SINCE 2016

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Background Esophageal squamous cell carcinoma is still a health burden in Taiwan. In R/M setting, the prognosis becomes worse. ESCC is still an immunogenic cancer. In randomized 2nd line ATTRACTION-3 study(nivolumab vs taxane after PF failure), median OS improved from 8.4 months in chemotherapy to 10.9 months in nivolumab(HR, 0.77; 95% CI, 0.62–0.96; p =0.019). The median duration of response was 3.9 months and 6.9 months. Nivolumab is a new 2nd line option for ESCC.

Methods From early 2016 to early 2020, 15 advanced ESCC patients had ever received immunotherapy-containing regimens in Yun-lin Branch of National Taiwan University Hospital and were analyzed.

Results The overall response to immunotherapy-containing regimens was 60%(9/15) and clinical benefit was 80%(12/15). 2nd line nivolumab was given in 3 cases; response rate was33% and clinical benefit was 67%. 2nd line afatinib combined with anti-PD1 was given in 9 case; response rate was 67% and clinical benefit was 78%. The response rate of 2nd line afatinib & pembrolizumab was 75%(3/4); however, Gr. III pneumonitis & Gr. II hepatitis were noted in the patient with progression. The response rate of 2nd line afatinib & nivolumab was 60%(3/5) and clinical benefit was 80%(4/5); skin rash and diarrhea were often found. 1st line afatinib combined with anti-PD1 was given in 3 patients; response rate was 67% and clinical benefit was 100%. The response rate of 1st line afatinib & nivolumab was 100%(2/2).

Conclusions EGFR TKIs have multiple immuno-modulatory effects and may increase immunotherapy benefits in ESCC. Anti-PD1 and anti-CTLA4, another possible rationale, could bring more benefits maybe in 1st line CheckMate649 study.

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Trial Registration N/A

Ethics Approval N/A

Consent Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

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Nil

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