As-treated analysis

Serious bacterial infection 48 3445 1.39 [1.03-1.85] 61 4629 1.32 [1.01-1.69] 1.04 [0.71-1.52]
Opportunistic infection 4 3489 0.11 [0.03-0.29] 23 4686 0.49 [0.25-0.80] 0.25 [0.10-0.52]
Serious zoster 62 3435 1.81 [1.38-2.31] 11 4682 0.24 [0.12-0.42] 0.74 [0.39-1.41].

365-day ITT

Serious bacterial infection 36 2260 1.59 [1.12-2.21] 61 4313 1.48 [1.07-1.92] 1.08 [0.75-1.56]
Opportunistic infection 3 2274 0.13 [0.03-0.39] 16 4155 0.39 [0.18-0.83] 0.35 [0.14-0.85]
Serious zoster 37 2263 1.64 [1.15-2.25] 12 4156 0.29 [0.15-0.50] 0.77 [0.33-1.79].

IR is per 100 person-years.
Background: Treatment effect of tumor necrosis factor α (TNF-α) inhibitors is still low in patients with rheumatoid arthritis (RA), around 50%-70%. Thus more drugs by targeting proliferation of synovial fibroblasts (FLS) and TNF-α induced inflammatory cytokine production are needed. Repurposed use of drugs that have been used in clinic is a quick and cost-effective way to find new drugs.

Objectives: This study aims to screen drugs that could inhibit the proliferation and inflammation induced by TNF-α in FLS from FDA approved on market drug library, then to assess the treatment effect of the identified drugs on collagen-induced arthritis (CIA) mouse model.

Methods: CCK8 assay was performed to screen the drugs that could inhibit FLS proliferation, followed by qRT-PCR and ELISA to select the drugs that could suppress TNF-α induced inflammatory cytokine production. Then, treatment effects of the identified drugs were assessed in CIA mouse model. 

Results: The first and second round drug library screening aimed to select out the drugs that could inhibit the proliferation of FLS. Results showed, from 1815 drugs, 372 drugs were identified at the initial screening (Figure 1A) and 121 drugs were identified from the second screening (Figure 1B). The second round screening. The drugs could inhibit more than 10% absorbance at 450nm, more than 20% absorbance at 450nm, under the red lines, were the target ones, n=372. (B) The second round screening. The drugs could inhibit more than 10% absorbance at 450nm, under the red lines, were the target ones, n=121. (C-F) The third round screening. (C-D) mRNA expression levels of IL-6 and IL-8. (E-F) the secretion levels of IL-6 and IL-8. (G-H) The confirmation of drugs inhibitory effect on the inflammation cytokone production. Red asterisk indicated the comparison between TNF-α group and DMSO group and blue pound signs suggested the comparison between drugs and TNF-α group. (G-H) the mRNA expression levels of IL-6 and IL-8. (I-J) the secretion levels of IL-6 and IL-8. CIA mouse model was established to test the treatment effect of SV (10mg/kg), PDL (10mg/kg), ALM (5mg/kg), CCC (10mg/kg), and AOM (10mg/kg), and MTX (2mg/kg) was set as the positive control. (K) clinical score of joint swelling (L) H&E staining of knee joint (M) H&E staining of ankle joint (N) pathological scoring of H&E staining for joint inflammation and bone erosion.

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Disclosure of Interests: None Declared.

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POS0839

AGOMELATINE IDENTIFIED FROM THE FDA-APPROVED DRUG LIBRARY IS THERAPEUTIC AGAINST COLLAGEN INDUCED ARTHRITIS

Keywords: Rheumatoid arthritis, Cytokines and chemokines

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Background: ToFA, apart from its anti-inflammatory activity, improves endothelial dysfunction and cardiovascular risk in active RA without clinical overt cardiovascular disease. Thus, JAK inhibition with TOFA has vasculoprotective and cardioprotective effect mediated through anti-inflammatory and probably other mechanisms.

REFERENCE:

Disclosure of Interests: None Declared.

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POS0839

THE COMPARISON OF MALIGNANCY RISK BETWEEN JAK INHIBITORS AND TNF INHIBITORS IN MULTI-CENTER COHORT STUDY

Keywords: Targeted synthetic drugs, Rheumatoid arthritis, Safety

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Background: Ytterberg et al. demonstrated the concern about the incidence of malignancy during treatment with tofacitinib [1]. However, there is few published data of such adverse events in clinical settings.

Objectives: We aimed to compare the incidence of malignancies in RA patients treated with JAK inhibitors and TNF inhibitors in real-world settings.

Methods: We enrolled 499 RA patients treated with JAK inhibitors (tacitofinib, n=192 or baricitinib, n=104) or TNF inhibitors (adalimumab, n=88 or etanercept, n=115). The standardized incidence ratio (SIR) of malignancies were determined using the general Japanese population. After adjusting the clinical characteristic imbalance by propensity score weighting, we compared the risk of malignancy between JAK inhibitors and TNF inhibitors using Cox proportional hazard models.

Results: Observational period was 961.9 patient-years (PY), and median observational period was 1.3 years. We identified 11 cases (3.7%) of malignancies in JAK inhibitors and 4 cases (2.0%) in TNF inhibitors. The SIR for overall malignancies in TNF inhibitors was comparable with general population (0.94, 95%CI: 0.26–2.41), and the SIR in JAK inhibitors was higher than the general population but no significant difference (1.61/100PY, 95%CI: 0.80–2.88). The adjusted hazard ratio was 0.38 (95%CI: 0.09–1.55) between JAK inhibitors and TNF inhibitors in the risk of malignancies (Figure 1).

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