

## Press Release

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### Medac at EULAR 2019

## Get the most out of MTX therapy

### **Medac EULAR Symposium in Madrid with new data on how to improve therapy with the gold standard methotrexate<sup>1</sup>**

*Madrid / Wedel (14. June 2019).* Even in the era of biologics and new therapies, there is no doubt that methotrexate (MTX) remains the preferred initial antirheumatic drug and is considered the gold standard for the treatment of rheumatoid arthritis (RA). Doctor DARIO CAMELLINO, Italy, stressed that this is why methotrexate has kept its key position in current guidelines including the most recent ones from EULAR and ACR<sup>2,3,4</sup>. These strongly recommend DMARD monotherapy over combination therapy and state that MTX is the preferred initial DMARD. The value of MTX in combination therapies is well established. The reason why methotrexate is the gold standard is its reliability with respect to its efficacy and safety profile. Despite the significance and awareness of this, there has been criticism that methotrexate's potential is not being fully exploited – either in terms of frequency of use, doses or dosage form.<sup>5,6,7</sup> CAMELLINO outlined the proven advantages of the subcutaneous

<sup>1</sup> Medac satellite symposium “MTX remains gold standard in the era of biologics and new therapies”, European Congress of Rheumatology (EULAR), Madrid, 13<sup>th</sup> June 2019.

<sup>2</sup> Smolen JS et al., EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. *Ann Rheum Dis.* 2017;76:960-977.

<sup>3</sup> Combe B et al., 2016 update of the EULAR recommendations for the management of early arthritis. *Ann Rheum Dis.* 2017;76:948-959.

<sup>4</sup> Singh JA et al., 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Care Res.* 2016;68:1-25.

<sup>5</sup> Rohr MK et al., Underuse of Methotrexate in the Treatment of Rheumatoid Arthritis: A National Analysis of Prescribing Practices in the US. *Arthritis Care Res.* 2017;69:794-800.

<sup>6</sup> Moura CA & Moura CG, Methotrexate still works: comment on the articles by Rohr et al and Hirata et al. *Arthritis Care Res.* 2018;70:1118.

<sup>7</sup> Bello AE et al., Recommendations for optimizing methotrexate treatment for patients with rheumatoid arthritis. *Open Access Rheumatol.* 2017;9:67-79.

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route of administration. This shows a better bioavailability<sup>8,9,10</sup> due to the MTX polyglutamation<sup>11</sup> as well as a better efficacy and tolerability<sup>12,13</sup> caused by bypassing of the gastrointestinal tract. The latest improvement with the higher drug concentration of 50 mg/ml, and thus a smaller injection volume,<sup>14</sup> as well as the simplified handling with Medac's methotrexate autoinjectors (Metoject<sup>®</sup>, Metex<sup>®</sup> and Rasuvo<sup>™</sup>) are proven advantages for better patient adherence.<sup>15,16,17</sup>

Doctor CARTER THORNE, Canada, confirmed these aspects of subcutaneous MTX based on best practice findings in the real world setting. The observational Canadian Early Arthritis Cohort (CATCH) underlines the advantages of an optimised dosing regimen of methotrexate and the subcutaneous route of administration. Evidence showed that sc MTX in an optimised dosing schedule is associated with a better early outcome and lower rate of treatment failure

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- <sup>8</sup> O'Connor A et al., The rapid kinetics of optimal treatment with subcutaneous methotrexate in early inflammatory arthritis: an observational study. *BMC Musculoskelet Disord.* 2016;17:364.
- <sup>9</sup> Schiff MH et al., Head-to-head, randomised, crossover study of oral versus subcutaneous methotrexate in patients with rheumatoid arthritis: drug-exposure limitations of oral methotrexate at doses  $\geq 15$  mg may be overcome with subcutaneous administration. *Ann Rheum Dis.* 2014;73:1549-1551.
- <sup>10</sup> Pichlmeier U, Heuer KU, Subcutaneous administration of methotrexate with a prefilled autoinjector pen results in a higher relative bioavailability compared with oral administration of methotrexate. *Clin Exp Rheumatol.* 2014;32:563-571.
- <sup>11</sup> Kremer JM, Still Trying to Understand Methotrexate. *J Rheumatol.* 2014;41:2099-2101.
- <sup>12</sup> Rutkowska-Sak L et al., Oral vs. subcutaneous low-dose methotrexate treatment in reducing gastrointestinal side effects *Reumatologia* 2009;47:207-211.
- <sup>13</sup> Borman P et al., Letter to the Editor. Subcutaneous (SC) Methotrexate (MTX) is Better and Well-Tolerable than Oral MTX in Rheumatoid Arthritis Patients, Switched from Oral to SC Administration Due to Gastrointestinal Side Effects. *Open Rheumatol J.* 2014;8:18-19.
- <sup>14</sup> Mueller-Ladner U et al., Tolerability and patient/physician satisfaction with subcutaneously administered methotrexate provided in two formulations of different drug concentrations in patients with rheumatoid arthritis. *Open Rheumatol J.* 2010;4:15-22.
- <sup>15</sup> Demary W et al., Subcutaneously administered methotrexate for rheumatoid arthritis, by prefilled syringes versus prefilled pens: patient preference and comparison of the self-injection experience. *Patient Prefer Adherence.* 2014;8:1061-1071.
- <sup>16</sup> Pachon JA et al., Assessing usability, label comprehension, pen robustness and pharmacokinetics of a self-administered prefilled autoinjector pen of methotrexate in patients with rheumatoid arthritis. *SAGE Open Med.* 2014;2:2050312114564241.
- <sup>17</sup> Freundlich B et al., Nearly pain-free self-administration of subcutaneous methotrexate with an autoinjector: results of a phase 2 clinical trial in patients with rheumatoid arthritis who have functional limitations. *J Clin Rheumatol.* 2014;20:256-260.

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in early rheumatoid arthritis - especially in initial therapy<sup>18,19,20</sup>. The absorption of methotrexate is improved if given subcutaneously, particularly at doses > 15 mg/week. New data show that “Patients on SC MTX monotherapy changed less (45% vs 79%) and remained longer [...] on therapy than those on oral MTX”.<sup>20</sup>

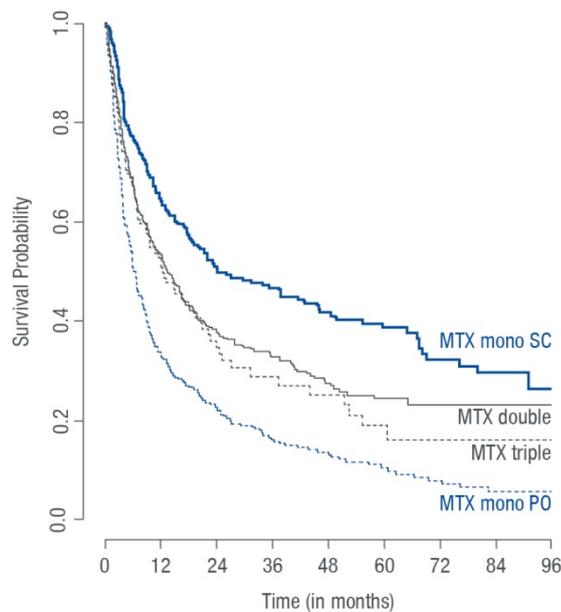


Figure: Kaplan Meier survival curves for treatment duration per treatment group of initial MTX-based treatment strategy after Moura CS et al. *Arthritis Care Res* 2019<sup>20</sup>, © medac

With regard to the dosing regimen, THORNE concluded that “optimal methotrexate dosing of 25 mg given subcutaneously weekly from initiation of therapy, allows better outcomes to be achieved.”

<sup>18</sup> Hazlewood GS et al., The comparative effectiveness of oral versus subcutaneous methotrexate for the treatment of early rheumatoid arthritis. *Ann Rheum Dis* 2016;75:1003-1008.

<sup>19</sup> O'Connor A et al., The rapid kinetics of optimal treatment with subcutaneous methotrexate in early inflammatory arthritis: an observational study. *BMC Musculoskelet Disord*. 2016;17:364.

<sup>20</sup> Moura CS et al., Treatment strategies in early rheumatoid arthritis methotrexate management: Results from a prospective cohort. *Arthritis Care Res*. 2019 May 21 [Epub ahead of print]. doi: 10.1002/acr.23927.

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The improved efficacy of methotrexate according to the dose and route of administration also applies to the treatment of children with juvenile idiopathic arthritis (JIA), Professor PAVLA DOLEŽALOVÁ, Czech Republic, added. Even in the era of biologics, MTX remains the first choice for JIA as well as for rare diseases such as juvenile dermatomyositis and paediatric uveitis. The position of methotrexate as the first-line treatment is down to its therapeutic efficacy and favourable toxicity profile. DOLEŽALOVÁ stressed the importance of optimised MTX therapy focusing on the treat-to-target approach and the therapeutic target of remission. In order to achieve the best outcome and sustained remission, the early start of therapy with a more intensive therapeutic regimen and subcutaneous methotrexate around 15 mg/m<sup>2</sup>/week is crucial.<sup>21</sup>

Addressing new therapeutic strategies, THORNE drew attention to the measurable aspects of effective rheumatoid arthritis therapy. “Latest CATCH data support the use of subcutaneous MTX monotherapy or MTX combination as initial MTX-based therapy in early RA patients and the use of additional therapy (either biologic or csDMARDs) in RA patients who failed initial MTX-based therapy”.<sup>20</sup>

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<sup>21</sup> Fráňová J et al., Methotrexate efficacy, but not its intolerance, is associated with the dose and route of administration. *Pediatric Rheumatology*. 2016;14:36

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