ACTEMRA®
tocilizumab

Roche

FIRST CHOICE

New EULAR Guidelines Recommend ACTEMRA® as the First Biological Choice[1]

ACTEMRA® **now in SC**[2]
Proven comparable efficacy and safety to IV formulation[3]

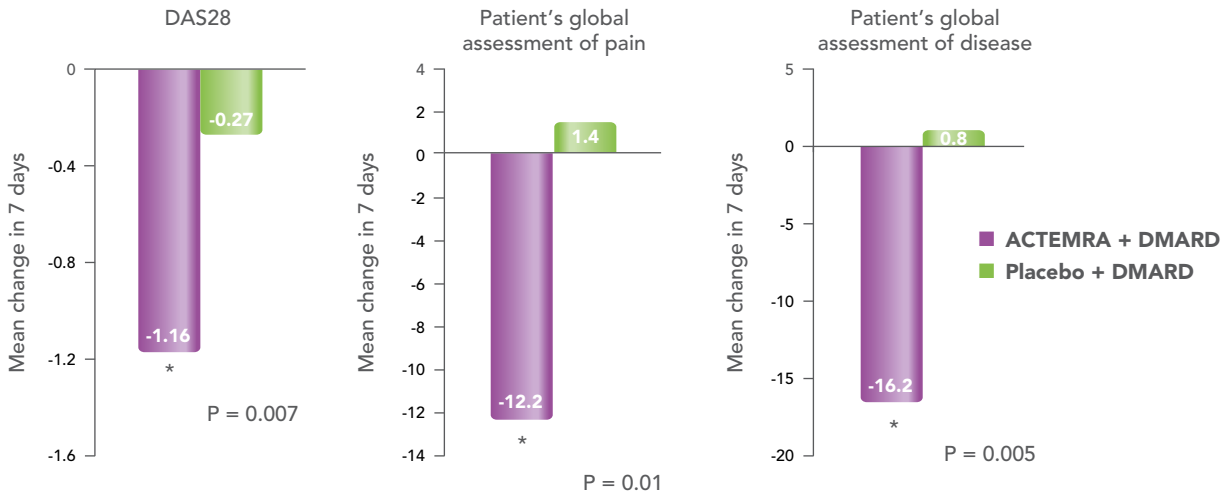
ACTEMRA® first choice: Now recommended by EULAR as the first biological treatment choice for RA

In the EULAR 2013 guidelines:[1]

- ACTEMRA® is recommended as the first biological treatment choice for rheumatoid arthritis (RA) after failure of conventional disease-modifying antirheumatic drugs (DMARD)
- ACTEMRA®'s unique efficacy as monotherapy is highlighted
- ACTEMRA®'s long-term safety profile, similar to that of TNF's, is highlighted

ACTEMRA® provides rapid improvement in clinical outcomes after just 1 week[4]

Clinical improvements with ACTEMRA® after 7 days' treatment



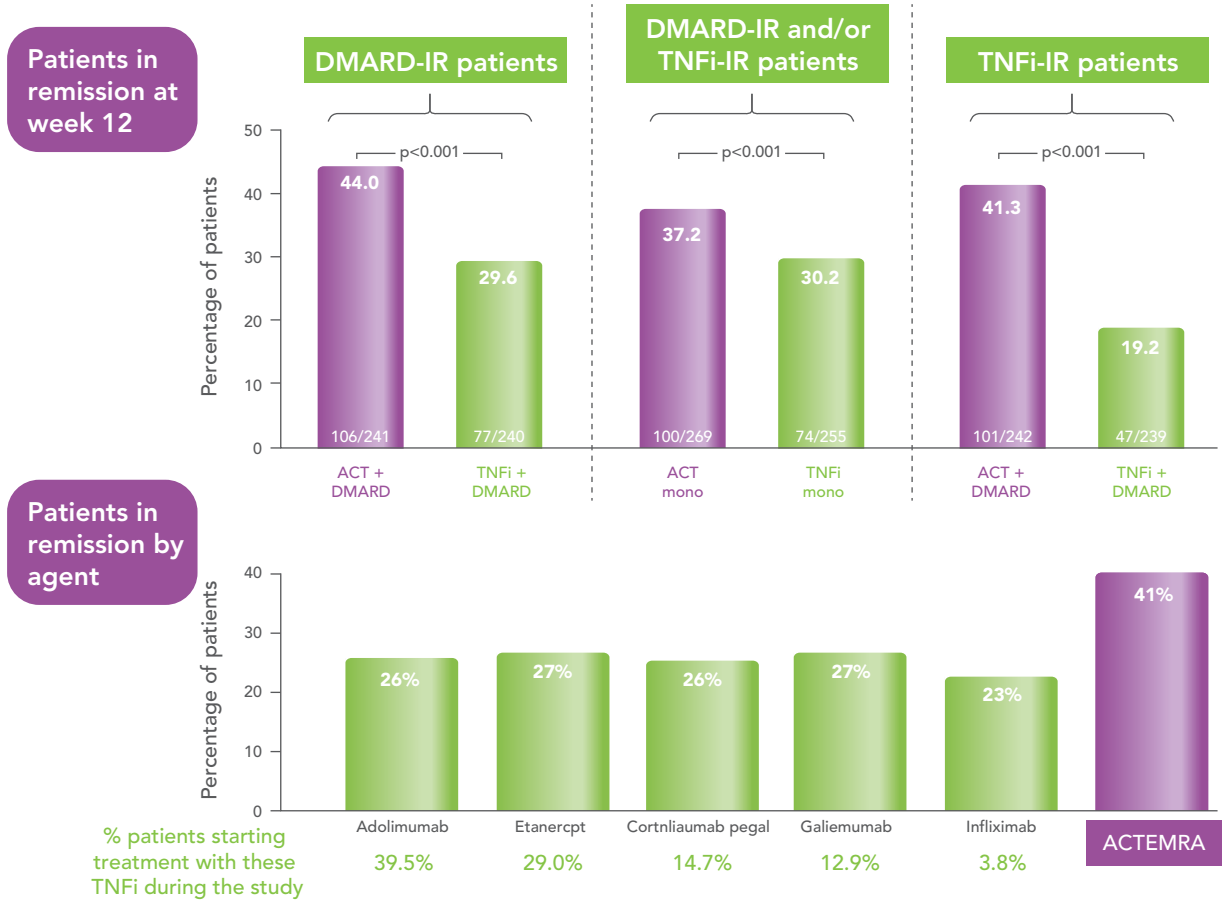
Yazici Y, et al. *Ann Rheum Dis* 2012.[4] Data are from ROSE clinical trial early disease activity control substudy (N = 62). DAS, disease activity score

With ACTEMRA®, symptoms improve RAPIDLY – in as little as one week

ACTEMRA® first choice: Real-world clinical experience with ACTEMRA® & TNFi in Germany[5]

Patients achieved DAS28 remission ranging from 37%-44% with ACTEMRA® and 19%-30% with TNFi, as combination or monotherapy[5]

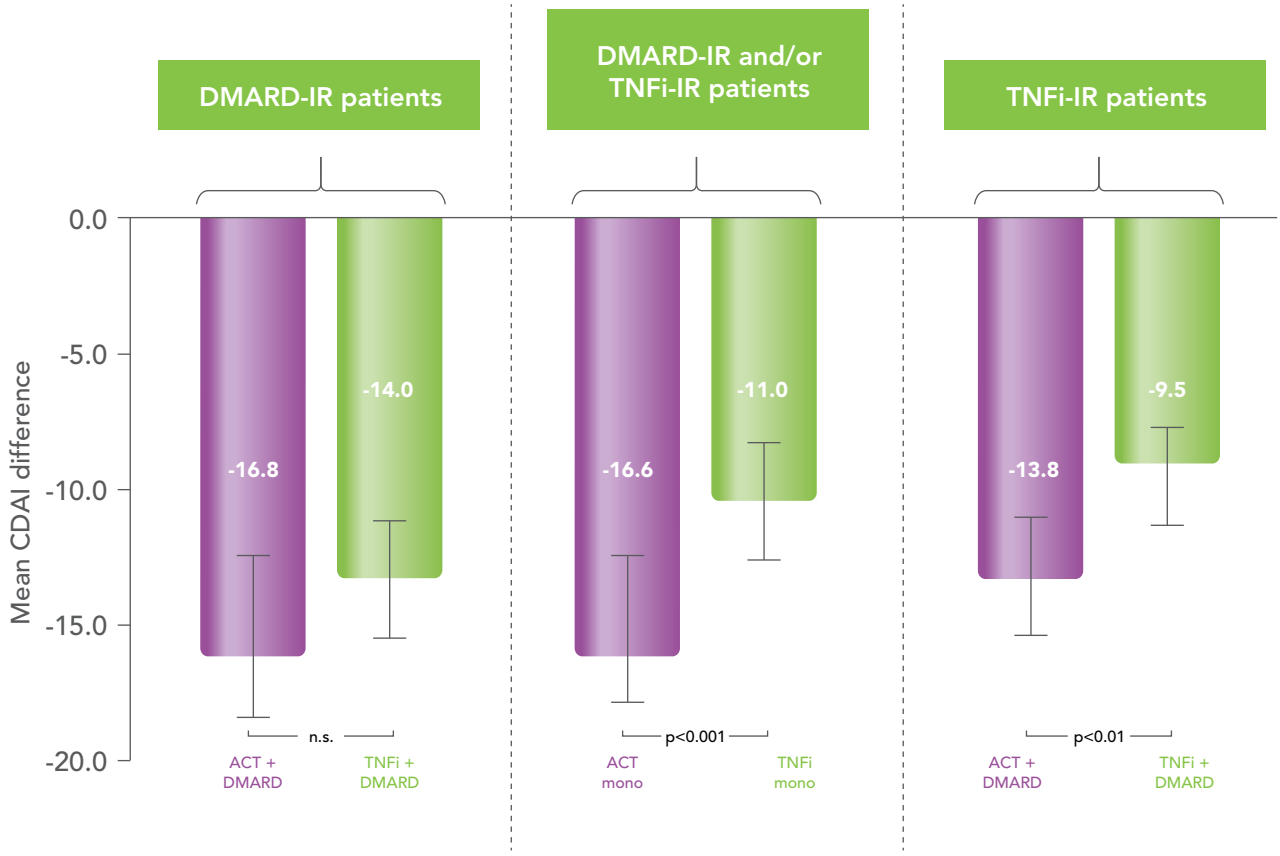
DAS28 remission at Week 12 with ACTEMRA® or TNFi



Adapted from Backhaus M, et al. *Clin Rheumatol* 2015.[5] In a retrospective study, 1,603 patients from 70 centres who had previous insufficient treatment responses were divided into six study treatment groups: 1. DMARD-IR patients starting treatment with ACTEMRA® + DMARD; 2. DMARD-IR patients starting treatment with a TNFi + DMARD; 3. DMARD-IR and/or TNFi-IR patients starting treatment with ACTEMRA® monotherapy; 4. DMARD-IR and/or TNFi-IR patients starting treatment with TNFi monotherapy; 5. TNFi-IR patients starting treatment with ACTEMRA® + DMARD (TNFi-IR ACT); 6. TNFi-IR patients starting treatment with TNFi + DMARD. Data are the percentage of patients in remission at week 12 according to the disease activity score (DAS) 28 erythrocyte sedimentation rate (ESR). ACT, ACTEMRA®; DMARD, disease modifying antirheumatic drugs; IR, insufficient response; mono, monotherapy; TNFi, tumour necrosis factor inhibitor

ACTEMRA® first choice: Real-world clinical experience with ACTEMRA® & TNFi in Germany[5]

Disease activity improvement at Week 12 with ACTEMRA® or TNFi

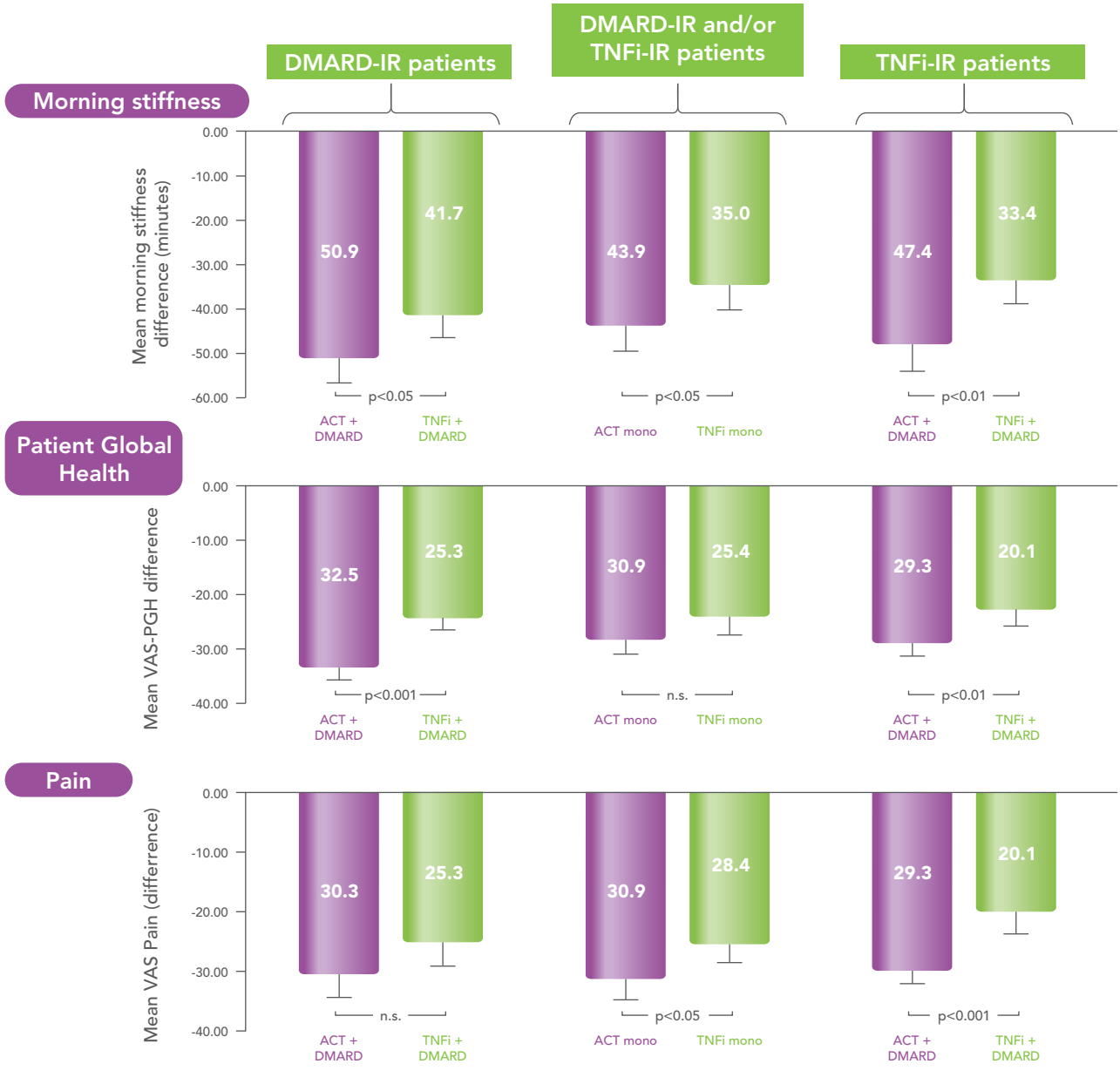


Adapted from Backhaus M, et al. *Clin Rheumatol* 2015.[5] A total of 1,603 patients who had previous insufficient treatment responses were divided into six study treatment groups as described on page 1. Data are mean change in CDAI (95 % CI) at week 12 versus baseline by treatment group. ACT, ACTEMRA®; CDAI, clinical disease activity score; DMARD, disease modifying antirheumatic drugs; IR, insufficient response; mono, monotherapy; TNFi, tumour necrosis factor inhibitor

ACTEMRA® first choice: Patients themselves report clinical benefits with ACTEMRA®

Irrespective of prior unsuccessful treatment, patients reported improvements with ACTEMRA® monotherapy and combination treatment[5]

Patient-reported outcomes with ACTEMRA® or TNFi at Week 12

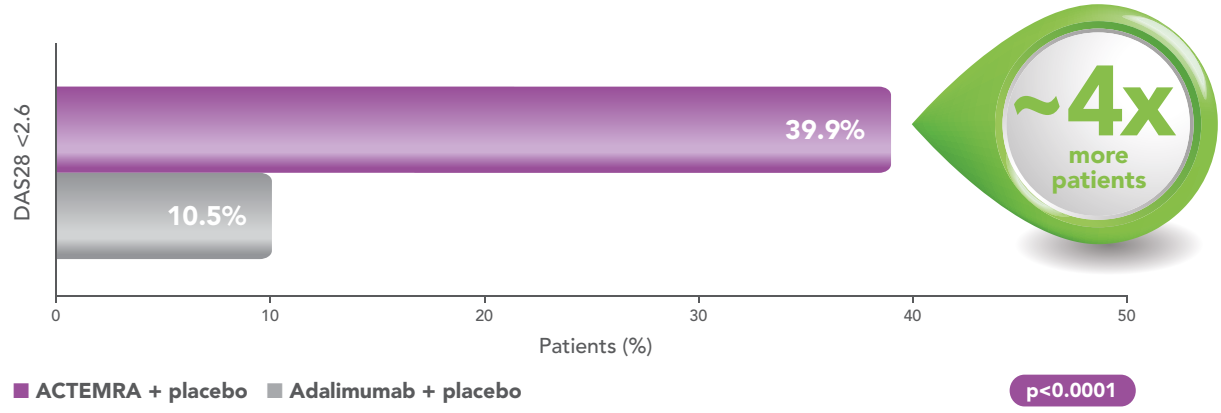


Adapted from Backhaus M, et al. *Clin Rheumatol* 2015.[3] A total of 1,603 patients who had previous insufficient treatment responses were divided into six study treatment groups as described on page 1. Data are patient-reported outcomes at Week 12 for morning stiffness, VAS patient global health (100 units) and VAS pain (100 units). ACT, ACTEMRA®; DMARD, disease modifying antirheumatic drugs, IR, insufficient response; mono, monotherapy; n.s., not significant; TNFi, tumour necrosis factor inhibitor; VAS, visual analogue scale

ACTEMRA® first choice: ACTEMRA® is the only biologic proven superior to a TNFi (adalimumab)

ADACTA study: Four times more patients achieved remission with ACTEMRA® than with adalimumab[6]

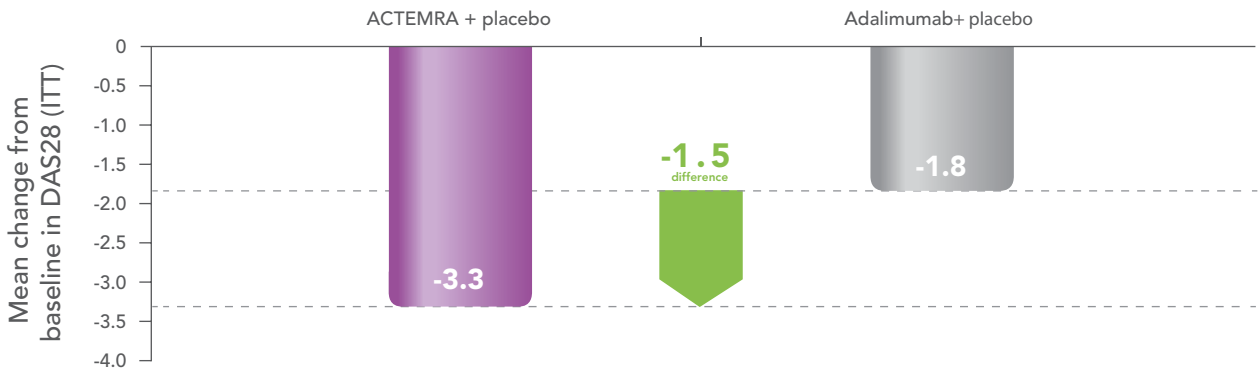
DAS 28<2.6 remission at Week 24



Adapted from Gabay C, et al. *Lancet* 2013.[6] Data are from ADACTA (24-week, double-blind, phase IV, randomized, controlled study), the first head-to-head superiority trial in biologic monotherapy, involving 325 methotrexate-intolerant or -inappropriate patients. DAS, disease activity score

ACTEMRA® led to a significantly greater reduction in mean DAS28 at Week 24 versus adalimumab (p<0.0001)[6]

Mean change from baseline in DAS 28 at Week 24

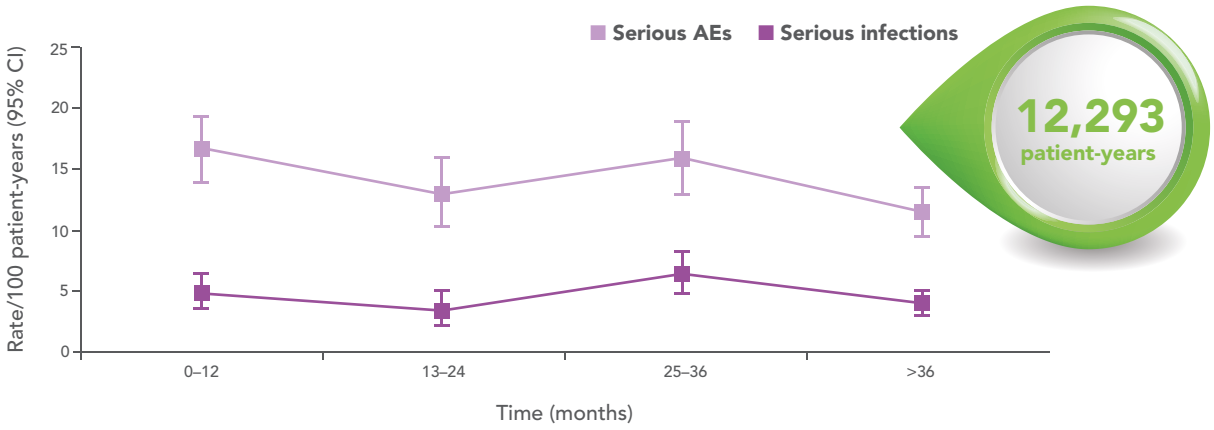


Adapted from Gabay C, et al. *Lancet* 2013.[6] Data are from ADACTA (24-week, double-blind, phase IV, randomized, controlled study), the first head-to-head superiority trial in biologic monotherapy, involving 325 methotrexate-intolerant or -inappropriate patients. DAS, disease activity score

ACTEMRA® first choice: ACTEMRA® safety

ACTEMRA® has a well-established long-term safety profile[7]

Serious AEs and serious infections per 100 patient-years with ACTEMRA® over 12-month consecutive periods in 4,009 patients (mean treatment duration 3.1 years)



Adapted from Genovese M et al. *J Rheumatol* 2013.[7] Data from clinical trials (OPTION, TOWARD, RADIATE, AMBITION and LITHE in combination therapy and monotherapy) were pooled. A total of 4,009 patients received ACTEMRA® with a mean duration of 3.1 years and a total observation time of 12,293 patient-years.
AE, adverse event

No tuberculosis was observed in three non-TB-screened studies in Japan[8-10]

Study	No. of patients	Patient type	Outcome
SATORI[8]	N = 125	MTX-IR	TB not observed
SAMURAI[6]	N = 306	DMARD-IR	TB not observed
STREAM[7]	N = 143	DMARD-IR	1. No systemic opportunistic infection or TB was observed 2. At least two patients with TB history were treated with ACTEMRA®. Neither had any recurrence nor exacerbation of TB, even without prophylactic use of anti-TB drugs

DMARD, disease modifying antirheumatic drugs; IR, insufficient response; MTX, methotrexate; TB, tuberculosis

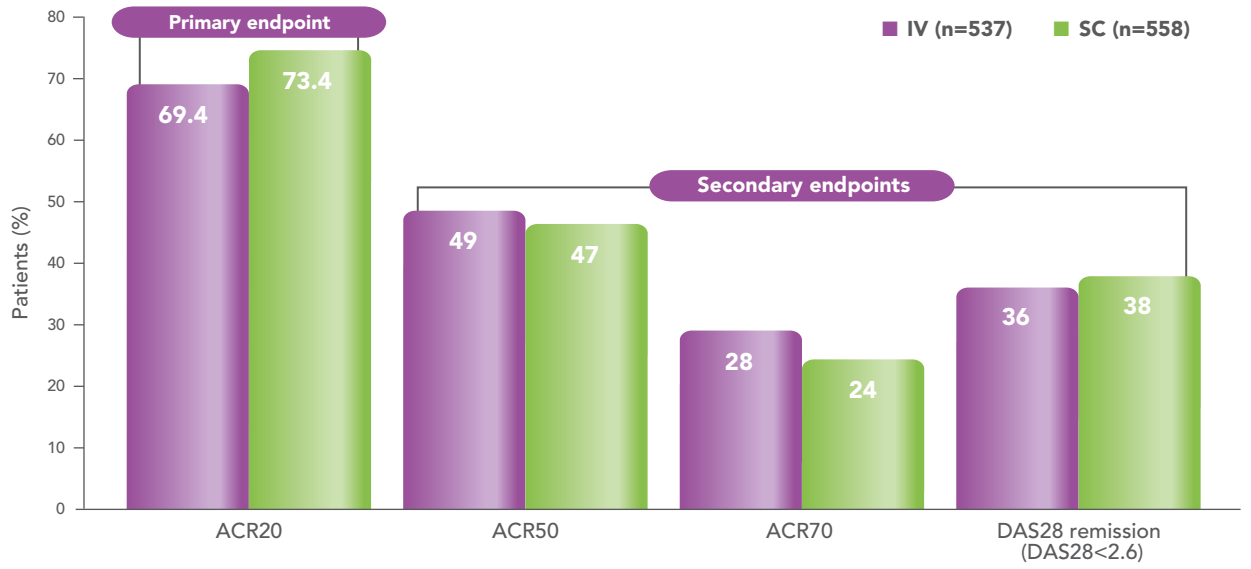
ACTEMRA® first choice: Now in SC

New ACTEMRA® SC has comparable efficacy and safety to the proven IV formulation[3]

In a phase III, double-blind trial involving 1,262 patients, ACTEMRA® SC demonstrated:[3]

- Comparable ACR responses
- Comparable DAS28 remission

SUMMACTA: Comparable endpoints at Week 24



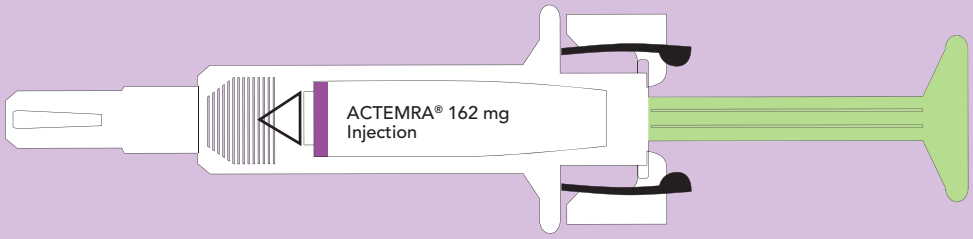
Adapted from Burmester GR, et al. *Ann Rheum Dis* 2014.[3] Data from SUMMACTA study in 1,262 patients treated with ACTEMRA® IV 8 mg/kg IV q4w + DMARD or ACTEMRA® SC 162 mg qw + DMARD for 24 weeks. Primary endpoint weighted difference: -4.0% (95% CI, -9.2 to 1.2). ACR, American College of Rheumatology; DAS, disease activity score, IV, intravenous; SC, subcutaneous

Safety profiles for SC and IV groups were comparable, consistent with previous studies, and no new clinically meaningful safety signals were identified[3]

Injection-site reactions occurred more frequently in the SC group than the IV group[3]

ACTEMRA® first choice: ACTEMRA® SC is a convenient alternative option for patients[2]

Simple	Convenient
One fixed dose for all patients **162 mg**	Once weekly, at home* **q1w**



*The first dose should be administered in the clinic under the supervision of a healthcare practitioner for both new ACTEMRA® patients and those switching from IV

ACTEMRA® first choice: ACTEMRA® is recommended as the first biological choice in recently published EULAR guidelines[1]

- ACTEMRA®: Blockade of IL-6R affects a range of pathological processes, even as monotherapy[11]
- ACTEMRA® delivered significantly improved clinical outcomes in a real-world setting in Germany[5]
- ACTEMRA® is the only biologic proven to be superior to a TNF inhibitor (adalimumab) as RA biologic monotherapy[6]
- ACTEMRA® now in SC:[2] Proven comparable efficacy and safety to the IV formulation[3]

The Joy of Living

ACTEMRA® SC is now available:

Now more of your patients can benefit from ACTEMRA®

Abbreviated prescribing information

ACTEMRA® (tocilizumab) 162mg solution for injection in pre-filled syringe
Indications: Treatment of moderate to severe active rheumatoid arthritis in adult patients. ACTEMRA® can be given in combination with methotrexate (MTX), or can be given as monotherapy in case of intolerance to MTX or if continued treatment with MTX is inappropriate. ACTEMRA® has been shown to reduce the rate of progression of joint damage as measured by X-ray and to improve physical function when given in combination with methotrexate.

Dosage & administration: The recommended posology is subcutaneous 162mg once every week. No dose adjustment is required in elderly patients, or in patients with mild renal impairment. ACTEMRA® has not been studied in patients with hepatic impairment and the safety and efficacy of subcutaneous formulation in children from birth to less than 18 years have not been established. Dose adjustments are recommended in the event of liver enzyme abnormalities, low absolute neutrophil count or low platelet count (see full Prescribing Information for details).

Contraindications: Hypersensitivity to tocilizumab or to any of the excipients.

Warnings & Precautions:
Infections: If serious infection develops, interrupt therapy until infection is controlled. Exercise caution in patients with a history of recurring infection or other underlying conditions which may predispose to infection. **Complications of Diverticulitis:** Use with caution in patients with a history of intestinal ulceration or diverticulitis. Patients with symptoms of complicated diverticulitis should be evaluated promptly. **Tuberculosis:** Screen for latent TB prior to starting therapy; treat latent TB with standard therapy before initiating ACTEMRA®. **Vaccination:** Live and live attenuated vaccines should not be given concurrently. Patients should be brought up to date with all immunizations in agreement with current immunization guidelines prior to initiating tocilizumab therapy. **Hypersensitivity reactions:** Stop infusion immediately and discontinue permanently if anaphylactic reaction or serious hypersensitivity reaction occurs. **Active hepatic disease/impairment:** Use with caution in patients with active hepatic disease or hepatic impairment. Viral reactivation: Viral reactivation has been reported. **Neurological disorders:** Physicians to be vigilant for indicative symptoms. **Haematological abnormalities:** Not recommended in patients with ANC < 0.5 x 109/l or platelet count < 50 x 103/ml. Use with caution in patients with low platelet count; monitor neutrophils and platelets according to Prescribing Information. If reduced, follow recommendations for dose modification. **Hepatic transaminase elevations:** Not recommended in patients with baseline ALT or AST > 5xULN; use with caution in patients with ALT or AST > 1.5xULN. Monitor ALT/AST levels according to Prescribing Information, if raised follow recommendations for dose modification. **Lipid parameters:** Lipid parameters should be assessed according to Prescribing Information, if elevated, patients should be managed according to local guidelines for hyperlipidaemia.

Drug Interactions: MTX, NSAIDs or corticosteroids had no effect on tocilizumab clearance. Co-administration with MTX had no significant effect on MTX exposure. Tocilizumab has not been studied in combination with other biological DMARDs. Patients taking medicines which are individually adjusted and metabolized via CYP450 3A4, 1A2 or 2C9 should be monitored when starting or stopping ACTEMRA®, as doses of these products may need to be adjusted.

Use in Pregnancy & Lactation: No adequate data from use in pregnant women. Animal study showed a higher number of spontaneous abortion/ embryo-foetal death at high dose. ACTEMRA® should not be used during pregnancy unless clearly necessary. A decision on whether to continue/discontinue breast-feeding or ACTEMRA® therapy should be made taking into account the relative benefits to mother and child.

Undesirable effects: RA - Common adverse reactions: Most commonly reported ADRs were URTI, nasopharyngitis, headache, hypertension and increased ALT. The most serious ADRs were serious infections, complications of diverticulitis, and hypersensitivity reactions. A double-blind, controlled, multicenter study was conducted. Injection site reaction: These injection site reactions were mild to moderate in severity. The majority was resolved without any treatment and none necessitated drug discontinuation. Immunogenicity: No correlation of antibody development to clinical response or adverse events was observed. Haematological abnormalities: a decrease in neutrophil count below 1 × 109/L occurred in 2.9% of patients and there was no clear relationship between decreases in neutrophils and the occurrence of serious infections. No patient had a decrease in platelet count to ≤50 × 103 / µl. Elevation in ALT or AST ≥3 x ULN occurred in 6.5% and 1.4% of patients. 19% of patients experienced sustained elevations in total cholesterol > 6.2 mmol/l, with 9% experiencing a sustained increase in LDL to≥ 4.1 mmol/l.

Date of preparation: June 2015
Full prescribing information should be viewed prior to prescribing

References

1. Smolen JS, et al. *Ann Rheum Dis* 2014;73:492-509.
2. ACTEMRA® (tocilizumab) Hong Kong Prescribing Information Jan 2015.
3. Burmester GR, et al. *Ann Rheum Dis* 2014;73:69-74.
4 Yazici Y, et al. *Ann Rheum Dis* 2012;71:198-205.
5. Backhaus M, et al. *Clin Rheumatol* 2015;34:673-681.
6. Gabay C, et al. *Lancet* 2013;381:1541-1550.
7. Genovese MC, et al. *J Rheumatol* 2013;40:768-780.
8. Nishimoto N, et al. *Ann Rheum Dis* 2007;66:1162-1167.
9. Nishimoto N, et al. *Ann Rheum Dis* 2009;68:1580-1584.
10. Nishimoto N, et al. *Mod Rheumatol* 2009;19:12-19.
11. Witte T. Z *Clin Rheumatol* 2015;34:629-634

Roche Hong Kong Ltd.
G.P.O. Box 11331 Hong Kong
Tel: (852) 2723 2832
Fax: (852) 2877 6557

ACTEMRA®
tocilizumab

HK-ROC-435