OPEN-LABEL EXTENSION DATA

When It's Time for a Change, Target IL-6R with KEVZARA

KEVZARA LONG-TERM TREATMENT FOLLOW-UP:

UP TO 7 YEARS OF SAFETY AND 5 YEARS OF EFFICACY DATA

KEVZARA®
(sarilumab) injection
200 mg | 150 mg

OVERVIEW OF OPEN-LABEL EXTENSION POPULATIONS

36 patients (1.2%) were treated for >360 weeks (7 years) and 212 patients (7.3%) were treated for >312 weeks (6 years).[1]

IL-6R=interleukin-6 receptor; CRP=C-reactive protein.

INDICATION

KEVZARA is indicated for treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to one or more disease-modifying antirheumatic drugs (DMARDs).

IMPORTANT SAFETY INFORMATION

WARNING: RISK OF SERIOUS INFECTIONS

Patients treated with KEVZARA are at increased risk for developing serious infections that may lead to hospitalization or death. Opportunistic infections have also been reported in patients receiving KEVZARA. Most patients who developed infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.

Avoid use of KEVZARA in patients with an active infection.

Reported infections include:

- **Active tuberculosis, which may present with pulmonary or extrapulmonary disease. Patients should be tested for latent tuberculosis before KEVZARA use and during therapy. Treatment for latent infection should be initiated prior to KEVZARA use.**
- **Invasive fungal infections, such as candidiasis, and pneumocystis. Patients with invasive fungal infections may present with disseminated, rather than localized, disease.**
- **Bacterial, viral and other infections due to opportunistic pathogens.**

Closely monitor patients for signs and symptoms of infection during treatment with KEVZARA. If a serious infection develops, interrupt KEVZARA until the infection is controlled.

Consider the risks and benefits of treatment with KEVZARA prior to initiating therapy in patients with chronic or recurrent infection.

Please see Important Safety Information throughout and click here to see full Prescribing Information, including **Boxed WARNING.**

WHEN IT'S TIME FOR A CHANGE, TARGET IL-6R WITH

KEVZARA®
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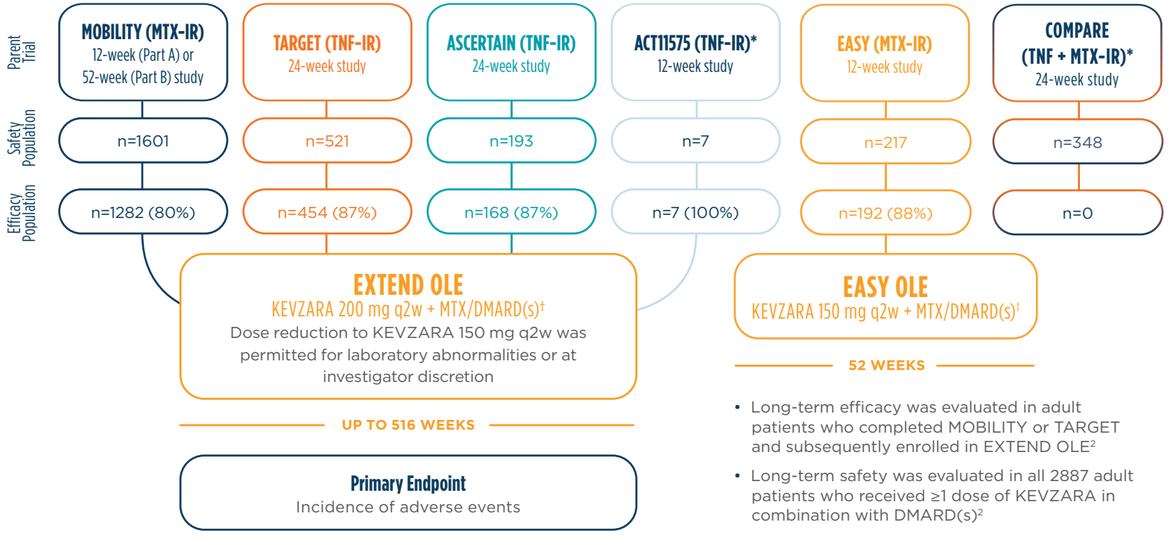
KEVZARA + MTX/DMARD(s) SAFETY AND EFFICACY EVALUATED OVER TIME[2]



- Long-term efficacy was evaluated in adult patients who completed MOBILITY or TARGET and subsequently enrolled in EXTEND OLE[2]
- Long-term safety was evaluated in all 2887 adult patients who received ≥1 dose of KEVZARA in combination with DMARD(s)[2]

*These 2 studies were discontinued due to low enrollment[3,4]; †Patients participating in the EXTEND OLE trial received KEVZARA 200 mg regardless of prior treatment in the placebo-controlled trials, except for patients who were previously dose-reduced to KEVZARA 150 mg due to safety issues, who continued on KEVZARA 150 mg[2]; ‡Patients in the EASY OLE study received KEVZARA 150 mg regardless of their prior treatment.[1]

OPEN-LABEL EXTENSION (OLE) STUDY LIMITATIONS AND ADDITIONAL STUDY CONTEXT

- These data are not included in the US Prescribing Information. Data presented are truthful and not misleading
- Open-label extension studies tend to include patients who respond to treatment and exclude those who discontinue treatment for any reason. As such, evaluating long-term efficacy using continuous variables can be influenced by progressively smaller numbers of patients remaining in the study
- Data presented are descriptive in nature, and no statistical comparisons are made
- Clinical data were analyzed based on all available data as observed

LONG-TERM SAFETY ANALYSIS

- This was a comprehensive safety analysis from pooled studies of patients who received at least 1 dose of sarilumab in combination with DMARD(s)

LONG-TERM EFFICACY ANALYSIS

- Efficacy assessments in this analysis did not include all of the primary endpoints from the placebo-controlled period of the pivotal trials analyzed
- For analysis of no radiographic progression, linear extrapolation was used to impute missing data. Patients with missing data after the imputation were considered progressors

Given the limitations and context described above, caution should be used in interpreting these data.

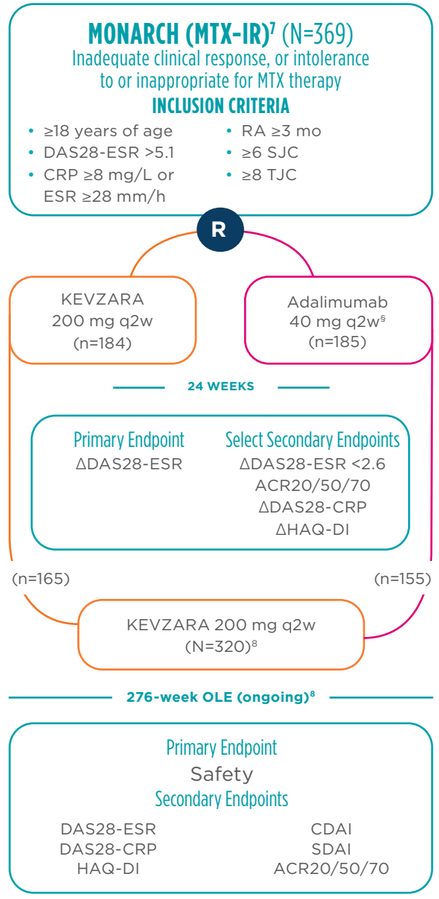
STUDY DESIGNS FOR PIVOTAL TRIALS:

MOBILITY Study Design: A 52-week, randomized, double-blind, placebo-controlled, multicenter study (N=1197) assessing the efficacy and safety of KEVZARA 200 mg + MTX and 150 mg + MTX in patients with moderate to severe active RA (duration of ≥3 months) who had been on MTX 10 mg to 25 mg/week ≥6 weeks. Primary endpoints were reduction of signs and symptoms (ACR20) at 24 weeks, change in van der Heijde mTSS at 52 weeks, and change from baseline in HAQ-DI at 16 weeks. After week 16 in MOBILITY, patients with an inadequate response could have been treated with open-label KEVZARA 200 mg every 2 weeks.[5]

TARGET Study Design: A 24-week, randomized, double-blind, parallel group, placebo-controlled, multicenter study (N=546) assessing the efficacy and safety of KEVZARA 200 mg and 150 mg added to background conventional DMARD(s) in adult patients with moderate to severe active RA (≥6 months duration) with inadequate response and/or intolerance to 1 or more TNF antagonists, when administered with background conventional DMARD(s). Primary endpoints were reduction of signs and symptoms (ACR20) at 24 weeks and change from baseline in HAQ-DI at 12 weeks. After week 12 in TARGET, patients with an inadequate response could have been treated with open-label KEVZARA 200 mg every 2 weeks.[6]

KEVZARA MONOTHERAPY EVALUATED OVER TIME*

MONARCH: A randomized, double-blind, double-dummy phase 3 superiority study to evaluate the safety and efficacy of KEVZARA monotherapy vs adalimumab monotherapy[7†‡]



MONARCH ADDITIONAL STUDY CONTEXT

- MONARCH data are not included in the KEVZARA full Prescribing Information
- DAS28-ESR and FACIT-Fatigue were endpoints in MONARCH; however, there are no DAS28-ESR or FACIT-Fatigue data in the KEVZARA USPI

USE OF ADALIMUMAB

- Adalimumab and KEVZARA have different indications and can be used differently in clinical practice
- Dose escalation from adalimumab 40 mg q2w to qw was permitted after week 16 in patients who had not achieved at least 20% improvement in TJC and SJC. By week 24, dosing for 8.6% of patients on adalimumab was adjusted

STUDY LIMITATIONS (MONARCH)

- KEVZARA and adalimumab can be used as monotherapy or in combination with nonbiologic DMARD(s). In MONARCH, both agents were only used as monotherapy
- The efficacy of KEVZARA monotherapy has not been compared to that of KEVZARA + MTX or adalimumab + MTX
- MONARCH did not evaluate radiographic outcomes in either treatment group

MONARCH OPEN-LABEL EXTENSION (OLE) STUDY LIMITATIONS AND ADDITIONAL STUDY CONTEXT

- These data are not included in the USPI. Data presented are truthful and not misleading
- Long-term safety analysis included all patients who received at least 1 dose of KEVZARA monotherapy
- Analysis of clinical data were based on all available data as observed
- Data presented are descriptive in nature and no statistical comparisons are made
- Open-label extension studies tend to include patients who respond to treatment and exclude those who discontinue treatment for any reason. As such, evaluating long-term efficacy using continuous variables can be influenced by progressively smaller numbers of patients remaining in study

Given the limitations and context described above, caution should be used in interpreting these data.

MONARCH OLE: An extension designed to assess the safety and efficacy of long-term continuous KEVZARA monotherapy and switching from adalimumab monotherapy to KEVZARA monotherapy[8]

*KEVZARA monotherapy evaluated over time includes the MONARCH OLE and ONE OLE studies; †Efficacy analyses were conducted in the ITT population, which included all randomized patients, including those who increased the dose frequency of adalimumab or matching placebo. Data collected after permanent treatment discontinuation period were excluded; ‡After week 16, dose escalation to adalimumab qw was permitted for patients who did not achieve ≥20% improvement in TJC and SJC; §The recommended dose of adalimumab SC is 40 mg q2w. Some patients not taking concomitant MTX may derive additional benefit from increasing the SC dosing frequency to 40 mg qw; see adalimumab full Prescribing Information.[7,9]

MTX=methotrexate; MTX-IR=methotrexate inadequate response; TNF-IR=tumor necrosis factor inhibitor inadequate response or intolerant; TNF=tumor necrosis factor; q2w=once every 2 weeks; ACR20=American College of Rheumatology 20% improvement criteria; mTSS=modified total Sharp score; HAQ-DI=Health Assessment Questionnaire-Disability Index; DAS28-ESR=disease activity score 28-erythrocyte sedimentation rate; SJC=swollen joint count; TJC=tender joint count; CDAI=Clinical Disease Activity Index; SDAI=Simple Disease Activity Index; USPI=United States Prescribing Information; ITT=intent to treat; SC=subcutaneous.

IMPORTANT SAFETY INFORMATION (cont'd)

CONTRAINDICATION

Do not use KEVZARA in patients with known hypersensitivity to sarilumab or any of the inactive ingredients.

WARNINGS AND PRECAUTIONS

- ***Infections.*** Serious and sometimes fatal infections due to bacterial, mycobacterial, invasive fungal, viral, or other opportunistic pathogens have been reported in patients receiving immunosuppressive agents for rheumatoid arthritis (RA). The most frequently observed serious infections with KEVZARA included pneumonia and cellulitis. Among opportunistic infections, TB, candidiasis, and pneumocystis were reported with KEVZARA.
  - Hold treatment with KEVZARA if a patient develops a serious infection or an opportunistic infection.

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KEVZARA® (sarilumab) injection
200 mg | 150 mg

OPEN-LABEL EXTENSION DATA

CLINICAL RESPONSE OVER 5 YEARS

These data should be interpreted with caution. There are limitations associated with open-label study design, including decreasing sample size and potential continued involvement of responders and attrition of non-responders. Data presented are descriptive in nature and no statistical comparisons are made.

PIVOTAL TRIAL DATA[5,6,10]:

ACR20 RESPONSE IN MOBILITY AND TARGET (CO-PRIMARY ENDPOINT)

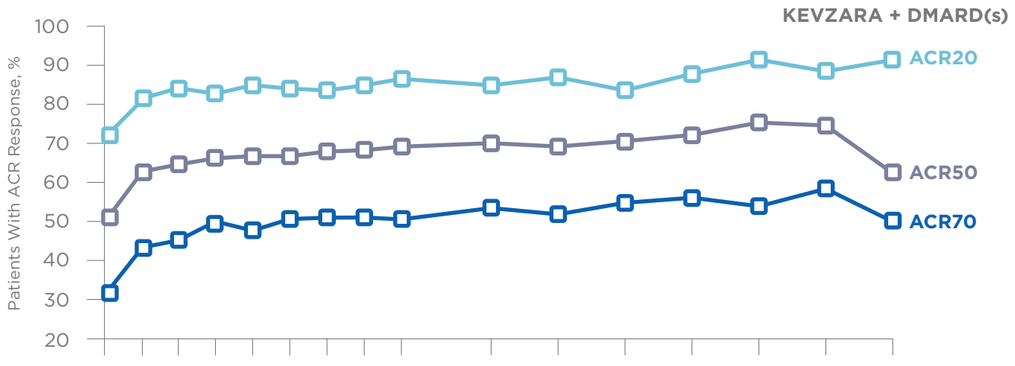
ACR20 response at week 24 was the primary endpoint in MOBILITY (MTX-IR) and TARGET (TNF-IR).

Patients achieved:

- 66%* with KEVZARA 200 mg + MTX compared to 33% with placebo + MTX (MOBILITY)
- 61%* with KEVZARA 200 mg + DMARD(s) compared to 34% with placebo + DMARD(s) (TARGET)

*$P<0.0001$.

POOLED ACR20/50/70 RESPONSE OVER TIME[1]



Number of subjects																
ACR20	1318	1470	1482	1431	1379	1275	1156	1084	975	860	519	242	179	163	110	37
ACR50	824	1065	1078	1074	1037	952	888	819	749	664	391	192	141	132	89	25
ACR70	435	625	690	694	673	623	577	531	493	446	268	131	102	88	64	18

Please see the EXTEND open-label extension study design on page 2.

Patients achieved consistent ACR response **over time with KEVZARA[1]**

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

- Patients with latent TB should be treated with standard antimycobacterial therapy before initiating KEVZARA. Consider anti-TB therapy prior to initiation of KEVZARA in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed, and for patients with a negative test for latent TB but having risk factors for TB infection.
- Consider the risks and benefits of treatment prior to initiating KEVZARA in patients who have: chronic or recurrent infection, a history of serious or opportunistic infections, underlying conditions in addition to RA that may predispose them to infection, been exposed to TB, or lived in or traveled to areas of endemic TB or endemic mycoses.
- Viral reactivation has been reported with immunosuppressive biologic therapies. Cases of herpes zoster were observed in clinical studies with KEVZARA.

OPEN-LABEL EXTENSION DATA

HAQ-DI OVER 5 YEARS

These data should be interpreted with caution. There are limitations associated with open-label study design, including decreasing sample size and potential continued involvement of responders and attrition of non-responders. Data presented are descriptive in nature and no statistical comparisons are made.

Data in patients who received initial treatment with KEVZARA compared with those who initially received placebo.

PIVOTAL TRIAL DATA[1,10]:

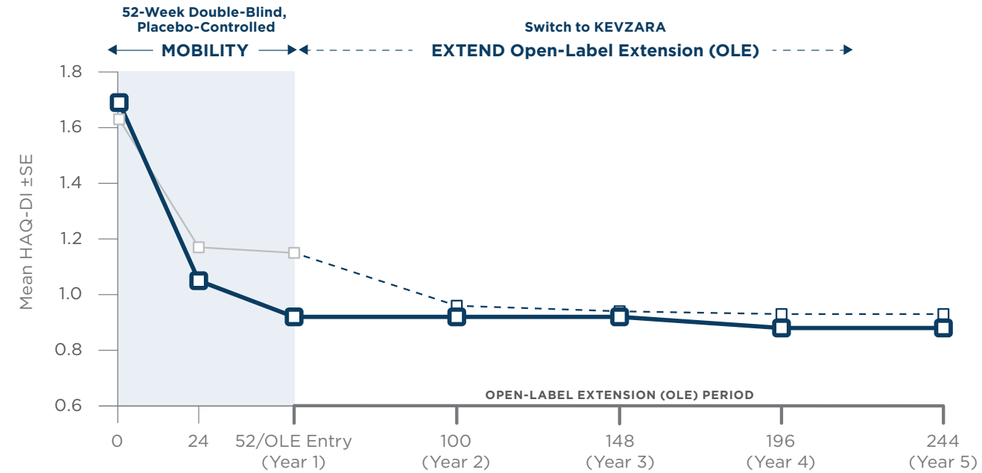
ΔHAQ-DI IN MOBILITY AND TARGET (CO-PRIMARY ENDPOINT)

Mean change from baseline in HAQ-DI at week 16 in MOBILITY and week 12 in TARGET was a co-primary endpoint.

- -0.58* with KEVZARA 200 mg + MTX compared to -0.30 with placebo + MTX (MOBILITY)
- -0.49† with KEVZARA 200 mg + DMARD(s) compared to -0.29 with placebo + DMARD(s) (TARGET)

*$P<0.0001$; †$P<0.001$.

MEAN HAQ-DI OVER TIME[1,11‡] MOBILITY → EXTEND



Number of subjects							
Placebo	398	369	331	269	250	227	211
Sarilumab 200 mg	399	348	310	262	237	227	212

Placebo + MTX → KEVZARA 200 mg q2w + MTX

KEVZARA 200 mg q2w → KEVZARA 200 mg q2w

This analysis has not been performed for the TNF-IR population.

‡Mean HAQ-DI scores were calculated based on observed cases, without imputation of missing data.

HAQ-DI was measured in patients who continued **treatment with KEVZARA for up to 5 years[1,11]**

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KEVZARA® (sarilumab) injection 200 mg | 150 mg

OPEN-LABEL EXTENSION DATA

INHIBITION OF RADIOGRAPHIC PROGRESSION OVER 5 YEARS

These data should be interpreted with caution. There are limitations associated with open-label study design, including decreasing sample size and potential continued involvement of responders and attrition of non-responders. Data presented are descriptive in nature and no statistical comparisons are made.

Data in patients who received initial treatment with KEVZARA compared with those who initially received placebo.

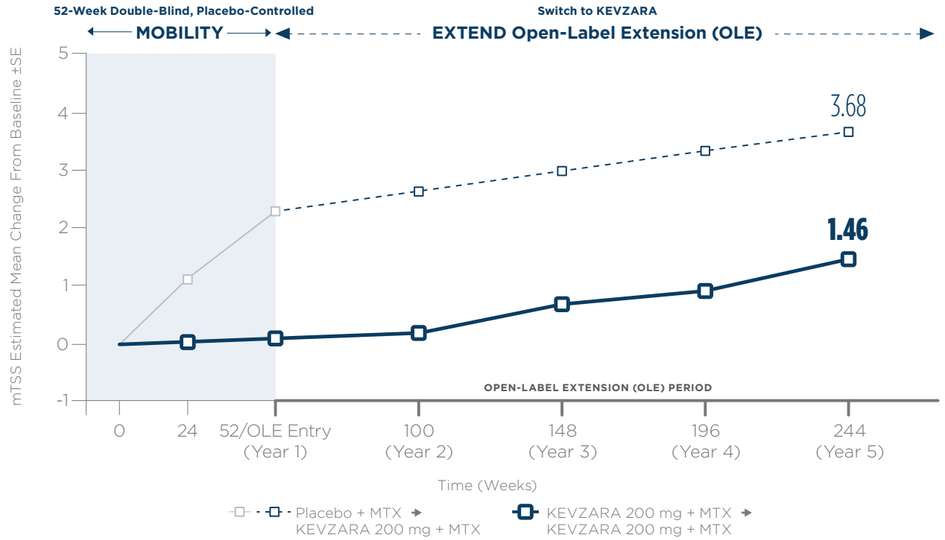
PIVOTAL TRIAL DATA[5,10]:

In MOBILITY, ΔmTSS from baseline at week 52 was 0.25 with KEVZARA 200 mg vs 2.78 with placebo* (CO-PRIMARY ENDPOINT)

- KEVZARA 200 mg + MTX provided an absolute difference of -2.52 units (CI: -3.38, -1.66) in mean ΔmTSS relative to placebo + MTX

*$P<0.0001$.

CHANGE FROM BASELINE IN RADIOGRAPHIC PROGRESSION (mTSS)[11†]
MOBILITY → EXTEND



In MOBILITY, **56% of MTX-IR patients receiving KEVZARA 200 mg** had no radiographic progression (ΔmTSS ≤0) vs 39% of placebo patients at week 52[10]

SE=standard error.

†Radiographic progression was assessed by change from baseline in mTSS, reported using a post hoc integrated analysis of 4 separate reading campaigns. Change from baseline in mTSS was recorded in 1 campaign during the randomized controlled phase and 3 campaigns during the OLE. A post hoc integrated analysis was conducted to analyze radiographic progression based on all available campaign data.[11]

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

- ***Laboratory Abnormalities.*** Treatment with KEVZARA was associated with decreases in absolute neutrophil counts (including neutropenia), and platelet counts; and increases in transaminase levels and lipid parameters (LDL, HDL cholesterol, and/or triglycerides). Increased frequency and magnitude of these elevations were observed when potentially hepatotoxic drugs (e.g., MTX) were used in combination with KEVZARA. Assess neutrophil count, platelet count, and ALT/AST levels prior to initiation with KEVZARA. Monitor these parameters 4 to 8 weeks after start of therapy and every 3 months thereafter. Assess lipid parameters 4 to 8 weeks after start of therapy, then at 6 month intervals.

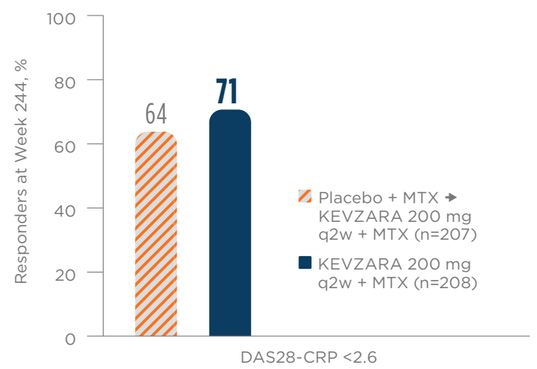
OPEN-LABEL EXTENSION DATA

DAS28-CRP OVER 5 YEARS

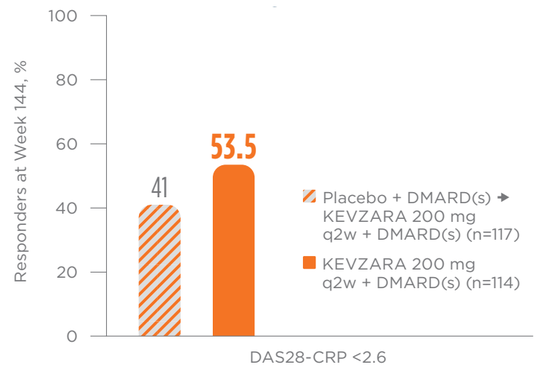
These data should be interpreted with caution. There are limitations associated with open-label study design, including decreasing sample size and potential continued involvement of responders and attrition of non-responders. Data presented are descriptive in nature and no statistical comparisons are made.

Data in patients who received initial treatment with KEVZARA compared with those who initially received placebo.

DISEASE ACTIVITY AT 244 WEEKS (DAS28-CRP <2.6)[11]
MOBILITY → EXTEND



DISEASE ACTIVITY AT 144 WEEKS (DAS28-CRP <2.6)[12]
TARGET → EXTEND



PIVOTAL TRIAL DATA[5,6,10]:

PERCENTAGE OF PATIENTS ACHIEVING DAS28-CRP <2.6 IN MOBILITY AT 24 WEEKS

- 34% with KEVZARA 200 mg + MTX compared to 10% with placebo + MTX

PERCENTAGE OF PATIENTS ACHIEVING DAS28-CRP <2.6 IN TARGET AT 24 WEEKS

- 29% with KEVZARA 200 mg + DMARD(s) compared to 7% with placebo + DMARD(s)

CONTROL OF IL-6–RELATED SIGNS AND SYMPTOMS

RAPIDLY NORMALIZED CRP LEVELS

CRP levels returned to normal (<10 mg/L) as early as 2 weeks after the first dose of KEVZARA.[10,13]

LS mean change from baseline in CRP levels at week 24 was -16.7 with KEVZARA 200 mg + MTX vs 0.1 with placebo + MTX in MOBILITY and -23.3 with KEVZARA 200 mg + DMARD(s) vs -3.6 with placebo + DMARD(s) in TARGET.[1]

CRP was studied as part of ACR20/50/70 response endpoints in these studies.[10]*

*Not a prespecified endpoint.

REDUCTIONS IN MORNING STIFFNESS

LS mean change from baseline in morning stiffness VAS at week 24 was -33.8 with KEVZARA 200 mg + DMARD(s) vs -21.7 with placebo + DMARD(s) in TARGET.[14] Morning stiffness was not assessed in MOBILITY.

REDUCTIONS IN PAIN

LS mean change from baseline in pain VAS at week 24 was -31.8 with KEVZARA 200 mg + MTX vs -15.4 with placebo + MTX in MOBILITY and -33.7 with KEVZARA 200 mg + DMARD(s) vs -21.3 with placebo + DMARD(s) in TARGET.[14,15]

LS=least squares; VAS=visual analogue scale.

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WHEN IT'S TIME FOR A CHANGE, TARGET IL-6R WITH

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PROVEN SAFETY PROFILE

COMMON ADVERSE REACTIONS IN PRE-RESCUE, PLACEBO-CONTROLLED TRIALS[10]*

Preferred Term	Placebo + DMARD(s) N=579	KEVZARA 150 mg + DMARD(s) N=579	KEVZARA 200 mg + DMARD(s) N=582
Neutropenia	0.2%	7%	10%
ALT increased	2%	5%	5%
Injection site erythema	0.9%	5%	4%
Injection site pruritus	0.2%	2%	2%
Upper respiratory tract infection	2%	4%	3%
Urinary tract infection	2%	3%	3%
Hypertriglyceridemia	0.5%	3%	1%
Leukopenia	0%	0.9%	2%

*Adverse reactions occurring in ≥2% of patients administered KEVZARA 200 mg or KEVZARA 150 mg + DMARD(s) and greater than observed in patients on placebo + DMARD(s).

- Medically relevant AE occurring at an incidence of less than 2% in patients with RA treated with KEVZARA in controlled studies was oral herpes[10]
- Decrease in ANC was not associated with higher incidence of infections, including serious infections[10]
- In the long-term safety population, the overall rates of serious infections, GI perforations, neutrophil counts, platelets counts, and lipid parameters were consistent with what was observed in the placebo-controlled trials[10]

ALT=alanine aminotransferase; ANC=absolute neutrophil count; GI=gastrointestinal.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

- ***Gastrointestinal Perforation.*** GI perforation risk may be increased with concurrent diverticulitis or concomitant use of NSAIDs or corticosteroids. Gastrointestinal perforations have been reported in clinical studies, primarily as complications of diverticulitis. Promptly evaluate patients presenting with new onset abdominal symptoms.
- ***Immunosuppression.*** Treatment with immunosuppressants may result in an increased risk of malignancies. The impact of treatment with KEVZARA on the development of malignancies is not known but malignancies have been reported in clinical studies.
- ***Hypersensitivity Reactions.*** Hypersensitivity reactions have been reported in association with KEVZARA. Hypersensitivity reactions that required treatment discontinuation were reported in 0.3% of patients in controlled RA trials. Injection site rash, rash, and urticaria were the most frequent hypersensitivity reactions. Advise patients to seek immediate medical attention if they experience any symptoms of a hypersensitivity reaction. If anaphylaxis or other hypersensitivity reaction occurs, stop administration of KEVZARA immediately. Do not administer KEVZARA to patients with known hypersensitivity to sarilumab.
- ***Active Hepatic Disease and Hepatic Impairment.*** Treatment with KEVZARA is not recommended in patients with active hepatic disease or hepatic impairment, as treatment with KEVZARA was associated with transaminase elevations.
- ***Live Vaccines.*** Avoid concurrent use of live vaccines during treatment with KEVZARA due to potentially increased risk of infections. No data are available on the secondary transmission of infection from persons receiving live vaccines to patients receiving KEVZARA.

ADVERSE REACTIONS

- The most common serious adverse reactions were infections. The most frequently observed serious infections included pneumonia and cellulitis. The most common adverse reactions (occurred in at least 3% of patients treated with KEVZARA + DMARDs) are neutropenia, increased ALT, injection site erythema, upper respiratory infections, and urinary tract infections.

AN ESTABLISHED SAFETY PROFILE UP TO 7 YEARS, WITHOUT UNEXPECTED SAFETY SIGNALS

Studied in ≈3000 MTX-IR and TNF-IR patients with more than 8100 patient-years of exposure[1,2,10]

Mean duration of treatment in the safety population (N=2887) was 2.8 years (max 7.3 years), representing 8188 cumulative PY of exposure

- 773 patients (27%) were treated for ≥240 weeks (4.6 years)
- 36 patients (1.2%) were treated for >360 weeks (7 years)

Incidence rate of AEs was generally stable over time, with no indication of increased incidence rate in serious AEs and serious infections[1,2]

MOBILITY (MTX-IR), TARGET (TNF-IR), LONG-TERM SAFETY POPULATIONS[1,2]

	Placebo-Controlled Population			Long-Term Safety Population
Adverse Event (IR/100 PY)*	Placebo + MTX/DMARD(s) n=661	KEVZARA 150 mg q2w MTX/DMARD(s) n=660	KEVZARA 200 mg q2w MTX/DMARD(s) n=661	KEVZARA 200 mg or 150 mg q2w MTX/DMARD(s) N=2887
Cumulative total TEAE observation period, years†	382.3	440.7	441.4	8187.7
Any TEAE	173.3	215.7	252.0	144.2
Serious TEAE	8.3	9.7	13.8	9.4
TEAE leading to discontinuation	8.2	16.8	19.4	8.7
TEAE leading to death	0.8	0.5	0.2	0.4
Overall infections	75.1	80.8	84.5	54.4
Serious infections	3.9	3.6	5.2	3.7
Upper respiratory tract infection	10.2	12.3	12.5	7.7
Urinary tract infection	7.8	7.0	10.9	5.9
Neutropenia	0.8	22.9	31.0	13.8
ALT increased	4.4	11.6	10.9	5.0
Injection site erythema‡	1.6	29.3	23.8	13.3
Injection site pruritus‡	0.5	9.3	9.3	6.9
Hypertriglyceridemia	1.3	4.5	3.2	2.8
Leukopenia	0	4.1	7.9	3.7

In the long-term safety population, the rates of thromboembolic events (MedDRA high-level group term "embolism and thrombosis") were 0.8 per 100 PY (as reported and evaluated post hoc; not a prespecified AESI)[2]

- Rate of DVT was 0.2 per 100 PY; rate of PE was 0.2 per 100 PY

Safety observations in the open-label extension population were consistent with those in the placebo-controlled trials.[1,2]

*Incidence rate per 100 PY at risk of first event; †TEAE period, period from day of first treatment dose to 60 days after the last treatment dose[2]; ‡Injection site reactions (including erythema and pruritus) were mild in severity for the majority of patients and necessitated drug discontinuation in 3 (<0.5%) patients receiving KEVZARA.[1]

PY=patient-years; TEAE= treatment-emergent adverse event; AESI=adverse event of special interest; DVT=deep vein thrombosis; PE=pulmonary embolism.

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200 mg | 150 mg

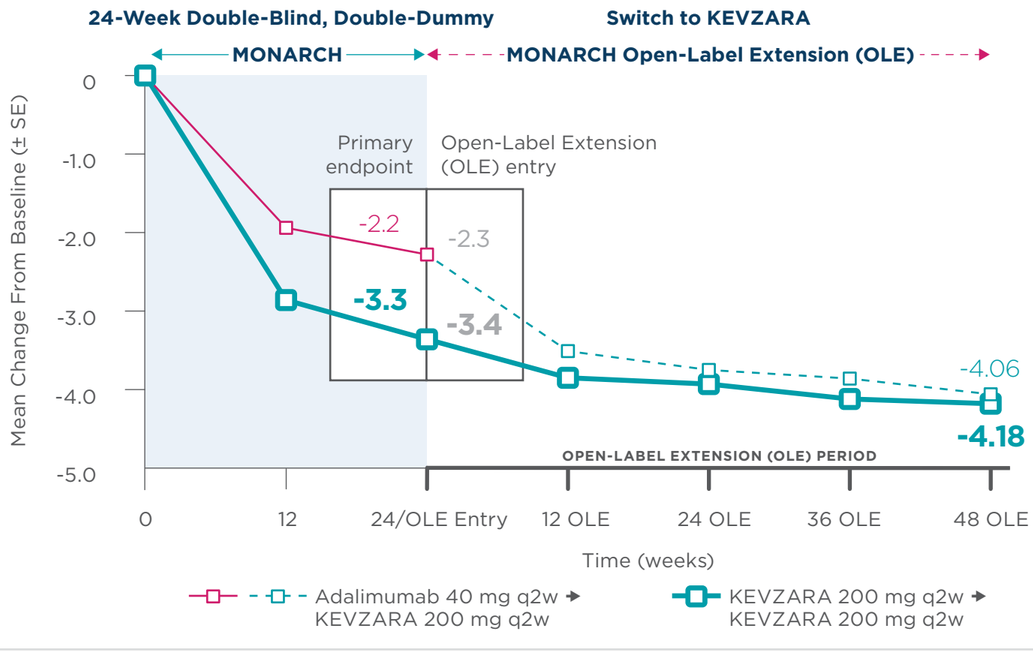
MONARCH OPEN-LABEL EXTENSION DATA

CHANGE IN DISEASE ACTIVITY

These data should be interpreted with caution. There are limitations associated with open-label study design, including decreasing sample size and potential continued involvement of responders and attrition of non-responders. Data presented are descriptive in nature and no statistical comparisons are made.

See additional MONARCH study limitations on page 3.

MEAN CHANGE FROM BASELINE IN DAS28-ESR[7,8]



Changes in disease activity were measured in both patients who continued treatment with KEVZARA monotherapy and in those who switched treatment from adalimumab to KEVZARA

CONTROL OF IL-6–RELATED SIGNS AND SYMPTOMS

RAPIDLY NORMALIZED CRP LEVELS

CRP levels returned to normal (<10 mg/L) as early as 2 weeks after the first dose of KEVZARA.[10,13]

LS mean change from baseline in CRP levels at week 24 was -17 with KEVZARA 200 mg monotherapy vs -2.9 with adalimumab 40 mg monotherapy in MONARCH.[7]*

CRP was studied as part of ACR20/50/70 response endpoints.[7]

*Not a prespecified endpoint.

REDUCTIONS IN MORNING STIFFNESS

LS mean change from baseline in morning stiffness VAS at week 24 was -35.1 with KEVZARA 200 mg monotherapy vs -29.3 with adalimumab 40 mg monotherapy in MONARCH.[16]

REDUCTIONS IN PAIN

LS mean change from baseline in pain VAS at week 24 was -36.2 with KEVZARA 200 mg monotherapy vs -27.4 with adalimumab 40 mg monotherapy in MONARCH.[16]

MONARCH: NO UNEXPECTED SAFETY SIGNALS

OVERALL, KEVZARA MONOTHERAPY LONG-TERM SAFETY WAS STUDIED IN 471 PATIENTS, WITH ≈800 PATIENT-YEARS OF EXPOSURE AND DATA WAS CONSISTENT WITH MONARCH STUDIES[2]

Mean exposure in the long-term safety population was 1.7 years (max 3.5 years)

- 320 patients (87%) were treated for ≥72 weeks

Incidence rate of AEs was generally stable over time, with no indication for increased incidence rate[1,7]

MONARCH (MTX-IR) AND MONARCH LONG-TERM SAFETY POPULATIONS[1,7*†]

	Randomized, Controlled Population		Long-Term Safety Population
	Adalimumab 40 mg q2w[‡] n=184 % (n_E/100 PY)[§]	KEVZARA 200 mg q2w n=184 % (n_E/100 PY)[§]	KEVZARA 200 mg q2w n=320 % (n_E/100 PY)[§]
Any TEAE	63.6% (326.9)	64.1% (462.0)	73.4% (247.9)
Serious TEAE	6.5% (14.9)	4.9% (18.7)	7.2% (9.5)
TEAE leading to discontinuation	7.1% (19.9)	6.0% (21.2)	6.9% (7.8)
TEAE leading to death[‖]	0% (0)	0.5% (3.7)	0.9% (1.1)
Infections	27.7% (82.0)	28.8% (86.2)	38.8% (59.5)
Serious infections[¶]	1.1% (2.5)	1.1% (2.5)	0.9% (0.9)
Bronchitis	3.8% (8.7)	6.5% (18.7)	7.5% (7.2)
Nasopharyngitis	7.6% (18.6)	6.0% (13.7)	11.9% (13.5)
Upper respiratory tract infection	3.8% (11.2)	1.6% (3.7)	6.6% (6.9)
Neutropenia	0.5% (1.2)	13.6% (54.9)	13.1% (28.2)
Headache	6.5% (17.4)	3.8% (11.2)	2.8% (5.5)
Rheumatoid arthritis	3.8% (8.7)	0.5% (1.2)	3.8% (4.3)
Injection site erythema	3.3% (8.7)	7.6% (87.4)	7.8% (35.1)
ALT increase	3.8% (12.4)	3.8% (8.7)	4.4% (5.8)
Accidental overdose[#]	6.0% (14.9)	3.3% (7.5)	5.3% (6.6)
Dyslipidemia**	4.3% (9.9)	1.6% (3.7)	3.1% (3.2)

In MONARCH, the safety profiles of KEVZARA and adalimumab were generally comparable, except for neutropenia and injection site erythema for KEVZARA and headache and RA for adalimumab[7]

Safety observations in the long-term population were generally consistent with those in the randomized, controlled population.[8]

*Adverse events reported for the long-term safety population were selected based on occurrence in ≥3% of patients in the randomized, controlled population in any treatment group; †Patients from the KEVZARA ONE study population were included in these long-term monotherapy safety data; ‡One patient was randomized, but not treated, in the adalimumab group and was not included in the safety population; §Patient years per group are as follows: 80.5 (adalimumab 40 mg), 80.1 (KEVZARA 200 mg), and 348.1 (long-term safety population for KEVZARA 200 mg); ‖In the randomized trial, 1 patient in the KEVZARA group died of acute cardiac failure secondary to aortic dissection and papillary muscle rupture on day 36; ¶In the randomized trial, 1 patient receiving KEVZARA was diagnosed with infective bursitis and another patient was diagnosed with mastitis, and 1 patient receiving adalimumab was diagnosed with bacterial arthritis and another patient was diagnosed with a respiratory tract infection; #Protocol defined as ≥2 doses within 11 calendar days or within 6 days for adalimumab-treated patients who switched to weekly dosing; **Dyslipidemia was defined by standardized MedDRA query.[1,7]

IMPORTANT SAFETY INFORMATION (cont'd)

DRUG INTERACTIONS

- Exercise caution when KEVZARA is co-administered with CYP substrates with a narrow therapeutic index (e.g. warfarin or theophylline), or with CYP3A4 substrates (e.g. oral contraceptives or statins) as there may be a reduction in exposure which may reduce the activity of the CYP3A4 substrate.
- Elevated interleukin-6 (IL-6) concentration may down-regulate CYP activity such as in patients with RA and hence increase drug levels compared to subjects without RA. Blockade of IL-6 signaling by IL-6Rα antagonists such as KEVZARA might reverse the inhibitory effect of IL-6 and restore CYP activity, leading to altered drug concentrations.

Please see Important Safety Information throughout and click here to see full Prescribing Information, including **Boxed WARNING.**

For your adult patients with moderately to severely active RA who have had an inadequate response/intolerance to 1 or more DMARD(s)

When It's Time for a Change, Target IL-6R with KEVZARA

VISIT KEVZARAhcp.com TO LEARN MORE ABOUT KEVZARA

KEVZARA®
(sarilumab) injection
200 mg | 150 mg

IMPORTANT SAFETY INFORMATION (cont'd)

USE IN SPECIFIC POPULATIONS

- KEVZARA should be used in pregnancy only if the potential benefit justifies the potential risk to the fetus. Because monoclonal antibodies could be excreted in small amounts in human milk, the benefits of breastfeeding and the potential adverse effects on the breastfed child should be considered along with the mother's clinical need for KEVZARA.
- There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to KEVZARA during pregnancy. Physicians are encouraged to register patients and pregnant women are encouraged to register themselves by calling 1-877-311-8972.
- Use caution when treating the elderly.

Advise patients to read the FDA-approved patient labeling (Medication Guide and Instructions for Use).

KEVZARA is available by prescription only.

References: 1. Data on file, Sanofi/Regeneron. Integrated summary. October 25, 2019. **2.** Fleischmann R, Genovese M, Lin Y, et al. Long-term safety of sarilumab in rheumatoid arthritis: an integrated analysis with up to 7 years' follow-up. *Rheumatology (Oxford).* 2019. doi:10.1093/rheumatology/kez265. [Epub ahead of print]. **3.** NIH. Effect of SAR153191 (REGN88) with methotrexate in patients with active rheumatoid arthritis who failed TNF-α blockers. https://clinicaltrials.gov/ct2/show/NCT01217814. Accessed February 11, 2020. **4.** National Library of Medicine. An evaluation of sarilumab plus methotrexate compared to etanercept plus methotrexate in RA patients not responding to adalimumab plus methotrexate (RA-COMPARE). https://clinicaltrials.gov/ct2/show/NCT01764997. Accessed February 11, 2020. **5.** Genovese MC, Fleischmann R, Kivitz AJ, et al. Sarilumab plus methotrexate in patients with active rheumatoid arthritis and inadequate response to methotrexate: results of a phase III study. *Arthritis Rheumatol.* 2015;67(6):1424-1437. **6.** Fleischmann R, van Adelsberg J, Lin Y, et al. Sarilumab and nonbiologic disease-modifying antirheumatic drugs in patients with active rheumatoid arthritis and inadequate response or intolerance to tumor necrosis factor inhibitors. *Arthritis Rheumatol.* 2017;69(2):277-290. **7.** Burmester GR, Lin Y, Patel R, et al. Efficacy and safety of sarilumab monotherapy versus adalimumab monotherapy for the treatment of patients with active rheumatoid arthritis (MONARCH): a randomised, double-blind, parallel-group phase III trial. *Ann Rheum Dis.* 2017;76(5):840-847. **8.** Burmester GR, Strand V, Rubbert-Roth A, et al. Safety and efficacy of switching from adalimumab to sarilumab in patients with rheumatoid arthritis in the ongoing MONARCH open-label extension. *RMD Open.* 2019;5(2):e001017. doi: 10.1136/rmdopen-2019-001017. **9.** Humira [package insert]. North Chicago, IL: AbbVie Inc; 2019. **10.** KEVZARA [prescribing information]. Bridgewater, NJ: Sanofi/Regeneron Pharmaceuticals, Inc. **11.** Genovese MC, van der Heijde D, Lin Y, et al. Long-term safety and efficacy of sarilumab plus methotrexate on disease activity, physical function and radiographic progression: 5 years of sarilumab plus methotrexate treatment. *RMD Open.* 2019;5(2):e000887. doi:10.1136/ rmdopen-2018-000887. **12.** Data on file, Sanofi/Regeneron. EULAR poster SAT0172. June 2018. **13.** Center for Devices and Radiological Health. Guidance for industry and FDA staff: review criteria for assessment of c-reactive protein (CRP), high sensitivity c-reactive protein (hsCRP) and cardiac c-reactive protein (cCRP) assays. https://www.fda.gov/media/71337/download. Accessed February 11, 2020. **14.** Strand V, Reaney M, Chen CI, et al. Sarilumab improves patient-reported outcomes in rheumatoid arthritis patients with inadequate response/intolerance to tumour necrosis factor inhibitors. *RMD Open.* 2017;3:e000416. doi:10.1136/rmdopen-2016-000416. **15.** Strand V, Kosinski M, Chen CI, et al. Sarilumab plus methotrexate improves patient-reported outcomes in patients with active rheumatoid arthritis and inadequate responses to methotrexate: results of a phase III trial. *Arthritis Res Ther.* 2016;18:198. doi:10.1186/s13075-016-1096-9. **16.** Strand V, Gossec L, Proudfoot CWJ, et al. Patient-reported outcomes from a randomized phase III trial of sarilumab monotherapy versus adalimumab monotherapy in patients with rheumatoid arthritis. *Arthritis Res Ther.* 2018;20(1):129. doi:10.1186/s13075-018-1614-z.

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