Conclusion: FIL treatment provided rapid and deep disease control including higher rates of remission and other clinical outcomes, improved physical function, and less radiographic progression compared with MTX alone in MTX-naive pts with 4 PPF, W24 remission rates following FIL 200 mg vs MTX mono and numerically higher vs FIL 100 mg + MTX.

Figure 2. Rates of DAS28(CRP) <2.6, CDAI <2.8, SDAI <3.3, and Boolean remission at W24 in FINCH 3 patients with 4 PPF and at all FINCH 3 patients.

Results:

In the INBUILD trial, the rate of FVC decline was numerically greater in patients taking vs not taking DMARDs and/or glucocorticoids at baseline (Figure). The effect of nintedanib vs placebo on reducing the rate of decline in FVC was numerically more pronounced in patients taking vs not taking DMARDs and/or glucocorticoids at baseline than in those who were not. The rate of FVC decline was slower in patients treated with nintedanib than placebo both in patients who were and were not using DMARDs and/or glucocorticoids at baseline (Figure). The effect of nintedanib vs placebo on reducing the rate of decline in FVC in the placebo group was numerically greater in patients taking vs not taking DMARDs and/or glucocorticoids at baseline (yes/no).

Background: In the INBUILD trial in patients with progressive fibrosing ILDs, nintedanib reduced the rate of decline in forced vital capacity (FVC) vs placebo over 52 weeks in the overall population and in the subgroup with autoimmune disease-related ILDs. Patients taking stable doses of medications to treat RA or CTD were eligible, but the protocol excluded enrolment of patients treated with azathioprine, cyclosporine, mycophenolate, tacrolimus, cyclophosphamide, or oral glucocorticoids >20 mg/day.

Objectives: Assess the influence of DMARDs and/or glucocorticoids at baseline on the efficacy and safety of nintedanib in patients with progressive autoimmune disease-related ILDs.

Methods: In patients with progressive autoimmune disease-related ILDs in the INBUILD trial, the rate of decline in FVC (mL/year) and adverse events (AEs) over 52 weeks of treatment (or until 28 days after last trial drug intake for patients who discontinued drug before week 52) were assessed in subgroups by use of DMARDs and/or glucocorticoids (any dose) at baseline (yes/no).

Results: 170 patients in the INBUILD trial (82 nintedanib, 88 placebo) had autoimmune disease-related ILDs (89 RA-ILD, 39 SSC-ILD, 19 MCTD-ILD, 23 other). The baseline characteristics of patients taking (n=131) and not taking (n=39) DMARDs and/or glucocorticoids are shown in the Table. All but 1 patient taking glucocorticoids at baseline was taking <20 mg/day.

Conclusion: In the INBUILD trial, the rate of FVC decline was numerically greater in placebo-treated patients who were taking DMARDs and/or glucocorticoids at baseline than in those who were not. The rate of FVC decline was slower in patients treated with nintedanib than placebo both in patients who were and were not taking DMARDs and/or glucocorticoids at baseline. Nintedanib had an acceptable safety profile both in patients who were and were not using DMARDs and/or glucocorticoids at baseline.

References:


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Objectives: Assess the influence of DMARDs and/or glucocorticoids at baseline on the efficacy and safety of nintedanib in patients with progressive autoimmune disease-related ILDs.

Methods: In patients with progressive autoimmune disease-related ILDs in the INBUILD trial, the rate of decline in FVC (mL/year) and adverse events (AEs) over 52 weeks of treatment (or until 28 days after last trial drug intake for patients who discontinued drug before week 52) were assessed in subgroups by use of DMARDs and/or glucocorticoids (any dose) at baseline (yes/no).

Results: 170 patients in the INBUILD trial (82 nintedanib, 88 placebo) had autoimmune disease-related ILDs (89 RA-ILD, 39 SSC-ILD, 19 MCTD-ILD, 23 other). The baseline characteristics of patients taking (n=131) and not taking (n=39) DMARDs and/or glucocorticoids are shown in the Table. All but 1 patient taking glucocorticoids at baseline was taking <20 mg/day.

Conclusion: In the INBUILD trial, the rate of FVC decline was numerically greater in placebo-treated patients who were taking DMARDs and/or glucocorticoids at baseline than in those who were not. The rate of FVC decline was slower in patients treated with nintedanib than placebo both in patients who were and were not taking DMARDs and/or glucocorticoids at baseline. Nintedanib had an acceptable safety profile both in patients who were and were not using DMARDs and/or glucocorticoids at baseline.
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Most common biologic DMARDs, non-biologic DMARDs and glucocorticoids were abatacept

Glucocorticoids, % 87.8 –
Non-biologic DMARDs, % 46.6 –
Biologic DMARDs, % 15.3 –

ILD diagnosis, %

RA-ILD 60.3 25.6
SSc-ILD 15.3 48.7
MCTD-ILD 10.7 12.8
Other 13.7 12.8

Biologic DMARDs, % 15.3 –
Non-biologic DMARDs, % 46.6 –
Glucocorticoids, % 87.8 –

Most common biologic DMARDs, non-biologic DMARDs and glucocorticoids were abatacept (4.6%), hydroxychloroquine/hydroxychloroquine sulphate (19.8%) and prednisone (37.4%), respectively.

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**THU0190 METHOTREXATE THERAPY IS NOT ASSOCIATED WITH AN INCREASED RISK OF LIVER FIBROSIS ASSESSED BY THE FIBROSIS-4 INDEX**

J. Avouac 1, R. Degrave 1, J. Vergneault 1, Y. Allano 1, 1 AP-HC CUP Cochin Hospital, Rheumatology, Paris, France

Background: Methotrexate (MTX) holds a unique place in the management of rheumatoid arthritis (RA) given its favorable balance between efficacy and safety. However, conflicting data still suggest a potential risk of MTX-induced long-term liver fibrosis. The fibrosis-4 (Fib-4) index was originally proposed as a simple and non-invasive marker of liver fibrosis in HIV/HCV coinfection. In patients with RA, FIB-4 values have been correlated to the amount of histologic liver lesions, suggesting that this index may be a valuable marker to diagnose liver disease in RA patients (1).

Objectives: To estimate the amount of scarring in the liver with the Fib-4 index in RA patients on maintenance therapy with MTX.

Methods: We performed a cross-sectional study including successive RA patients hospitalized in the Rheumatology department of Cochin Hospital for a 12-month period. Data on liver function, disease activity, hepatotoxic and cardiovascular risk factors were systematically collected. The Fib-4 index was calculated according the following formula: (age(years) x AST(UL)/platelet (PLT) (109/L) x ALT(U/L)). Using a lower cutoff value of 1.45, a Fib-4 score >1.45 had a negative predictive value of 90% for advanced fibrosis in the patient cohort in which this formula was first validated. In contrast, a Fib-4 >3.25 had a 97% specificity and a positive predictive value of 65% for advanced fibrosis (2).

Results: We included 170 patients with established RA: 141 (83%) were women, the mean age was 59±12 years and the mean disease duration was 15±11 years. Positive rheumatoid factors and anti-CCP antibodies were detected in 134 patients (79%), 102 patients (60%) were treated with methotrexate, with a mean dose of 10.0+/−8.4mg/week, a mean treatment duration of 9.5+/−10.3 years and a cumulative dose of 5.3+/−5.1g. 23 patients (13.5%) received conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) other than MTX, 112 (66%) corticosteroids (99 with a dose <10 mg/day) and 85 targeted biologic DMARDs (bDMARDs) (50%). The mean Fib-4 value was 1.24+/−0.57, with 120 patients (71%) with value <1.45, 49 (29%) with values ranging from 1.45 to 3.25 and a single patient with Fib-4 >3.25. The Fib-4 was low and not significantly different between patients receiving MTX, patients previously treated with MTX and patients never treated with MTX (median 1.1, 1.25 and 1.16, respectively, p=0.709). This result was not modified after adjustment on treatments with other csDMARDs, corticosteroids, and bDMARDs. No correlation was observed between Fib-4 values and the cumulative dose of MTX (r=0.09, p=0.271). The Fib-4 index was low and similar between patients receiving cumulative MTX doses <5g, between 5 and 10g and 10g (Figure 1). The cumulative dose of MTX was not significantly higher in patients with a Fib-4 index >1.45 (median cumulative MTX dose 5.5g vs. 3.5g, p=0.302). No association was detected between the Fib-4 index and parameters of disease activity (DAS28, ESR and CRP levels), the body mass index, traditional cardiovascular risk factors and metabolic syndrome.

References:

**Figure 1. Fibrosis-4 index according to the cumulative dose of methotrexate in patients with rheumatoid arthritis**