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Medac at DGRh 2017

Enhancing the potential of methotrexate

Optimise rheumatism treatment with **Metobject[®]** and ensure long-term success of therapy

Stuttgart / Wedel (September 11, 2017). There is room for improvement in drug treatment of rheumatoid arthritis (RA) with the gold standard methotrexate (MTX). Current analyses of the CAPEA cohort suggest that German rheumatology exploits the potential of methotrexate as initial treatment¹ and follows the treatment guidelines closely^{2,3}: “After 3 months, 82 % of patients with a diagnosis of RA were given first line treatment with methotrexate.⁴ [...] In 78 % of the patients treated with methotrexate, the starting dose was 15 mg weekly”¹. Long-term data from the core documentation also confirm at 61 % the great importance of MTX in the treatment of RA.^{5,6} Current data from a German health insurance, however, paint a dramatically different picture nationwide. Given that csDMARDS account for 35 % of drug

¹ Albrecht K et al. Klinische Remission bei rheumatoider Arthritis. Daten aus der Früharthritids-Kohorten Studie CAPEA. *Z Rheumatol.* 2016;75:90-6.

² Krüger K et al. S1-Leitlinie der DGRh zur sequenziellen medikamentösen Therapie der rheumatoiden Arthritis 2012. Adaptierte EULAR-Empfehlungen und aktualisierter Therapiealgorithmus. *Z Rheumatol* 2012;71:592-603.

³ 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.

⁴ Please see as well: Schneider M. Neue Optionen für die Praxis. Update S1/S2-Leitlinie Rheumatoide Arthritis? *Z Rheumatol* 2017;76:125-32.

⁵ Deutsches Rheuma-Forschungszentrum, Daten der Kerndokumentation 2015, Berlin o.J., slide 14, URL: <http://www.drfg.de/versorgungsforschung> (as at 06.09.2017).

⁶ Albrecht K et al. Versorgung der rheumatoiden Arthritis 2014. Aktuelle Daten aus der Kerndokumentation. *Z Rheumatol.* 2017;76:50-7.

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treatment, Germany is some way from appropriate therapeutic treatment of patients with rheumatoid arthritis.⁷

The symposium on methotrexate sponsored by Medac at the DGRh congress in Stuttgart addressed this issue. As well as a new research project on the actual medical treatment situation, various options for improving the first line therapy with MTX were revealed.

Optimised initial treatment – is the potential of methotrexate exploited to the full?⁸

With reference to the current guidelines, Professor FRANK BUTTGEREIT from Berlin and Professor TORSTEN WITTE from Hannover emphasised that higher dosages and administration under the skin can increase the efficacy and persistence of the anchor drug methotrexate.

Thus higher-dose and subcutaneous administration of MTX in the initial treatment of early RA are associated with improved therapy response and fewer therapy failures.^{9,10} Particularly at dosages ≥ 15 mg/week, pre-filled syringes or pre-filled auto-injectors improve bioavailability.^{10,11,12} Professor DIAMANT THAÇI from Lübeck also refers to another aspect of the subcutaneous administration recently discovered in the field of dermatology – the

⁷ Albrecht K et al. Ambulante Versorgung und Krankheitslast der rheumatoiden Arthritis. Eine Analyse von Abrechnungsdaten und einer Versichertenbefragung. Z Rheumatol. 2017 Mar 21. [Epub ahead of print].

⁸ Medac satellite symposium “Optimierte Basistherapie – Methotrexat-Potenzial voll ausgeschöpft?“ anlässlich des 45. Kongresses der Deutschen Gesellschaft für Rheumatologie (DGRh), Stuttgart, 7. September 2017.

⁹ Hazlewood GS et al. The comparative effectiveness of oral versus subcutaneous methotrexate for the treatment of early rheumatoid arthritis. Ann Rheum Dis 2016;75:1003-8.

¹⁰ 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.

¹¹ 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 ≥ 15 mg may be overcome with subcutaneous administration. Ann Rheum Dis. 2014;73:1549-51.

¹² 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;32:563-71.

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immunomodulatory potential of methotrexate. The cellular mechanism of action was investigated in a sub-study using skin biopsies. The results show that MTX reduces the cutaneous expression of interleukin-17A mRNA by approx. 10 % and that of interferon- γ mRNA by approx. 25 %.¹³

General risk factors are another important aspect for the treatment success, underlined Professor CHRISTOPH FIEHN from Baden-Baden. Lifestyle factors such as smoking, obesity and poor dental health not only worsen the course of RA but also influence the therapy response and should therefore be discussed with patients.

Subcutaneous administration of methotrexate with the pre-filled pen

Moreover, use and treatment adherence are encouraged by easier self-administration provided by the auto-injectors Metoject[®], Metex[®] and Rasuvo[™].^{14,15,16} Documentation of current practice by Medac among German rheumatologists and rheumatoid arthritis patients confirms the high estimation that is known from studies to date. “97 % percent of all doctors and 89 %

¹³ Warren R B et al. An intensified dosing schedule of subcutaneous methotrexate in patients with moderate to severe plaque-type psoriasis (METOP): a 52 week, multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet*. 2017;389:528-37.

¹⁴ 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;8:1061-71.

¹⁵ 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.

¹⁶ 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;20:256-60.

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of patients with previous experience with pre-filled syringes rate the metex[®] PEN¹⁷ as “very beneficial” or “beneficial” compared to a pre-filled syringe.”¹⁸

Thereby right from the start, the methotrexate auto-injectors from Medac make easy and comfortable subcutaneous self-administration of MTX possible in daily clinical practice, which is rated by both doctor and patient as beneficial compared to the pre-filled syringe.

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Press Contact

Media Spokesperson
Volker Bahr
Tel. +49 (0)4103 – 8006 9111
Fax +49 (0)4103 – 8006 8934
press@medac.de

medac Gesellschaft für klinische Spezialpräparate mbH
Theaterstraße 6
22880 Wedel
Germany
www.medac.de

medac Gesellschaft für klinische Spezialpräparate mbH

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You can find further information on the company and its products on the internet under www.medac.de.

¹⁷ Equivalent to Metoject[®], Metex[®] and Rasuvo[™]

¹⁸ Hattesoehl M. et al. Handhabung eines Fertigpen zur subkutanen Selbstapplikation von Methotrexat. DGRh Abstract 2017. URL: <http://www.egms.de/static/de/meetings/dgrh2017/17dgrh244.shtml> (as at: 06.09.2017).