DEFINING THE CLINICAL UTILITY OF PET OR PET/CT IN IDIOPATHIC INFLAMMATORY MYOPATHIES: A SYSTEMATIC LITERATURE REVIEW

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Background: Positron emission tomography (PET), now often combined with computed tomography (CT), is a well-established tool for evaluating malignancy and inflammatory disease. The idiopathic inflammatory myopathies (IIM) are chronic, multi-system diseases characterised by skeletal muscle inflammation, the potential for extramuscular manifestations such as interstitial lung disease (ILD) and an increased risk of malignancy. PET or PET/CT thus has appeal as an imaging modality that may permit simultaneous assessment of multiple features of IIM, however its role in evaluation of these diseases remains poorly defined.

Objectives: This systematic review seeks to evaluate and describe the utility of PET or PET/CT in IIM, specifically for the detection of inflammatory muscle pathology, associated malignancy and extramuscular manifestations (e.g. ILD).

Methods: We performed a search of Medline and EMBASE from 1990-2021 using keywords related to IIM and PET. We included English language studies of adults with IIM who had PET or PET/CT as part of their diagnostic workup.

Results: Our search identified 910 potentially relevant abstracts, 18 of which were included. The majority of studies used fluorodeoxyglucose (FDG) PET or PET/CT scans, while the remainder used other radiotracers including [18F] flortetapir and [11C] Pittsburgh compound B ([11C] PIB). 1. Malignancy – PET vs. conventional screening Six studies investigated the ability of 18F-FDG PET or 18F-FDG PET/CT to detect malignancy in people with IIM. When reported, the sensitivity and specificity of PET or PET/CT for diagnosing malignancy compared with standard detection methods was 66.7-94% and 88.9-97.8%, respectively. 2. ILD Using high-resolution CT (HRCT) as the gold standard for detection of ILD, three studies reported the ability of PET or PET/CT to detect ILD. The sensitivity of 18F-FDG PET alone for ILD was 39%, while the sensitivity of 18F-FDG PET/CT for ILD was 93-100%. FDG lung uptake was significantly increased in people with rapidly progressive-ILD (RP-ILD) in comparison to those with non-RP-ILD in two studies. 3. Muscle disease activity Ten studies evaluated either 18F-FDG PET or 18F-FDG PET/CT for its ability to detect muscle inflammation in IIM. In the nine studies where controls were used, PET or PET/CT appeared to accurately detect the presence of muscle inflammation, although correlations with clinical measures of myositis disease activity, such as strength and serum creatine kinase were mixed. 4. A word on amyloid Skeletal muscle amyloid deposition was evaluated using [11C]PIB-PET in two studies and [18F]flortetapir PET/CT in one study. In all three studies, PET or PET/CT was able to differentiate sporadic inclusion body myositis (IBM) from non-IBM myositis.

Conclusion: PET or PET/CT performs relatively well as a malignancy screening tool for people with IIM in comparison to standard screening methods. While false positives for malignancy on PET can lead to unnecessary invasive investigations, this also occurs with conventional screening. PET/CT also appears to be a beneficial tool for detecting ILD in those with IIM and may predict its severity. While PET/CT may detect skeletal muscle inflammation in IIM, its utility beyond the standard and readily available diagnostic tests for measuring muscle disease activity remains unclear. Early evidence indicates PET-amyloid may be able to subtype IBM from non-IBM myopathic disease, although more data are needed. More research is needed to evaluate whether PET could be used as a tool for detecting cardiac involvement in IIM, or if extending the PET scan field of view might increase the cancer detection yield and permit a more accurate assessment of extramuscular manifestations in IIM. PET/CT holds promise as a single tool that can simultaneously evaluate multiple aspects of IIM early in the diagnostic process. These include screening for associated malignancy in high-risk patients, stratifying higher risk ILD, and providing information on muscle inflammation.

Disclosure of Interests: None declared


REFERENCES

POS0857 PHARMACOKINETICS, SAFETY, AND EFFICACY OF SUBCUTANEOUS BRODALUMAB FOR SYSTEMIC SCLEROSIS WITH MODERATE-TO-SEVERE SKIN THICKENING: A SINGLE-ARM, OPEN-LABEL, MULTI-DOSE, PHASE 1 TRIAL

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Background: Systemic sclerosis (SSc) is a rare autoimmune disease that causes fibrosis of the skin and internal organs. The mechanism of SSc pathogenesis and progression is not clear yet and SSc is therefore a disease with high unmet medical need. Though recent evidence reveals that interleukin-17 (IL-17) may play an essential role in the pathogenesis of multiple autoimmune inflammatory diseases, the role of IL-17 in SSc has not been established.

Objectives: This trial assessed the pharmacokinetics (PK), safety, and efficacy of multiple subcutaneous doses of brodalumab, a fully human anti-IL-17RA monoclonal antibody that inhibits the activity of IL-17A, IL-17C, IL-17F, IL-17A/F, and IL-17E (also called IL 25), in Japanese SSc patients with moderate-to-severe skin thickening.

Methods: In this trial, eligible patients (the modified Rodnan skin score (mRSS); 10-29, present with the first symptoms of SSc other than Raynaud's phenomenon within 60 months at enrolment) were enrolled and received subcutaneous brodalumab 210mg every 2 weeks (Q2W) during the 52-week period. Primary endpoints were PK and safety. Secondary endpoints included change from baseline in mRSS and Composite Response Index in SSc (CRiSS) score. Exploratory endpoints included lymphocyte subset testing.

Results: Eligible 8 patients were enrolled. Mean (SD) age was 53.6 (10.6) years. All patients had diffuse cutaneous SSc, total mRSS was 23.1 (5.1) at disease duration was 2.2 (1.9) years. Mean (SD) serum brodalumab trough concentration increased to 21.8 (16.7) μg/mL at week 2 and remained almost constant at week 52. Drug-related treatment-emergent adverse events were observed in three patients: oral candidiasis (n=3), vulvovaginal candidiasis (n=1), and arthralgia (n=1). A rapid decrease in mRSS was observed as early as week 4 ([1 vs baseline, p<0.005), which continued until week 52 ([1-0.125 vs baseline, p<0.0001]). Brodalumab reduced dermal thickness of the lesion skin consistent with the decrease in mRSS. All patients achieved a CRiSS score ≥0.6 at week 4, which continued until week 52. Brodalumab induced Th17/Treg balance to Treg dominance over 52 weeks (vs baseline, p<0.05). The rapid decrease in the number of immunoglobulin G class-switched memory B cells and plasmablasts (vs baseline, p<0.01) was accompanied by an increase in the number of transitional B cells (vs baseline, p<0.05) by week 52. Brodalumab demonstrated a rapid and sustained decrease in mRSS over 52 weeks in Japanese SSc patients with moderate-to-severe skin thickening, which could be attributed to its direct effects on fibroblasts and indirect effects via impacts on B and T cell subsets.

REFERENCES: None.