



# READY TO EXPLORE XELJANZ<sup>®</sup> ACROSS FIVE INDICATIONS?

RAPID RESPONSE  
STARTS HERE >



**XELJANZ<sup>®</sup>**   
[tofacitinib]

Not an actual patient.  
SmPC available at the booth / Ficha técnica disponible en el stand

May 2025  
PP-XEL-GLB-1950

## LEGACY

Approved indications



Clinical evidence and  
market experience



Oral formulations



## SAFETY

ORAL Surveillance



AESIs in RA, PsA, AS, and UC



JIA



## STUDY DESIGNS

All study designs



## HIGHER-RISK PATIENT POPULATION

Post hoc analysis of  
ORAL Surveillance



MACE



Malignancy



VTE



## EFFICACY

RA



PsA, AS, JIA, and UC



Rapid response



Durable response



Efficacy summary



## QUICK ACCESS

Summary

Limitations

References





XELJANZ<sup>®</sup> is approved for 5 indications



THE FIRST ORAL JAK INHIBITOR  
APPROVED FOR 5 INDICATIONS:

|                                                                                   |                                                                                                                                                  |                                                                                                                                        |                                                                                                                              |                                                                                                                                        |                                                                                                                                          |                                                                                     |                                             |                                                                                     |                                 |
|-----------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|---------------------------------------------|-------------------------------------------------------------------------------------|---------------------------------|
|  | <b>RA</b><br>Rheumatoid arthritis                                                                                                                |                                                       | <b>PsA</b><br>Psoriatic arthritis                                                                                            |                                                     | <b>AS</b><br>Ankylosing spondylitis                                                                                                      |  | <b>JIA</b><br>Juvenile idiopathic arthritis |  | <b>UC</b><br>Ulcerative colitis |
| Indicated for:                                                                    | MTX-IR/IT patients with moderate to severe RA <sup>1</sup><br> | DMARD-IR patients with active PsA <sup>1</sup><br> | Patients with active AS <sup>1</sup><br> | Patients ≥2 years of age with JIA <sup>1</sup><br> | Patients with moderate to severe UC <sup>1</sup><br> |                                                                                     |                                             |                                                                                     |                                 |
| Since:                                                                            | <b>2012</b> in the US <sup>2</sup><br><b>2017</b> in the EU <sup>7</sup>                                                                         | <b>2017</b> in the US <sup>3</sup><br><b>2018</b> in the EU <sup>8</sup>                                                               | <b>2021</b> in the US <sup>4</sup><br><b>2021</b> in the EU <sup>9</sup>                                                     | <b>2020</b> in the US <sup>5</sup><br><b>2021</b> in the EU <sup>10</sup>                                                              | <b>2018</b> in the US <sup>6</sup><br><b>2018</b> in the EU <sup>11</sup>                                                                |                                                                                     |                                             |                                                                                     |                                 |

Not actual patients.

AS, ankylosing spondylitis; DMARD, disease-modifying antirheumatic drug; IR, inadequate responder; IT, intolerance; JAK, Janus kinase; JIA, juvenile idiopathic arthritis; MTX, methotrexate; PsA, psoriatic arthritis; RA, rheumatoid arthritis; UC, ulcerative colitis.



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HIGHER-RISK  
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XELJANZ® is supported by **robust clinical evidence and market experience**

39

Global clinical trials

(phase 1–3/4b, LTE)

34 in rheumatology, 5 in gastroenterology<sup>1–6</sup>

>450,000 PY

of exposure in patients with RA and PsA globally<sup>8,d</sup>

>13,000

Patients in RCTs  
across 5 indications<sup>2–7</sup>

>38,000 PY

of exposure to XELJANZ  
in RCTs<sup>2,3,7,a–c</sup>



Not actual patients.

<sup>a</sup>Doses in RA included XELJANZ 1 mg, 3 mg, 5 mg, 10 mg, 15 mg, or 30 mg BID; 10 mg or 20 mg QD; or 11 mg MR QD. Doses in PsA included XELJANZ 5 mg and 10 mg BID. Doses in AS included XELJANZ 2 mg, 5 mg, and 10 mg BID. XELJANZ 5 mg BID or 11 mg prolonged release QD are the only approved dosages for the treatment of RA, PsA, and AS, which should not be exceeded. 10 mg BID is not licensed for RA, PsA, or AS.<sup>1,3</sup>

<sup>b</sup>Doses in UC included XELJANZ 0.5 mg, 2 mg, 3 mg, 5 mg, 10 mg, and 15 mg BID.<sup>1</sup>

<sup>c</sup>Doses in JIA included 5 mg BID or body weight-based equivalent of XELJANZ Oral Solution BID for patients weighing <40 kg.<sup>3,4</sup>

<sup>d</sup>PMS data from the Pfizer safety database were collected between 6 November 2012 and 6 November 2021 (RA) and between 14 December 2017 and 6 November 2021 (PsA).<sup>8</sup>

AS, ankylosing spondylitis; BID, twice daily; JIA, juvenile idiopathic arthritis; LTE, long-term extension; MR, modified release; PMS, post-marketing surveillance; PsA, psoriatic arthritis; PY, patient-year; QD, once daily; RA, rheumatoid arthritis; RCT, randomised controlled trial; UC, ulcerative colitis.



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XELJANZ® is offered in 3 oral formulations for flexible dosing across indications<sup>1</sup>

Tablets



5 mg



10 mg

Prolonged release tablets



11 mg

Oral solution



Weight-based dosing

Not actual size.

Approved doses and formulations by indication

- **RA, PsA, and AS:** 5 mg tablets and 11 mg prolonged release tablets
- **JIA:** 5 mg tablets and oral solution
- **UC:** 5 mg tablets and 10 mg tablets

XELJANZ® in combination with methotrexate (MTX) is indicated for the treatment of moderately to severely active rheumatoid arthritis (RA) in adult patients who have not responded adequately or who are intolerant to one or more disease-modifying antirheumatic drugs (DMARDs). XELJANZ® may be given as monotherapy in case of MTX intolerance or when MTX treatment is not adequate. XELJANZ in combination with MTX is indicated for the treatment of active PsA in adult patients who have had an inadequate response or who have been intolerant to a prior DMARD therapy. XELJANZ is indicated for the treatment of adult patients with active AS who have responded inadequately to conventional therapy. XELJANZ is indicated for the treatment of adult patients with moderately to severely active UC who have had an inadequate response, lost response, or were intolerant to either conventional therapy or a biologic agent. XELJANZ is indicated for the treatment of active pJIA (rheumatoid factor positive [RF+] or negative [RF-] polyarthritis and extended oligoarthritis), and jPsA in patients 2 years of age and older, who have responded inadequately to previous therapy with DMARDs. XELJANZ can be given in combination with MTX or as monotherapy in case of intolerance to MTX or where continued treatment with MTX is inappropriate.

PRESENTACIONES Y PRECIO XELJANZ 5 mg, 56 comprimidos recubiertos con película: PVL: 824€; PVP: 879,91€; PVP IVA: 915,11€. XELJANZ 10 mg, 56 comprimidos recubiertos con película: PVL: 1.648€; PVP: 1.703,91€; PVP IVA: 1.772,07€. XELJANZ 11 mg, 28 comprimidos de liberación prolongada: PVL: 824€; PVP: 879,91€; PVP IVA: 915,11€. XELJANZ 1 mg/ml solución oral, 1 frasco conteniendo 240 ml de solución oral: PVL: 706,29€; PVP: 762,20€; PVP IVA: 792,69€. CONDICIONES DE PRESCRIPCIÓN Y DISPENSACIÓN Con receta médica. Diagnóstico hospitalario. Fármaco de Dispensación Hospitalaria sin Cupón Precinto (DIHSC): se limita su dispensación, sin necesidad de visado, a los pacientes no hospitalizados, en los Servicios de Farmacia de los Hospitales <https://www.mscbs.gob.es/home.htm>.

AS, ankylosing spondylitis; DMARD, disease-modifying antirheumatic drug; JIA, juvenile idiopathic arthritis; jPsA, juvenile psoriatic arthritis; MTX, methotrexate; pJIA, polyarticular juvenile idiopathic arthritis; PsA, psoriatic arthritis; RA, rheumatoid arthritis; RF, rheumatoid factor; UC, ulcerative colitis.

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# Study designs

## Rheumatoid arthritis

**ORAL Solo:** A 6-month, randomised, double-blind, placebo-controlled, multicentre study in which 610 patients with moderately to severely active RA who had an inadequate response to  $\geq 1$  DMARD received XELJANZ 5 mg BID or 10 mg BID, or placebo. At Month 3, all patients randomised to placebo were switched to XELJANZ. The co-primary endpoints were ACR20 response, HAQ-DI change, and rate of DAS28-4(ESR)  $< 2.6$  at Month 3.<sup>1</sup>

**ORAL Start:** A 24-month, randomised, double-blind, active-controlled, multicentre, parallel-group trial in which 956 patients with moderately to severely active RA who were MTX naïve and who had  $\geq 3$  hand or foot erosions or were seropositive received XELJANZ 5 mg BID or 10 mg BID, or MTX. Stable low-dose oral glucocorticoids were allowed. MTX dose started at 10 mg/week, titrated by 5 mg Q4W as tolerated to 20 mg/week by Week 8. All DMARDs were washed out before baseline visit, but stable doses of antimalarial agents were permitted (XELJANZ 5 mg 12%; MTX 16%). The primary endpoints were change in mTSS and ACR70 response rate at Month 6.<sup>2</sup>

**ORAL Sync:** A 12-month, randomised, double-blind, placebo-controlled, multicentre study in which 792 patients with moderately to severely active RA who had an inadequate response to  $\geq 1$  csDMARD or bDMARD received XELJANZ 5 mg BID or 10 mg BID, or placebo with background csDMARD. At Month 3, placebo patients who were considered nonresponders were randomly assigned to receive XELJANZ + csDMARD. At Month 6, all remaining placebo patients were switched to XELJANZ + csDMARD. The co-primary endpoints were ACR20 response and DAS28-4(ESR)  $< 2.6$  at Month 6 and HAQ-DI at Month 3.<sup>3</sup>

**ORAL Standard:** A 12-month, randomised, double-blind, placebo-controlled, multicentre trial in which 717 patients with moderately to severely active RA who had an inadequate response to MTX (but not to a TNFi) received XELJANZ 5 mg BID or 10 mg BID, Humira® 40 mg SC Q2W, or placebo (all patients on stable background MTX, the only permitted background DMARD). Stable low-dose oral glucocorticoids allowed. At 3 months, nonresponding placebo patients were advanced blindly to XELJANZ 5 mg or 10 mg BID. At 6 months, all remaining placebo patients were advanced similarly. The primary endpoints were ACR20 response rate and rate of DAS28-4(ESR)  $< 2.6$  at Month 6 and HAQ-DI change at Month 3. This study was not designed as a head-to-head comparison between XELJANZ and Humira®.<sup>4</sup>

XELJANZ 5 mg BID or 11 mg prolonged release QD are the only approved dosages for the treatment of RA and PsA, which should not be exceeded. 10 mg BID is not licensed for RA or PsA.<sup>11</sup>

ACR20/50/70,  $\geq 20/50/70\%$  improvement in American College of Rheumatology score; ; bDMARD, biologic disease-modifying antirheumatic drug; BID, twice daily; csDMARD, conventional synthetic disease-modifying antirheumatic drug; DAS28-4(ESR), Disease Activity Score in 28 joints with 4 variables, erythrocyte sedimentation rate; DMARD, disease-modifying antirheumatic drug; HAQ-DI, Health Assessment Questionnaire–Disability Index; mTSS, modified Total Sharp/van der Heijde Score; MTX, methotrexate; OPAL, Oral Psoriatic Arthritis Trial; ORAL, Oral Rheumatoid Arthritis Trial; PsA, psoriatic arthritis; QD, once daily; Q2W, every 2 weeks; Q4W, every 4 weeks; RA, rheumatoid arthritis; SC, subcutaneous; TNFi, tumour necrosis factor inhibitor.

Humira is a registered trademark of AbbVie Inc.

**ORAL Scan:** A 24-month, randomised, double-blind, placebo-controlled, multicentre trial in which 797 patients with moderately to severely active RA who had an inadequate response to MTX and who had  $\geq 3$  hand or foot erosions or were seropositive received XELJANZ 5 mg BID or 10 mg BID, or placebo (all patients on stable background MTX, the only permitted background DMARD). Stable low-dose oral glucocorticoids were allowed. At 3 months, nonresponding placebo patients were advanced blindly to XELJANZ 5 mg or 10 mg BID. At 6 months, all remaining placebo patients were advanced similarly. The primary endpoints were ACR20 response rate, change in mTSS, and rate of DAS28-4(ESR)  $< 2.6$  at Month 6 and HAQ-DI change at Month 3.<sup>5</sup>

**ORAL Step:** A 6-month, double-blind, placebo-controlled, parallel-group study in which 399 patients with moderately to severely active RA who had an inadequate response to TNFis received XELJANZ 5 mg BID or 10 mg BID, or placebo, all with MTX. At Month 3, patients given placebo were switched to either XELJANZ 5 mg BID or 10 mg BID. The primary endpoints were ACR20 response rate, mean change in HAQ-DI, and DAS28-4(ESR)  $< 2.6$ , all at Month 3.<sup>6</sup>

**ORAL Strategy:** A 1-year, double-blind, triple-dummy, phase 3b/4, active comparator, head-to-head controlled trial in which 1146 patients with moderately to severely active RA who had an inadequate response to MTX received XELJANZ 5 mg BID, XELJANZ 5 mg BID + MTX, or Humira® 40 mg SC Q2W + MTX. The primary endpoint was the proportion of patients achieving ACR50 at Month 6 powered to test noninferiority through independent comparisons of XELJANZ 5 mg BID to Humira® 40 mg SC Q2W + MTX, XELJANZ 5 mg BID + MTX to Humira® 40 mg SC Q2W + MTX, and XELJANZ 5 mg BID to XELJANZ 5 mg BID + MTX.<sup>7,8</sup>

## Psoriatic arthritis

**OPAL Broaden:** A 12-month, randomised, multicentre, double-blind trial in which 422 patients with PsA who had an inadequate response to at least one csDMARD and were TNFi naïve received either XELJANZ 5 mg BID, XELJANZ 10 mg BID, Humira® 40 mg SC Q2W, or placebo. At Month 3, all patients randomised to placebo treatment were advanced in a blinded fashion to either XELJANZ 5 mg BID or XELJANZ 10 mg BID. Primary endpoints were ACR20 response and the change from baseline in HAQ-DI at Month 3.<sup>9</sup>

**OPAL Beyond:** A randomised, 6-month, double-blind trial in which 394 patients with PsA who had an inadequate response to at least one TNFi received either XELJANZ 5 mg BID, XELJANZ 10 mg BID, or placebo. At Month 3, all patients randomised to placebo were advanced in a blinded fashion to either XELJANZ 5 mg BID or XELJANZ 10 mg BID. Primary endpoints were ACR20 response rate and the change from baseline in HAQ-DI at Month 3.<sup>10</sup>

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# Study designs (cont'd)

## Ankylosing spondylitis

**Study AS-I:** A 48-week, randomised, phase 3 study (consisting of a 16-week double-blind phase, followed by a 32-week open-label phase) including 269 adult patients with active AS and an inadequate response to ≥2 NSAIDs. Randomisation was stratified by bDMARD treatment history in patients who were bDMARD naïve (~80%) or patients who had inadequate response to ≤2 TNFi or had prior bDMARD (TNFi or non-TNFi) use without IR (~20%). At baseline, 207 patients were bDMARD naïve, and 62 patients were TNFi-IR or prior bDMARD users (non-IR). NSAIDs/COX-2 inhibitors, MTX, SSZ, or oral corticosteroids were allowed if patients were on a stable dosage at baseline. For patients taking XELJANZ, the mean age was 42.2 years (40 years for placebo), and most patients were male (87.2% for XELJANZ 5 mg BID, 79.4% for placebo). Patients taking XELJANZ in the trial had a mean disease duration since symptoms of 14.2 years (12.9 years for placebo), mean AS disease duration since diagnosis of 8.9 years (6.8 for placebo), and mean baseline BASDAI score of 6.4 (6.5 for placebo).<sup>1</sup>

The primary endpoint was to evaluate the proportion of patients who achieved an ASAS20 response at Week 16. To control for type I error at the 5% level for primary and certain secondary endpoints, 4 families of efficacy endpoints were tested in hierarchical sequences with a step-down approach. The first family, the global type I error-controlled endpoints at Week 16, included ASAS20 response, ASAS40 response, ΔASDAS (CRP), ΔhsCRP, ΔASQoL, ΔSF-36v2 PCS score, ΔBASMI, and ΔFACIT-F total score. Upon meeting statistical significance for ASAS20 response at Week 16, the second family included ΔASAS components at Week 16, and included testing for ΔPtGA, Δtotal back pain, ΔBASFI, and Δmorning stiffness (inflammation). The third family, ASAS20 response over time, and the fourth family, ASAS40 response over time, were each tested in the following sequence: Weeks 16, 12, 8, 4, and 2. In each family, statistical significance could be declared only if the prior endpoint (or timepoint) in the sequence met the requirements for significance. Nonresponder imputation was applied to missing data for ASAS response rates.<sup>1</sup>

## Juvenile idiopathic arthritis

**Study JIA-I:** A 44-week, 2-part study (consisting of an 18-week, open-label, run-in phase, followed by a 26-week, double-blind, placebo-controlled, randomised phase<sup>a</sup>) in patients 2 to <18 years of age with pJIA (including RF-positive or RF-negative polyarthritis, eOA, and systemic JIA with active arthritis and no current systemic

symptoms) and patients 2 to <18 years of age with jPsA and ERA. However, the pJIA efficacy population only includes the subgroups with either RF-positive or RF-negative polyarthritis or eOA; inconclusive results have been seen in the subgroup of patients with systemic JIA with active arthritis and no current systemic symptoms. Patients with jPsA are included as a separate efficacy subgroup. ERA patients are not included in the efficacy analysis.<sup>2,3</sup>

A total of 225 patients were enrolled in the 18-week open-label run-in phase and received XELJANZ/ XELJANZ Oral Solution dosed at 5 mg BID or body weight-based equivalent BID. Only patients who achieved at least a JIA ACR30 response at the end of the run-in phase (Week 18) were randomised (1:1) to the double-blind phase. 173 patients (77%) met this criterion and were randomised into the double-blind phase to either XELJANZ/XELJANZ Oral Solution dosed at 5 mg BID or body weight-based equivalent BID (n=88) or placebo (n=85) for 26 weeks. Treatment with MTX was permitted but was not required during the study.<sup>3</sup>

The primary endpoint was JIA flare rate at Week 44. Flare is defined as a worsening of ≥30% in ≥3 of the 6 variables of the JIA core set, with ≤1 variable improving by ≥30%.<sup>2</sup>

## Ulcerative colitis

**OCTAVE Induction 1 and 2:** In 2 identical, 8-week induction phase 3 studies, 1139 patients with moderately to severely active UC (598 and 541 patients, respectively) were randomised to XELJANZ 10 mg BID or placebo (4:1 ratio). The primary endpoint was remission. Patients on stable doses of oral aminosalicylates and corticosteroids (prednisone daily dose up to 25 mg or equivalent) were permitted to continue on their stable dosing. Concomitant immunosuppressants (immunomodulators or biological therapies) were not permitted.<sup>3,4</sup>

**OCTAVE Sustain:** In a 52-week maintenance phase 3 study, 593 patients who had completed the induction studies and achieved clinical response<sup>b</sup> were re-randomised to XELJANZ 10 mg BID, XELJANZ 5 mg BID, or placebo (1:1:1 ratio). The primary endpoint was remission. Patients were permitted to use stable doses of oral aminosalicylates, but initiation of corticosteroid tapering was required upon entrance to this study for patients who were receiving corticosteroids at baseline. Concomitant immunosuppressants (immunomodulators or biological therapies) were not permitted.<sup>3,4</sup>

The recommended dose of XELJANZ for AS is 5 mg BID or 11 mg QD.<sup>3</sup> The recommended dose of XELJANZ for UC is 10 mg BID for 8-week induction and 5 mg BID for maintenance.<sup>3</sup> The recommended dose of XELJANZ for active pJIA (RF+ or RF- PA and eOA) and jPsA in patients 2 years of age and older who have responded inadequately to previous therapy with DMARDs is based upon the following weight categories: body weight 10–<20 kg, 3.2 mg BID; 20–<40 kg, 4 mg BID; ≥40 kg, 5 mg BID.<sup>3</sup> Refer to product label for full prescribing information and considerations for use based on the risk/benefit profile for individual patients and presence of risk factors for VTE, MACE, and malignancy.<sup>3</sup>

<sup>a</sup>The 26-week double-blind phase is from Week 18 through Week 44 (on and after randomisation day).<sup>2,b</sup> Clinical response in OCTAVE Induction 1 and 2 was defined as a decrease from baseline total Mayo score of ≥3 points and ≥30%, plus a decrease in rectal bleeding subscore of ≥1 point or an absolute rectal bleeding subscore of 0 or 1.<sup>5</sup>

ACR30, ≥30% improvement in American College of Rheumatology score; AS, ankylosing spondylitis; ASAS, Assessment of SpondyloArthritis International Society; ASDAS(CRP), Ankylosing Spondylitis Disease Activity Score based on C-reactive protein; ASQoL, Ankylosing Spondylitis Quality of Life; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; bDMARD, biologic disease-modifying antirheumatic drug; BID, twice daily; COX-2, cyclo-oxygenase 2; ERA, enthesitis-related arthritis; eOA, extended oligoarthritis; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; hsCRP, high-sensitivity C-reactive protein; IR, inadequate response; JIA, juvenile idiopathic arthritis; jPsA, juvenile psoriatic arthritis; MACE, major adverse cardiovascular events; MTX, methotrexate; NSAID, nonsteroidal anti-inflammatory drug; PA, polyarticular; PCS, Physical Component Summary; pJIA, polyarticular juvenile idiopathic arthritis; PtGA, Patient Global Assessment; QD, once daily; RF, rheumatoid factor; SF-36v2, 36-Item Short Form Health Survey, version 2; SSZ, sulfasalazine; TNFi, tumour necrosis factor inhibitor; UC, ulcerative colitis; VTE, venous thromboembolism.

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# Study designs (cont'd)

## Ulcerative colitis

**OCTAVE Open** was a phase 3, multicentre, open-label, long-term extension study. Eligible patients included OCTAVE Induction 1 and 2 nonresponders and OCTAVE Sustain completers and treatment failures.<sup>a</sup> Patients in remission at OCTAVE Open baseline received XELJANZ 5 mg BID (N=175). All other patients received XELJANZ 10 mg BID (N=769). Patients received XELJANZ for up to 7.0 years (median treatment duration: 4.2 years, XELJANZ 5 mg BID; 1.8 years, XELJANZ 10 mg BID). The primary and secondary objectives, respectively, were to assess the safety and tolerability and to evaluate efficacy of long-term XELJANZ therapy in patients with UC. This analysis investigated the maintenance of efficacy by examining a cohort of patients in remission after 52 weeks of XELJANZ treatment in OCTAVE Sustain who subsequently received open-label, long-term treatment with XELJANZ 5 mg BID in OCTAVE Open.<sup>1</sup>

The recommended dose of XELJANZ for UC is 10 mg BID for 8-week induction and 5 mg BID for maintenance. When induction treatment is complete, the dosage should be decreased from 10 mg BID to 5 mg BID, and the lowest effective dose needed to maintain response should be used. Refer to product label for full prescribing information and considerations for use based on the risk/benefit profile for individual patients and presence of risk factors for VTE, MACE, and malignancy.<sup>2</sup>

<sup>a</sup>Treatment failure in OCTAVE Sustain was defined as an increase in total Mayo score of ≥3 points from baseline of OCTAVE Sustain, accompanied by an increase in rectal bleeding subscore of ≥1 point and an increase of endoscopic subscore (centrally read) of ≥1 point (yielding an absolute endoscopic subscore of ≥2), after a minimum of 8 weeks of treatment in the study.<sup>1</sup>

BID, twice daily; MACE, major adverse cardiovascular events; UC, ulcerative colitis; VTE, venous thromboembolism.

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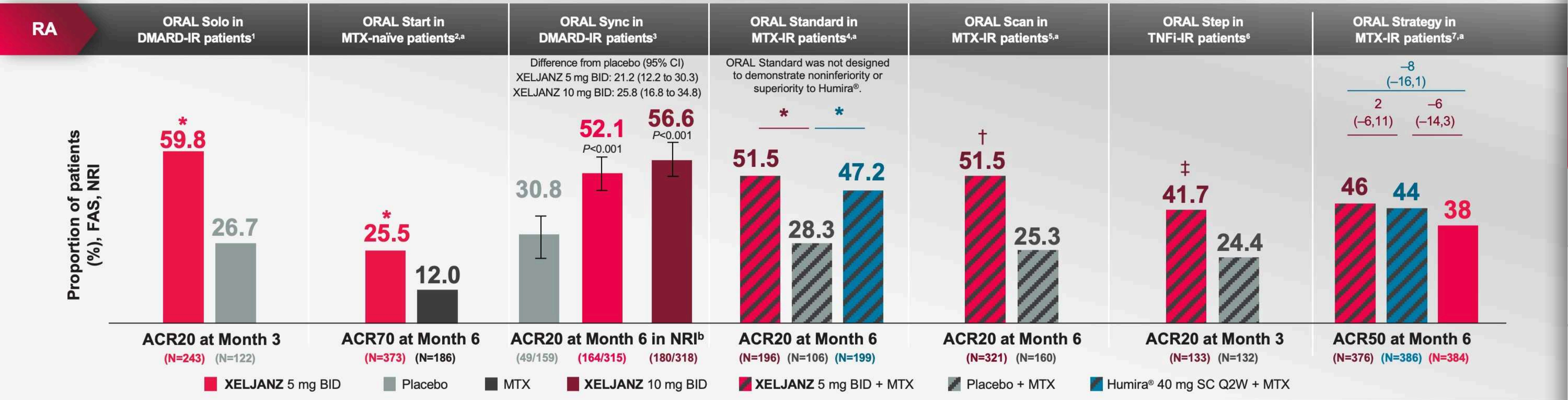
HIGHER-RISK  
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# XELJANZ<sup>®</sup> demonstrated efficacy across a wide range of patients with RA

## Primary endpoint results in RA clinical trials



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Rapid response

Durable response

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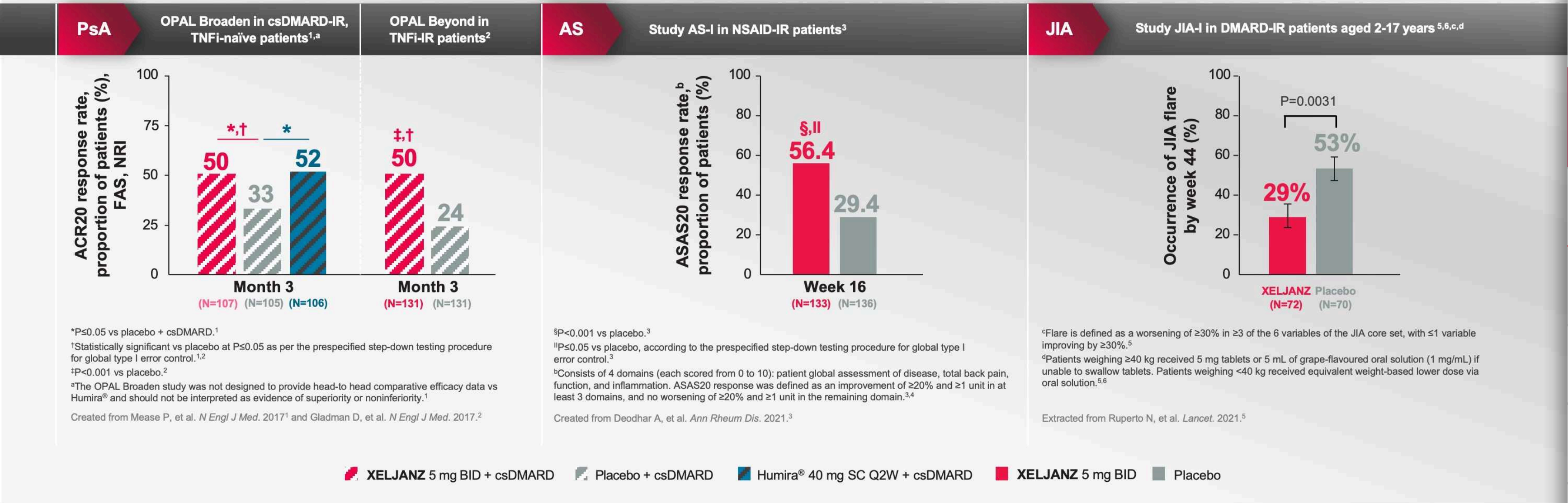
Limitations

References



# XELJANZ<sup>®</sup> demonstrated efficacy among patients with PsA, AS, and JIA

## Primary endpoint results in PsA, AS, and JIA clinical trials



ACR20, ≥20% improvement in American College of Rheumatology score; AS, ankylosing spondylitis; ASAS, Assessment of SpondyloArthritis international Society; BID, twice daily; csDMARD, conventional synthetic disease-modifying antirheumatic drug; DMARD, disease-modifying antirheumatic drug; FAS, full analysis set; IR, inadequate responder; JIA, juvenile idiopathic arthritis; NRI, nonresponder imputation; NSAID, nonsteroidal anti-inflammatory drug; OPAL, Oral Psoriatic Arthritis Trial; PsA, psoriatic arthritis; Q2W, every 2 weeks; SC, subcutaneous; TNFi, tumour necrosis factor inhibitor. Humira is a registered trademark of AbbVie Inc.



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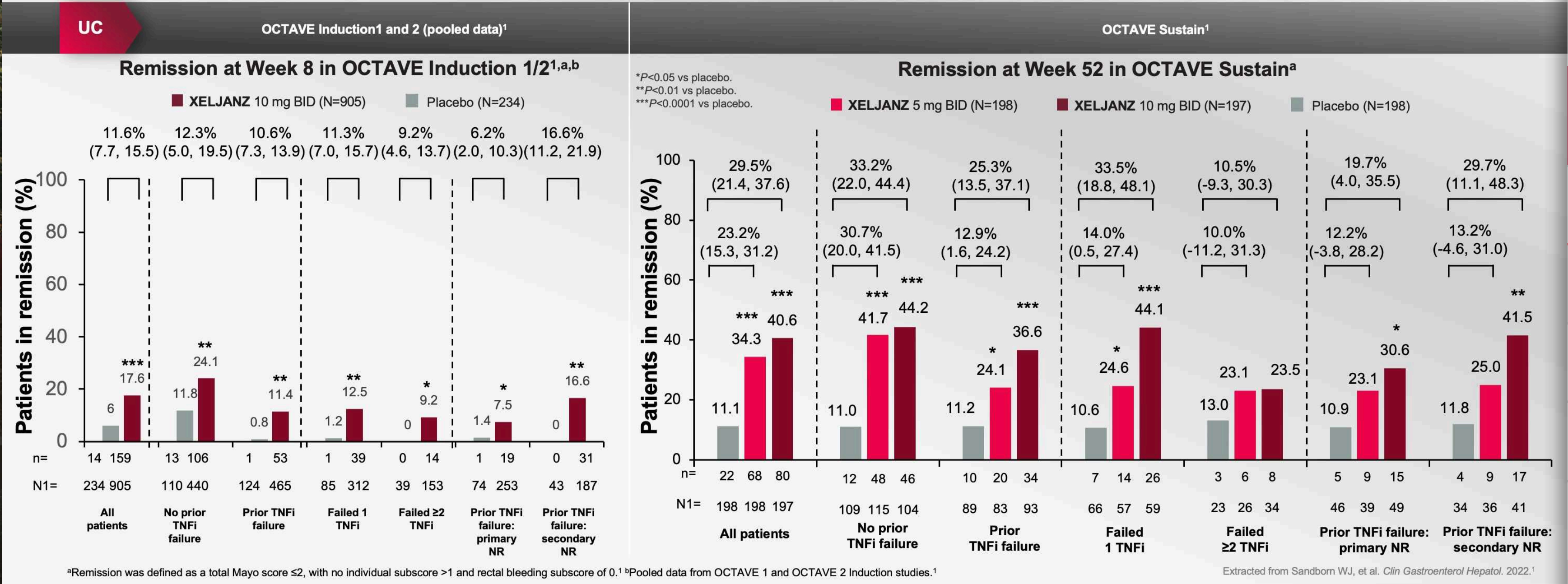
Limitations

References



# XELJANZ<sup>®</sup> demonstrated efficacy among patients with UC

## Primary endpoint results in UC clinical trials in patients with moderately to severely active UC





# XELJANZ<sup>®</sup> delivered rapid responses across 5 indications

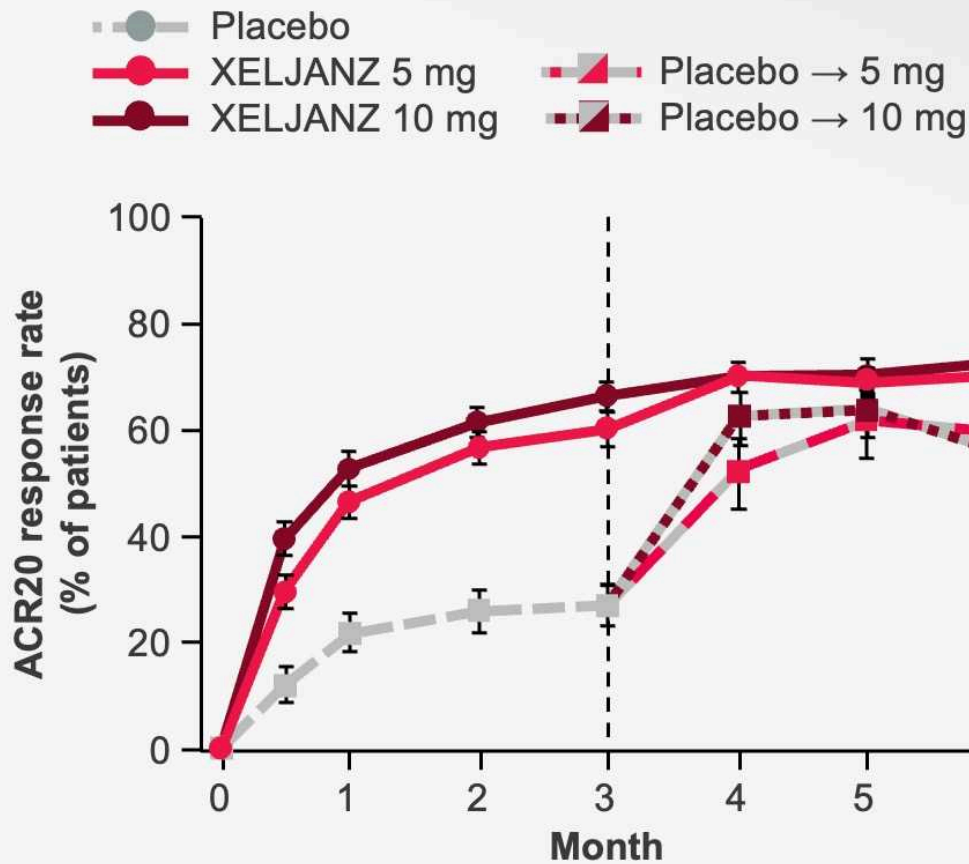


Results seen in  
**as early as 2 WEEKS** in RA and PsA  
Not actual patients.

RA

ORAL Solo in DMARD-IR patients<sup>1</sup>

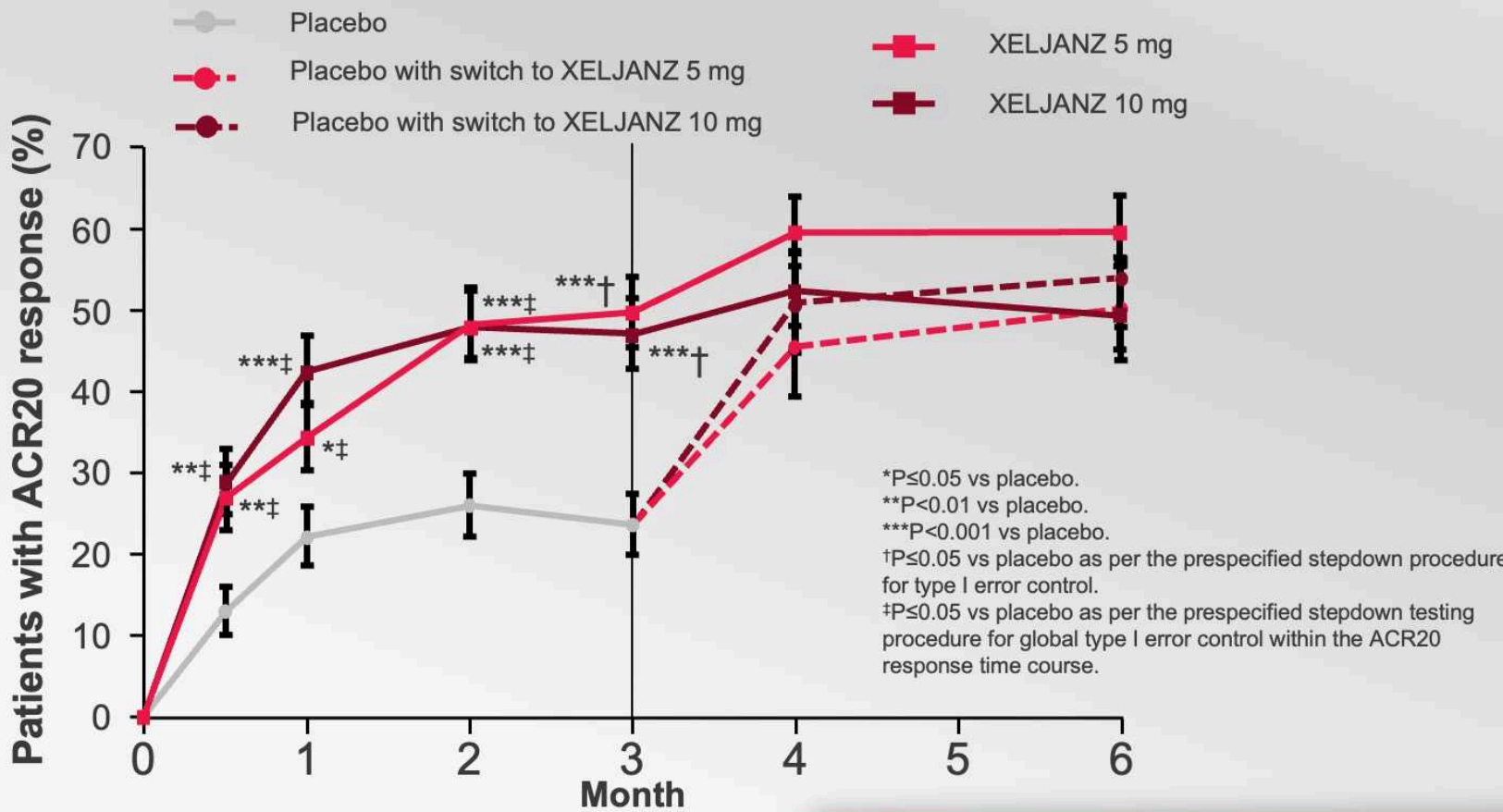
## Primary efficacy analysis<sup>1,a</sup>



PsA

OPAL Broaden<sup>b</sup> in csDMARD-IR patients<sup>2</sup>

## ACR20 response through 6 months<sup>2,b</sup>



Please see [study limitations](#)

XELJANZ 5 mg BID or 11 mg prolonged release QD are the only approved dosages for the treatment of RA and PsA, which should not be exceeded.<sup>3</sup>

<sup>a</sup>Analyses were performed in the modified intention-to-treat population (all patients who underwent randomisation and who received  $\geq 1$  dose of study medication). The dashed vertical line at the 3-month mark shows the time at which all the patients in the placebo group were switched to XELJANZ (either 5 mg or 10 mg dose). I bars indicate standard errors.<sup>1</sup>

<sup>b</sup>ACR20 was defined as a 20% reduction from baseline in the number of tender or swollen joints and a 20% improvement in  $\geq 3$  other important domains. Data from the placebo groups were pooled for visits at or before 3 months. The vertical line at 3 months indicates the end of the placebo-controlled period. Missing data regarding the ACR20 response were imputed as no response (at 3 months, data were missing for 15 patients in the pooled placebo group, for 7 patients in the XELJANZ 5 mg group, and for 12 patients in the XELJANZ 10 mg group).<sup>2</sup>

ACR20,  $\geq 20\%$  improvement in American College of Rheumatology score; BID, twice daily; csDMARD, conventional synthetic disease-modifying antirheumatic drug; IR, inadequate response; OPAL, Oral Psoriatic Arthritis Trial; ORAL, Oral Rheumatoid Arthritis Trial; PsA, psoriatic arthritis; QD, once daily; RA, rheumatoid arthritis.

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# XELJANZ<sup>®</sup> delivered rapid responses across 5 indications

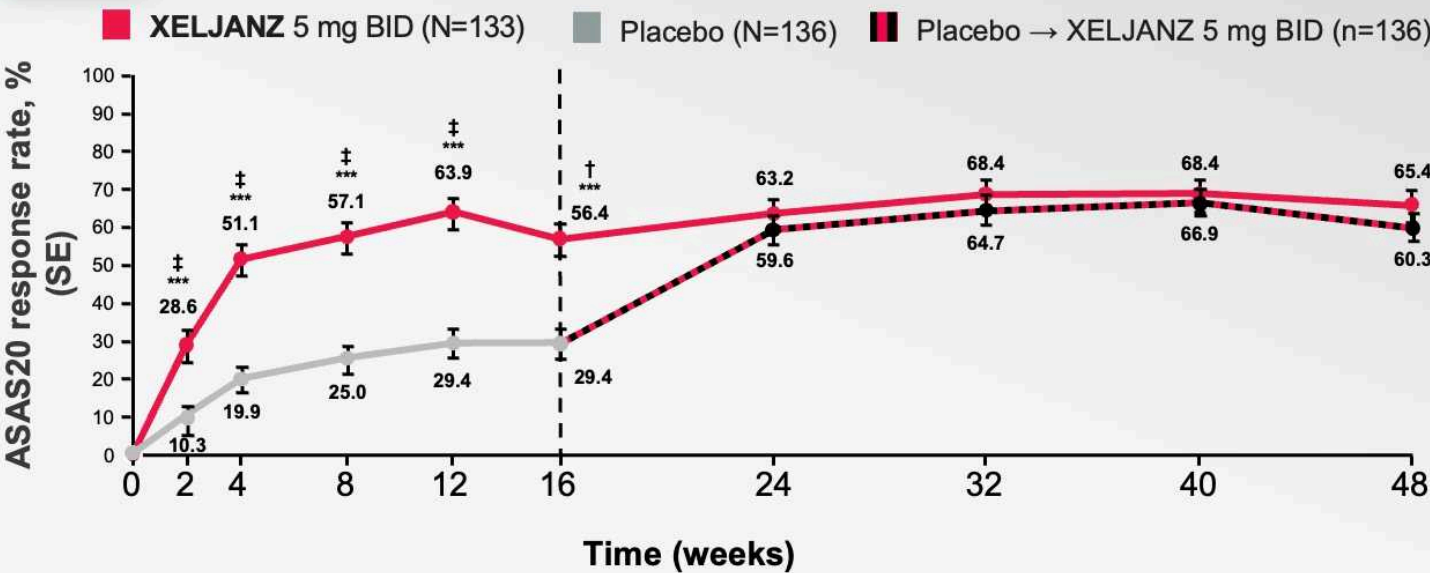


Results seen in  
**as early as 2 WEEKS** in AS and JIA  
Not actual patients.



Results seen in  
**as early as 3 DAYS** in UC  
Not an actual patient.

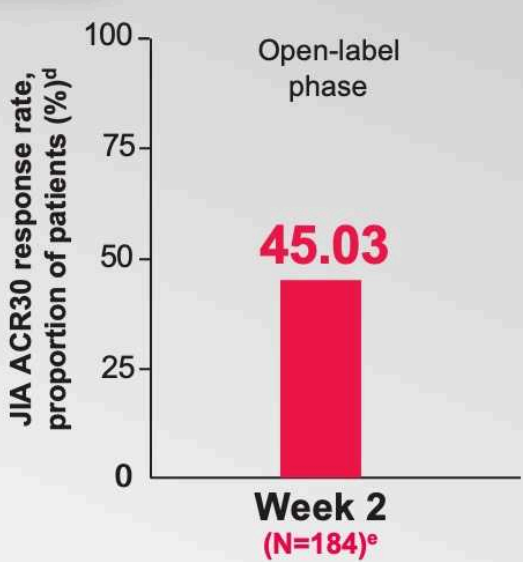
## AS ASAS20<sup>a</sup> | AS-I in NSAID-IR/IT patients<sup>1,b,c</sup>



\*\*\*P<0.001 vs placebo.<sup>1</sup>  
<sup>1</sup>P≤0.05 vs placebo, according to the prespecified step-down testing procedure for global type I error control.<sup>1</sup>  
<sup>2</sup>P≤0.05 vs placebo, according to the prespecified step-down testing procedure for type I error control of ASAS response over time.<sup>1</sup>

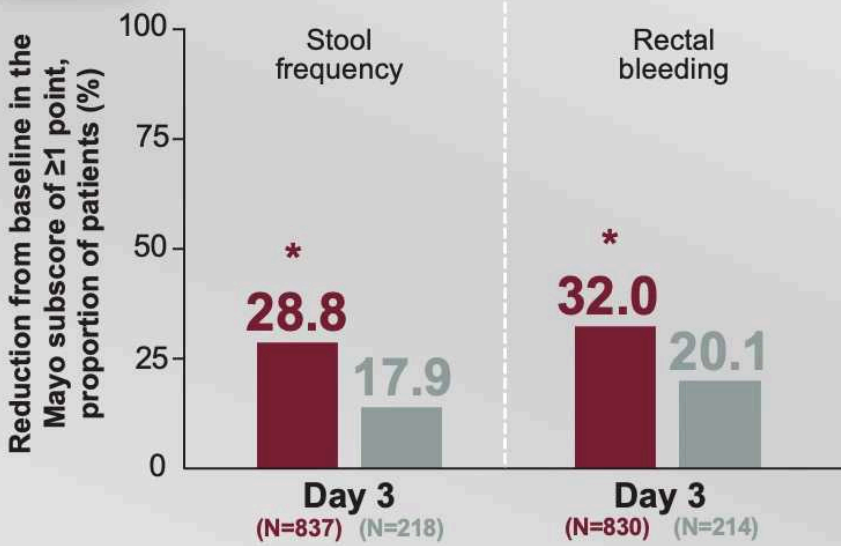
Extracted from Deodhar A, et al. *Ann Rheum Dis.* 2021.<sup>1</sup>

## JIA Study JIA-I in DMARD-IR patients aged 2-17 years<sup>2,3</sup>



Created from XELJANZ SmPC.<sup>2</sup>

## UC OCTAVE Induction 1 and 2 (pooled data)<sup>4</sup>



\*P<0.01 vs placebo.<sup>4</sup>

Created from Hanauer S, et al. *Clin Gastroenterol Hepatol.* 2019.<sup>4</sup>

XELJANZ 5 mg BID XELJANZ 10 mg BID Placebo

<sup>a</sup>ASAS20 at Week 16 was the primary endpoint. ASAS20 consists of 4 domains (each scored from 0 to 10): patient global assessment of disease, total back pain, function, and inflammation. ASAS20 response was defined as an improvement of ≥20% and ≥1 unit in ≥3 domains, and no worsening of ≥20% and ≥1 unit in the remaining domain.<sup>1,5</sup>  
<sup>b</sup>Data up to Week 16 are from the Week 16 analysis; data cut-off 19 December 2019; data snapshot 29 January 2020. Data for Weeks 24–48 are from the Week 48 final analysis. Patients receiving placebo advanced to XELJANZ 5 mg BID at Week 16 (dashed line). Up to Week 16, response rate was tested in hierarchical sequence to control for type I error: Weeks 16, 12, 8, 4, and 2. Statistical significance could be declared only if the prior timepoints in the sequence met the requirements for significance (P≤0.05). After Week 16, there was no type I error control. Normal approximation adjusting for the stratification factor (bDMARD treatment history: bDMARD naïve vs TNFi-IR or prior bDMARD use without IR) derived from the clinical database via the Cochran-Mantel-Haenszel approach was used. Missing response was considered as non response.<sup>1</sup>  
<sup>c</sup>Week 2 was the first measurement post-baseline.<sup>1</sup>  
<sup>d</sup>The JIA ACR30 response criteria are 3 of 6 JIA core set variables improving ≥30% with ≤1 out of 6 JIA core set variables worsening by ≥30%. For systemic JIA, the absence of spiking fever related to systemic JIA is also required.<sup>3</sup>  
<sup>e</sup>Patients received XELJANZ 5 mg BID or body weight-based equivalent of XELJANZ Oral Solution BID. Oral solution was used for patients weighing <40 kg.<sup>2,3</sup>

Please see [study limitations](#)

ACR20, ≥20% improvement in American College of Rheumatology score; AS, ankylosing spondylitis; ASAS, Assessment of SpondyloArthritis International Society; bDMARD, biologic disease-modifying antirheumatic drug; BID, twice daily; DMARD, disease-modifying antirheumatic drug; IR, inadequate response; IT, intolerant; JIA, juvenile idiopathic arthritis; NSAID, nonsteroidal anti-inflammatory drug; SE, standard error; SmPC, summary of product characteristics; TNFi, tumour necrosis factor inhibitor; UC, ulcerative colitis.

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# XELJANZ® delivered durable responses up to 8 years in patients with RA

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## Lasting symptom reduction up to 8 years

RA Proportion of patients achieving ACR50 response over time in the open-label LTE study<sup>1,2,a</sup>



RA Proportion of patients achieving ACR70 response over time in the open-label LTE study<sup>1,2,a</sup>



ACR50 and ACR70 were calculated with respect to qualifying index study data available for approximately 90% of patients. Italicised data were not reported in figure due to low patient numbers. Data for 12-month intervals are reported in the table. Database lock: 2 March 2017.<sup>1</sup>  
<sup>a</sup>Data are observed values with no imputation. Eligible patients began participation in the LTE studies upon conclusion of a qualifying phase 1/2/3 study; the exact time of entry varied from patient to patient.<sup>1</sup>  
<sup>b</sup>Includes all patients evaluable at each timepoint who received ≥1 dose of XELJANZ.<sup>1</sup>  
<sup>c</sup>XELJANZ 5 mg BID or 11 mg prolonged release QD are the only approved dosages for the treatment of RA, which should not be exceeded.<sup>3</sup>  
ACR50/70, ≥50/70% improvement in American College of Rheumatology score; BID, twice daily; LTE, long-term extension; QD, once daily; RA, rheumatoid arthritis.

Extracted from Wollenhaupt J, et al. *Arthritis Res Ther*. 2019 and supplementary appendix.<sup>2</sup>

Please see [limitations for all LTE studies](#)



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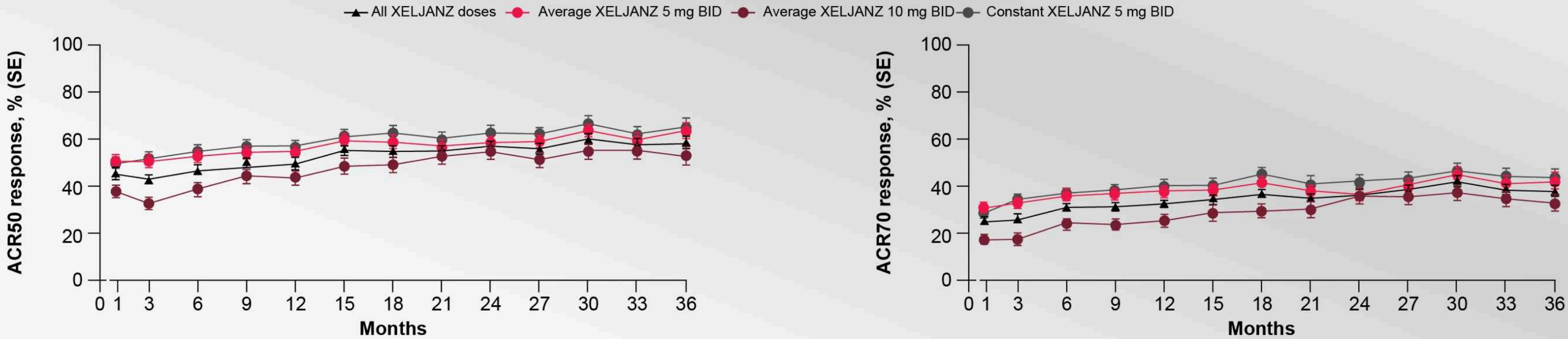
References



# XELJANZ® delivered durable responses up to 3 years in patients with PsA

## XELJANZ maintained efficacy up to 3 years

**PsA** Proportion of patients achieving ACR50/70 over time in the OPAL Balance LTE study<sup>1,a-c</sup>



| Number of patients                |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----------------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| All XELJANZ doses                 | 674 | 661 | 633 | 605 | 581 | 554 | 539 | 527 | 511 | 496 | 478 | 452 | 384 |
| Average XELJANZ 5 mg twice daily  | 391 | 381 | 359 | 346 | 333 | 320 | 313 | 307 | 299 | 291 | 278 | 259 | 207 |
| Average XELJANZ 10 mg twice daily | 283 | 280 | 274 | 259 | 248 | 234 | 226 | 220 | 212 | 205 | 200 | 193 | 177 |
| Constant XELJANZ 5 mg twice daily | 582 | 451 | 371 | 335 | 311 | 289 | 273 | 262 | 248 | 238 | 222 | 205 | 157 |

| Number of patients                |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----------------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| All XELJANZ doses                 | 676 | 662 | 636 | 607 | 582 | 555 | 538 | 527 | 512 | 496 | 476 | 453 | 384 |
| Average XELJANZ 5 mg twice daily  | 393 | 382 | 361 | 347 | 333 | 321 | 312 | 307 | 299 | 290 | 277 | 259 | 207 |
| Average XELJANZ 10 mg twice daily | 283 | 280 | 275 | 260 | 249 | 234 | 226 | 220 | 213 | 206 | 199 | 194 | 177 |
| Constant XELJANZ 5 mg twice daily | 584 | 452 | 373 | 336 | 311 | 290 | 272 | 262 | 248 | 237 | 221 | 205 | 157 |

<sup>a</sup>Datapoints are proportions with whiskers indicating SEs. Only evaluable patients at a visit of interest were included in the analysis, and missing values were not imputed. The dashed lines on the x-axes indicate the time between the baseline (Month 0) and Month 1, because baseline refers to the baseline visit of the qualifying study for patients who enrolled within the 14-day window from the last visit of the qualifying study, or the baseline visit of this LTE study for patients who enrolled outside of the 14-day window from the last visit of the qualifying study.<sup>1</sup>

<sup>b</sup>XELJANZ 5 mg BID or 11 mg prolonged release QD are the only approved dosages for the treatment of PsA, which should not be exceeded.<sup>2</sup>

<sup>c</sup>Data are observed values with no imputation. Eligible patients began participation in the LTE study upon conclusion of a qualifying phase 3 study; the exact time of entry varied from patient to patient.<sup>1</sup>

Extracted from Nash P, et al. *Lancet Rheumatol.* 2021.<sup>1</sup>

ACR50/70, ≥50/70% improvement in American College of Rheumatology score; BID, twice daily; LTE, long-term extension; OPAL, Oral Psoriatic Arthritis Trial; PsA, psoriatic arthritis; QD, once daily; SE, standard error.



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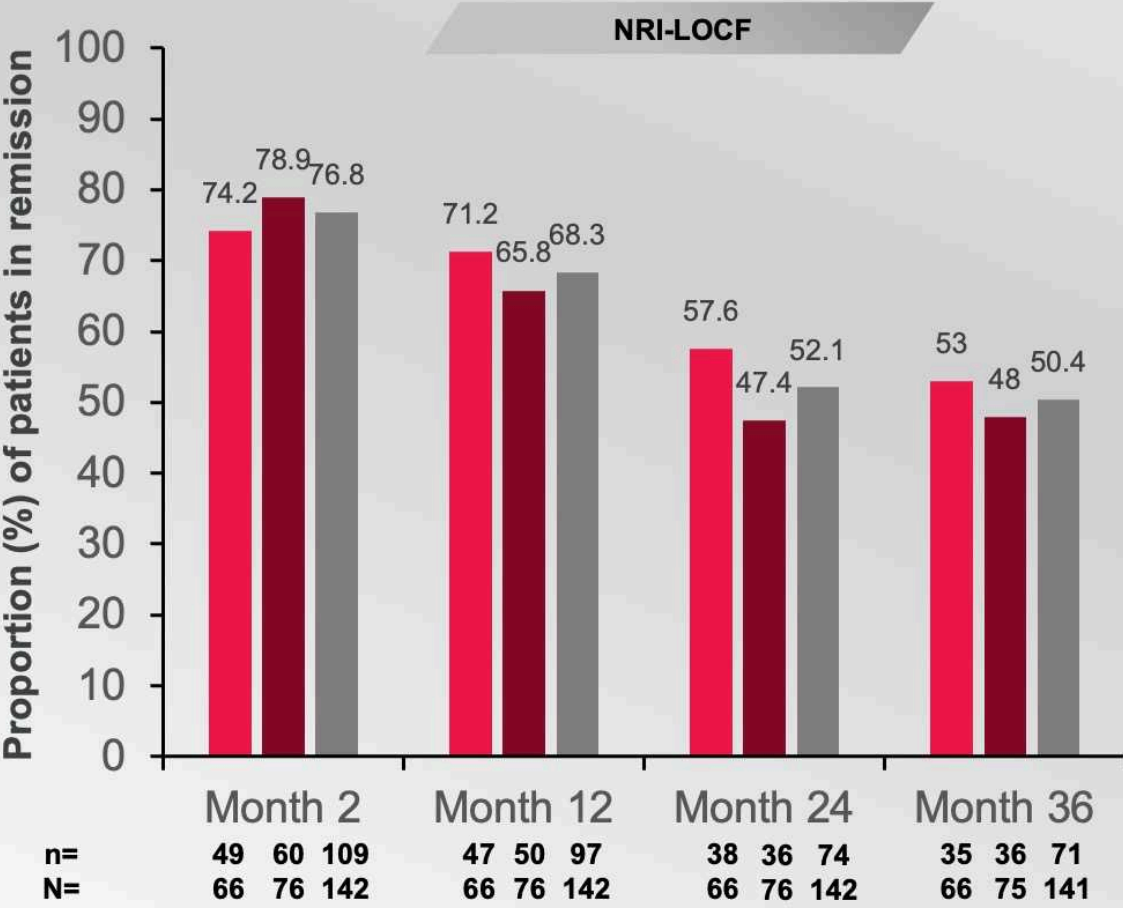
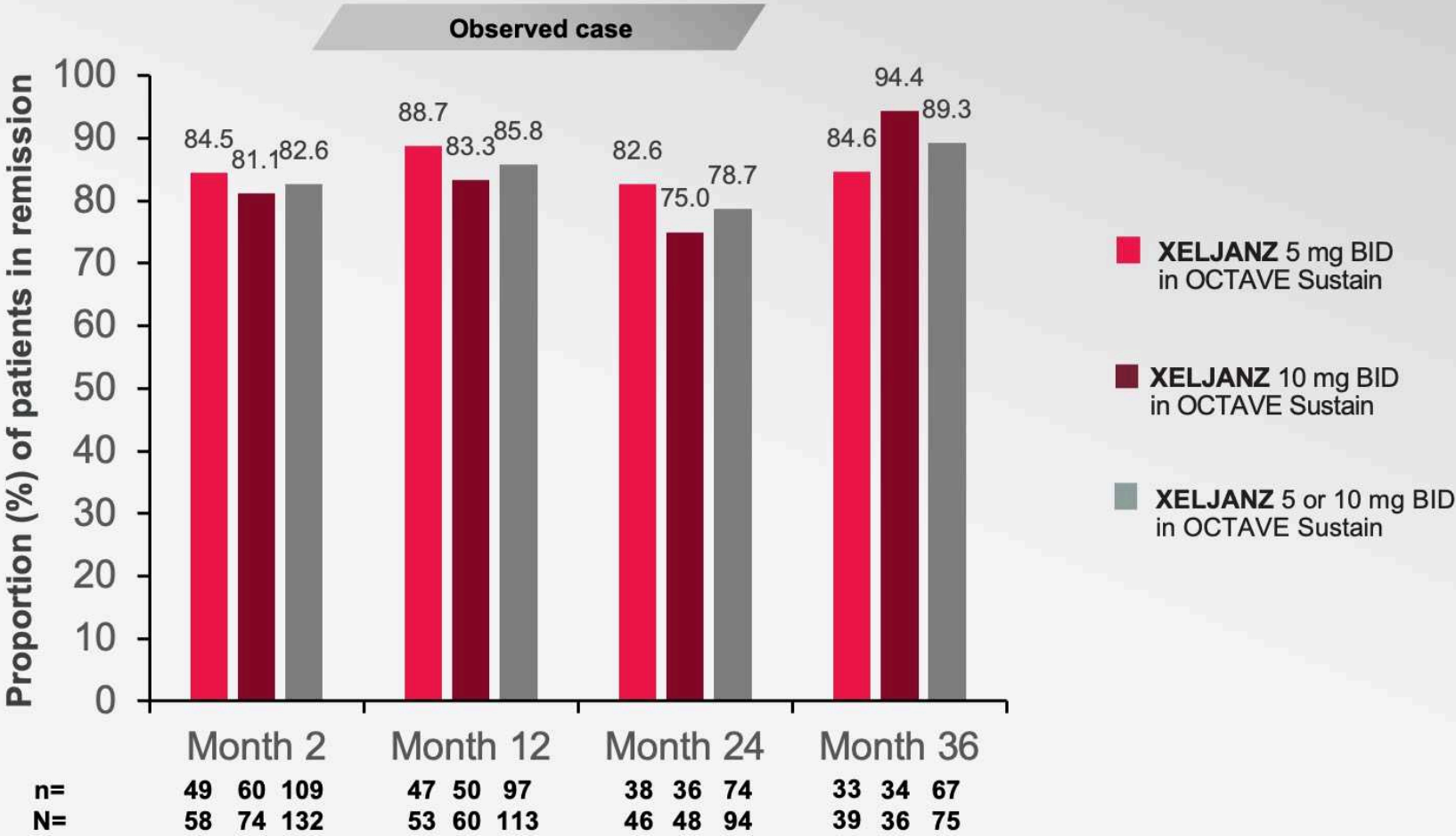




# XELJANZ® delivered durable responses up to 3 years in patients with UC

## Remission<sup>a</sup> maintained through 3 years

UC Proportion of patients achieving remission<sup>a</sup> in the open-label LTE study<sup>1</sup>



The recommended dose for maintenance treatment is XELJANZ 5 mg BID. When induction treatment is complete, the dosage should be decreased from 10 mg BID to 5 mg BID.<sup>2</sup>

<sup>a</sup>Clinical remission was defined as a total Mayo score ≤2, no individual subscore >1, and a rectal bleeding subscore of 0.<sup>1</sup>

Extracted from Colombel J-F, et al. *Clin Gastroenterol Hepatol.* 2022.<sup>1</sup>

BID, twice daily; LOCF, last observation carried forward; LTE, long-term extension; NRI, nonresponder imputation; UC, ulcerative colitis.



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# XELJANZ® delivered durable responses in AS and JIA

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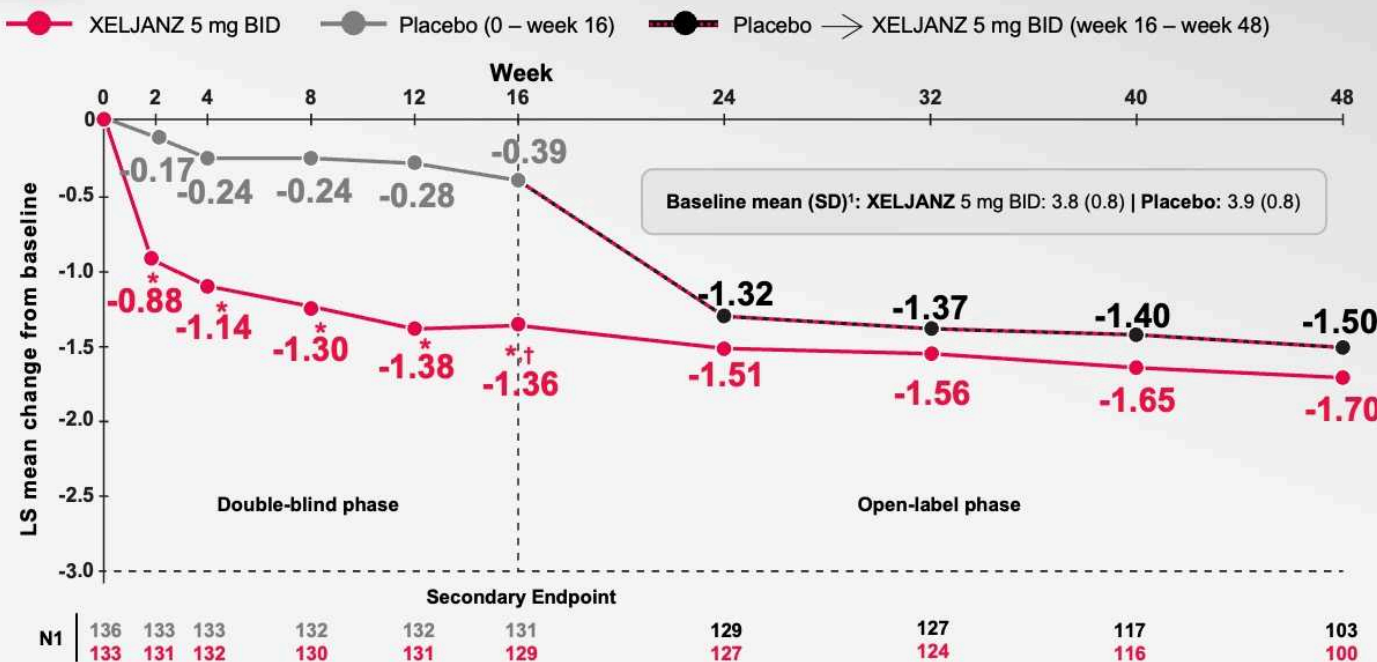
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## Improvement in disease activity was maintained from Week 16 through Week 48

AS ASDAS(CRP) in Study AS-I<sup>1,a,b</sup>



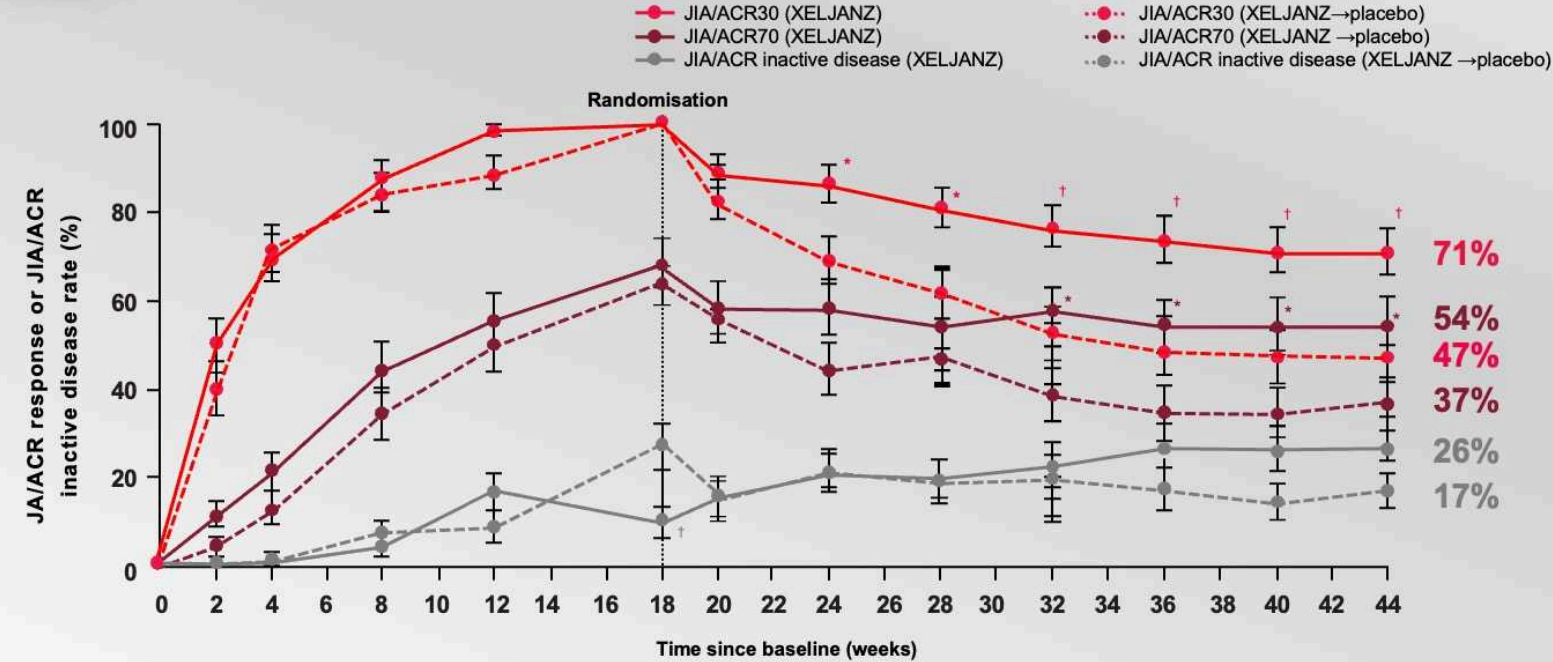
FAS: MMRM used without imputation for missing values.<sup>1</sup>  
\*P<0.001 vs placebo<sup>1</sup>  
†P≤0.05 vs placebo, according to the prespecified step-down testing procedure for global type I error control.<sup>1</sup>

<sup>a</sup>Post hoc analysis. Score calculated based on CRP level and patient-reported measures: patient global assessment of disease, total back pain, duration of morning stiffness, and peripheral joint pain/swelling. Higher scores indicate more disease activity. A score >3.5 points indicates very high disease activity. A score reduction of ≥1.1 points indicates a clinically important improvement in disease activity.<sup>1-4</sup>  
<sup>b</sup>The LLOQ of the hsCRP assay was 0.2 mg/L. For hsCRP values <LLOQ, they were set to 0.199 mg/L in all efficacy and safety analyses except for the ASDAS-related endpoints, where values <2 mg/L were set post hoc to 2 mg/L.<sup>1</sup>

In patients who achieved at least a JIA ACR30 response by the end of the open-label phase

## 71% of patients on XELJANZ maintained reduction of signs and symptoms of JIA through Week 44<sup>5</sup>

JIA ACR30 response rate in Study JIA-I<sup>5,c,d</sup>



\*P<0.05 vs placebo.<sup>5</sup>  
†P<0.01 vs placebo.<sup>5</sup>

<sup>c</sup>The JIA ACR30 response criteria are 3 of 6 JIA core set variables improving ≥30% with ≤1 out of 6 JIA core set variables worsening by ≥30%. For systemic JIA, the absence of spiking fever related to systemic JIA is also required.<sup>5</sup>  
<sup>d</sup>JIA ACR30 response rate at Week 44 was a type I error-controlled endpoint.<sup>5</sup>  
<sup>e</sup>Patients weighing ≥40 kg received 5 mg tablets or 5 mL of grape-flavoured oral solution (1 mg/mL) if unable to swallow tablets. Patients weighing <40 kg received equivalent weight-based lower dose via oral solution.<sup>5,6</sup>

ACR, American College of Rheumatology; ACR30/70, ≥30/70% improvement in American College of Rheumatology score; AS, ankylosing spondylitis; ASDAS, Ankylosing Spondylitis Disease Activity Score; ASDAS(CRP), Ankylosing Spondylitis Disease Activity Score based on C-reactive protein; BID, twice daily; CRP, C-reactive protein; FAS, full analysis set; hsCRP, high-sensitivity C-reactive protein; JIA, juvenile idiopathic arthritis; LLOQ, lower limit of quantification; LS, least squares; MMRM, mixed model for repeated measures; SD, standard deviation.



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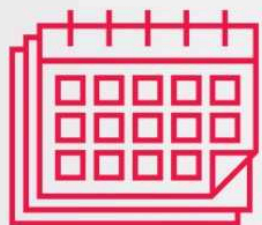
References



# Where rapid response meets durable efficacy



**Rapid response as early as 2 weeks** in patients with RA, PsA, AS, and JIA, and **3 days** in patients with UC<sup>1–6</sup>



**Durable response up to 8 years** in patients with RA and **3 years** in patients with PsA and UC<sup>7–9</sup>



**Robust clinical evidence and market experience** with **39 clinical trials** and **>450,000 PY of exposure in RA and PsA** globally<sup>4,5,10–15,a</sup>

<sup>a</sup>PMS data from the Pfizer safety database were collected between 6 November 2012 and 6 November 2021 (RA) and between 14 December 2017 and 6 November 2021 (PsA).<sup>15</sup>  
AS, ankylosing spondylitis; JIA, juvenile idiopathic arthritis; PMS, post-marketing surveillance; PsA, psoriatic arthritis; PY, patient-years; RA, rheumatoid arthritis; UC, ulcerative colitis.



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# ORAL Surveillance in patients with RA:

The prespecified noninferiority criterion was not met for the primary comparison of the combined XELJANZ doses with TNFi for adjudicated MACE and malignancies (excluding NMSC)<sup>1</sup>

Primary comparisons exceeded the prespecified noninferiority criterion of 1.8: for adjudicated MACE, the hazard ratio for the combined XELJANZ doses vs TNFi was 1.33 (95% CI 0.91–1.94); for adjudicated malignancies (excluding NMSC), the hazard ratio for the combined XELJANZ doses vs TNFi was 1.48 (95% CI 1.04–2.09).<sup>1</sup>

|                                                                  | XELJANZ 5 mg BID<br>(N=1455) | XELJANZ 10 mg BID<br>(N=1456) <sup>b</sup> | TNFi<br>(N=1451) |
|------------------------------------------------------------------|------------------------------|--------------------------------------------|------------------|
| Event <sup>a</sup>                                               |                              |                                            |                  |
| AE – no. (%)                                                     | 1333 (91.6)                  | 1344 (92.3)                                | 1308 (90.1)      |
| Serious AE – no. (%)                                             | 351 (24.1)                   | 390 (26.8)                                 | 306 (21.1)       |
| Discontinuation of trial treatment due to AE – no. (%)           |                              |                                            |                  |
| Permanent discontinuation <sup>c</sup>                           | 210 (14.4)                   | 304 (20.9)                                 | 210 (14.5)       |
| Temporary discontinuation <sup>d</sup>                           | 665 (45.7)                   | 736 (50.5)                                 | 576 (39.7)       |
| AEs of special interest                                          |                              |                                            |                  |
| Serious infection – no. (%)                                      | 141 (9.7)                    | 169 (11.6)                                 | 119 (8.2)        |
| Hazard ratio vs TNFi (95% CI)                                    | 1.17 (0.92, 1.50)            | 1.48 (1.17, 1.87)                          | Referent         |
| Adjudicated opportunistic infection – no. (%) <sup>e</sup>       | 39 (2.7)                     | 44 (3.0)                                   | 21 (1.4)         |
| Hazard ratio vs TNFi (95% CI)                                    | 1.82 (1.07, 3.09)            | 2.17 (1.29, 3.66)                          | Referent         |
| All herpes zoster, serious and nonserious – no. (%) <sup>f</sup> | 180 (12.4)                   | 178 (12.2)                                 | 58 (4.0)         |
| Hazard ratio vs TNFi (95% CI)                                    | 3.28 (2.44, 4.41)            | 3.39 (2.52, 4.55)                          | Referent         |
| Adjudicated hepatic event – no. (%)                              | 46 (3.2)                     | 72 (4.9)                                   | 35 (2.4)         |
| Hazard ratio vs TNFi (95% CI)                                    | 1.29 (0.83, 2.00)            | 2.14 (1.43, 3.21)                          | Referent         |
| Adjudicated NMSC – no. (%)                                       | 31 (2.1)                     | 33 (2.3)                                   | 16 (1.1)         |
| Hazard ratio vs TNFi (95% CI)                                    | 1.90 (1.04, 3.47)            | 2.16 (1.19, 3.92)                          | Referent         |
| Adjudicated pulmonary embolism – no. (%)                         | 9 (0.6)                      | 24 (1.6)                                   | 3 (0.2)          |
| Hazard ratio vs TNFi (95% CI)                                    | 2.93 (0.79, 10.83)           | 8.26 (2.49, 27.43)                         | Referent         |
| Adjudicated DVT – no. (%)                                        | 11 (0.8)                     | 15 (1.0)                                   | 7 (0.5)          |
| Hazard ratio vs TNFi (95% CI)                                    | 1.54 (0.60, 3.97)            | 2.21 (0.90, 5.43)                          | Referent         |
| Adjudicated VTE – no. (%)                                        | 17 (1.2)                     | 34 (2.3)                                   | 10 (0.7)         |
| Hazard ratio vs TNFi (95% CI)                                    | 1.66 (0.76, 3.63)            | 3.52 (1.74, 7.12)                          | Referent         |
| Adjudicated death from any cause – no. (%)                       | 26 (1.8)                     | 39 (2.7)                                   | 17 (1.2)         |
| Hazard ratio vs TNFi (95% CI)                                    | 1.49 (0.81, 2.74)            | 2.37 (1.34, 4.18)                          | Referent         |

- ORAL Surveillance was a randomised, open-label, noninferiority, post-authorisation safety study of XELJANZ in patients with RA ≥50 years of age with ≥1 additional CV risk factor<sup>1</sup>
- Incidence rates were observed to be higher for XELJANZ compared with TNFi<sup>1</sup>

XELJANZ 5 mg BID and 11 mg prolonged-release QD are the only approved dosages for the treatment of RA, which should not be exceeded. XELJANZ 10 mg BID is not licensed for RA.<sup>2</sup>

<sup>a</sup>Shown are AEs that emerged or worsened during the 28-day on-treatment period, which was defined as the minimum of the date of last contact or the date of the last dose of a trial treatment plus 28 days.<sup>1</sup>

<sup>b</sup>For patients assigned to receive XELJANZ at a dose of 10 mg BID who had their dose reduced to 5 mg BID, the data collected after patients had been switched to 5 mg BID were counted in the group receiving 10 mg BID.<sup>1</sup>

<sup>c</sup>Data are based on the AE and disposition case report forms.<sup>1</sup>

<sup>d</sup>At the discretion of the investigator, discontinuations of trial medication were allowed, not to exceed 2 months, for safety issues.<sup>1</sup>

<sup>e</sup>Also included are opportunistic herpes zoster and tuberculosis events.<sup>1</sup>

<sup>f</sup>Included are herpes zoster adjudicated as an opportunistic infection and nonadjudicated herpes zoster events.<sup>1</sup>

Extracted from Ytterberg SR, et al. *N Engl J Med*. 2022.<sup>1</sup>

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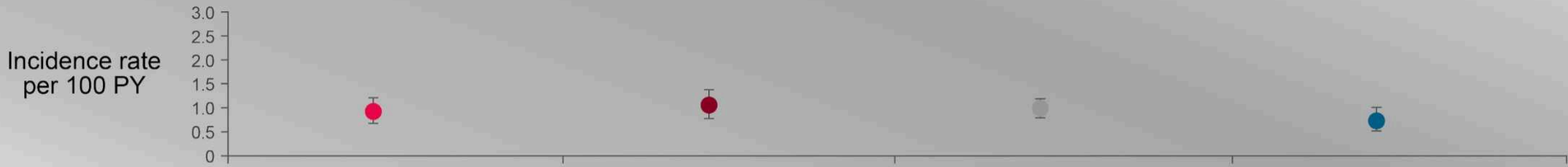




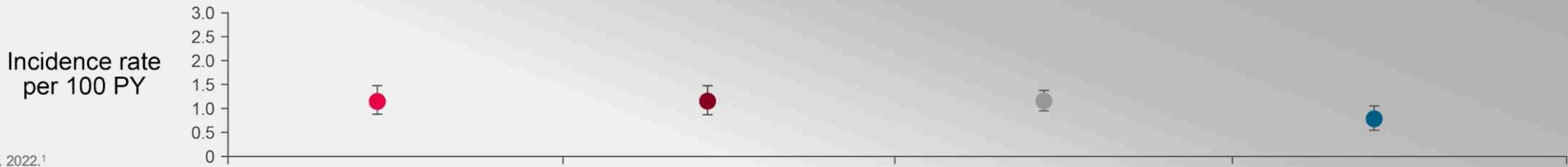
# ORAL Surveillance in patients with RA:

The prespecified noninferiority criterion was not met for the primary comparison of the combined XELJANZ doses with TNFi for adjudicated MACE and malignancies (excluding NMSC)<sup>1</sup>

| Adjudicated MACE                               | XELJANZ 5 mg BID | XELJANZ 10 mg BID | Combined XELJANZ doses | TNFi             |
|------------------------------------------------|------------------|-------------------|------------------------|------------------|
| No. of patients with first event/total no. (%) | 47/1455 (3.2)    | 51/1456 (3.5)     | 98/2911 (3.4)          | 37/1451 (2.5)    |
| No. of PY                                      | 5166.32          | 4871.96           | 10,038.28              | 5045.27          |
| Incidence rate per 100 PY (95% CI)             | 0.91 (0.67–1.21) | 1.05 (0.78–1.38)  | 0.98 (0.79–1.19)       | 0.73 (0.52–1.01) |
| NNH (PY) vs TNFi <sup>a</sup>                  | 567              | 319               | –                      | –                |
| NNH (over 5-year period) vs TNFi <sup>a</sup>  | 113              | 64                | –                      | –                |



| Adjudicated malignancies (excluding NMSC)      | XELJANZ 5 mg BID | XELJANZ 10 mg BID | Combined XELJANZ doses | TNFi             |
|------------------------------------------------|------------------|-------------------|------------------------|------------------|
| No. of patients with first event/total no. (%) | 62/1455 (4.3)    | 60/1456 (4.1)     | 122/2911 (4.2)         | 42/1451 (2.9)    |
| No. of PY                                      | 5491.48          | 5311.71           | 10,803.19              | 5482.30          |
| Incidence rate per 100 PY (95% CI)             | 1.13 (0.87–1.45) | 1.13 (0.86–1.45)  | 1.13 (0.94–1.35)       | 0.77 (0.55–1.04) |
| NNH (PY) vs TNFi <sup>a</sup>                  | 276              | 275               | –                      | –                |
| NNH (over 5-year period) vs TNFi <sup>a</sup>  | 55               | 55                | –                      | –                |



Extracted from Ytterberg et al. *N Engl J Med*. 2022.<sup>1</sup>

XELJANZ 5 mg BID and 11 mg prolonged-release QD are the only approved dosages for the treatment of RA, which should not be exceeded. XELJANZ 10 mg BID is not licenced for RA.<sup>2</sup>  
<sup>a</sup>NNH was the number of PY of exposure to XELJANZ required to have 1 additional adverse event, relative to a TNFi. NNH over a period of 5 years was the number of patients who would need to be treated for that duration with XELJANZ rather than a TNFi to result in 1 additional adverse event. Calculations were performed post hoc.<sup>1</sup>  
BID, twice daily; CI, confidence interval; MACE, major adverse cardiovascular events; NMSC, nonmelanoma skin cancer; NNH, number needed to harm; ORAL, Oral Rheumatoid Arthritis Trial; PY, patient-years; TNFi, tumour necrosis factor inhibitor.

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# ORAL Surveillance in patients with RA:

The incidence rates of AEs of special interest were higher with XELJANZ compared with TNFis<sup>1</sup>

IRs (95% CIs) of AEs of special interest and HRs (95% CIs) of XELJANZ dose comparisons (safety analysis set, 28-day on-treatment time)

|                                                         | XELJANZ<br>5 mg BID<br>(N=1455) | XELJANZ<br>10 mg BID <sup>a</sup><br>(N=1456) | TNFi<br>(N=1451)    |                                     | XELJANZ<br>5 mg BID<br>(N=1455) | XELJANZ<br>10 mg BID <sup>a</sup><br>(N=1456) | TNFi<br>(N=1451)    |                                        | XELJANZ<br>5 mg BID<br>(N=1455) | XELJANZ<br>10 mg BID <sup>a</sup><br>(N=1456) | TNFi<br>(N=1451)    |
|---------------------------------------------------------|---------------------------------|-----------------------------------------------|---------------------|-------------------------------------|---------------------------------|-----------------------------------------------|---------------------|----------------------------------------|---------------------------------|-----------------------------------------------|---------------------|
| <b>Serious infections</b>                               |                                 |                                               |                     | <b>Adjudicated hepatic events</b>   |                                 |                                               |                     | <b>Adjudicated DVT</b>                 |                                 |                                               |                     |
| Total PY of exposure                                    | 4931.40                         | 4641.93                                       | 4878.88             | Total PY of exposure                | 5109.65                         | 4755.30                                       | 4996.20             | Total PY of exposure                   | 5156.30                         | 4854.20                                       | 5032.05             |
| IR (95% CI)                                             | 2.86 (2.41 to 3.37)             | 3.64 (3.11 to 4.23)                           | 2.44 (2.02 to 2.92) | IR (95% CI)                         | 0.90 (0.66 to 1.20)             | 1.51 (1.18 to 1.91)                           | 0.70 (0.49 to 0.97) | IR (95% CI)                            | 0.21 (0.11 to 0.38)             | 0.31 (0.17 to 0.51)                           | 0.14 (0.06 to 0.29) |
| HR (95% CI) versus XELJANZ 5 mg BID                     | Referent                        | 1.26 (1.01 to 1.58)                           | –                   | HR (95% CI) versus XELJANZ 5 mg BID | Referent                        | 1.67 (1.15 to 2.41)                           | –                   | HR (95% CI) versus XELJANZ 5 mg BID    | Referent                        | 1.44 (0.66 to 3.14)                           | –                   |
| <b>Adjudicated opportunistic infections<sup>b</sup></b> |                                 |                                               |                     | <b>Adjudicated NMSC</b>             |                                 |                                               |                     | <b>Adjudicated VTE</b>                 |                                 |                                               |                     |
| Total PY of exposure                                    | 5117.24                         | 4822.21                                       | 5011.45             | Total PY of exposure                | 5115.64                         | 4811.57                                       | 5019.75             | Total PY of exposure                   | 5150.95                         | 4823.09                                       | 5024.75             |
| IR (95% CI)                                             | 0.76 (0.54 to 1.04)             | 0.91 (0.66 to 1.22)                           | 0.42 (0.26 to 0.64) | IR (95% CI)                         | 0.61 (0.41 to 0.86)             | 0.69 (0.47 to 0.96)                           | 0.32 (0.18 to 0.52) | IR (95% CI)                            | 0.33 (0.19 to 0.53)             | 0.70 (0.49 to 0.99)                           | 0.20 (0.10 to 0.37) |
| HR (95% CI) versus XELJANZ 5 mg BID                     | Referent                        | 1.19 (0.78 to 1.84)                           | –                   | HR (95% CI) versus XELJANZ 5 mg BID | Referent                        | 1.14 (0.70 to 1.86)                           | –                   | HR (95% CI) versus XELJANZ 5 mg BID    | Referent                        | 2.12 (1.18 to 3.79)                           | –                   |
| <b>All herpes zoster<sup>c,d</sup></b>                  |                                 |                                               |                     | <b>Adjudicated PE</b>               |                                 |                                               |                     | <b>Adjudicated all-cause mortality</b> |                                 |                                               |                     |
| Total PY of exposure                                    | 4802.96                         | 4514.39                                       | 4918.05             | Total PY of exposure                | 5157.43                         | 4836.57                                       | 5036.74             | Total PY of exposure                   | 5173.44                         | 4873.27                                       | 5044.04             |
| IR (95% CI)                                             | 3.75 (3.22 to 4.34)             | 3.94 (3.38 to 4.57)                           | 1.18 (0.90 to 1.52) | IR (95% CI)                         | 0.17 (0.08 to 0.33)             | 0.50 (0.32 to 0.74)                           | 0.06 (0.01 to 0.17) | IR (95% CI)                            | 0.50 (0.33 to 0.74)             | 0.80 (0.57 to 1.09)                           | 0.34 (0.20 to 0.54) |
| HR (95% CI) versus XELJANZ 5 mg BID                     | Referent                        | 1.03 (0.84 to 1.27)                           | –                   | HR (95% CI) versus XELJANZ 5 mg BID | Referent                        | 2.82 (1.31 to 6.06)                           | –                   | HR (95% CI) versus XELJANZ 5 mg BID    | Referent                        | 1.59 (0.97 to 2.61)                           | –                   |

Extracted from Ytterberg SR, et al. *N Engl J Med* Supplementary Appendix. 2022<sup>1</sup>

XELJANZ 5 mg BID and 11 mg prolonged-release QD are the only approved dosages for the treatment of RA, which should not be exceeded. XELJANZ 10 mg BID is not licensed for RA.<sup>2</sup>

<sup>a</sup>For patients assigned to receive XELJANZ at a dose of 10 mg BID who had their dose reduced to 5 mg BID, the data collected after patients had been switched to 5 mg BID were counted in the group receiving 10 mg BID.<sup>1</sup>

<sup>b</sup>Also included are opportunistic herpes zoster and tuberculosis events.<sup>1</sup>

<sup>c</sup>Includes nonserious and serious events.<sup>1</sup>

<sup>d</sup>Included are herpes zoster adjudicated as an opportunistic infection and nonadjudicated herpes zoster events.<sup>1</sup>

AE, adverse event; BID, twice daily; CI, confidence interval; DVT, deep vein thrombosis; HR, hazard ratio; IR, incidence rate; MACE, major adverse cardiovascular events; NMSC, nonmelanoma skin cancer; ORAL, Oral Rheumatoid Arthritis Trial; PE, pulmonary embolism; PY, patient-year; QD, once daily; RA, rheumatoid arthritis; TNFi, tumour necrosis factor inhibitor; VTE, venous thromboembolism.



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# AEs of special interest in the RA (excluding ORAL Surveillance), PsA, and UC clinical trial programmes

### Limitations of pooled and LTE data<sup>1</sup>

- LTE studies may provide useful data; however, conduct of open-label LTE studies where both treatment and dose are known to both investigator and patient is subject to certain biases and limitations. Most participants were known to have responded to and tolerated XELJANZ (all had completed a qualifying study), so our findings might not be generalisable to patients new to XELJANZ
- Biases include, but are not limited to, patient selection (patient willingness or ineligibility to enrol, which may be due to a prior serious AE), prior treatment, volunteer, observer, initial dose of study drug, investigator/patient expectation, and study duration. Limitations include, but are not limited to, AE frequencies and incidence rates subject to change over time due to patient entry/exit, dose changes influenced by both investigator and patient, dose restrictions in certain countries, the number of patients and exposure for a specific safety event possibly differing depending on the timing of censored events, and the number of observed patients with longer exposure times becoming lower

### IRs: patients with events/100 PY (95% CI) for safety events of interest<sup>1,a-d</sup>

| IRs (95% CI) for AEs of special interest                                    | RA (N=7964)                        | PsA (N=783)                    | UC (N=1157)                                              | PsO (N=3663)                   |
|-----------------------------------------------------------------------------|------------------------------------|--------------------------------|----------------------------------------------------------|--------------------------------|
| Total XELJANZ exposure, patient-years                                       | 23,497                             | 2038                           | 2581                                                     | 8950                           |
| Serious infections, IR (95% CI) (n)                                         | 2.5 (2.3 to 2.7) (592)             | 1.2 (0.7 to 1.7) (24)          | 1.7 (1.2 to 2.3) (45)                                    | 1.3 (1.1 to 1.5) (119)         |
| All HZ (non-serious and serious), IR (95% CI) (n)                           | 3.6 (3.3 to 3.8) (795)             | 1.8 (1.2 to 2.4) (36)          | 3.5 (2.8 to 4.3) (87)                                    | 2.4 (2.0 to 2.7) (209)         |
| Adjudicated OIs excluding tuberculosis, IR (95% CI) (n)                     | 0.4 (0.3 to 0.5) (95)              | 0.3 (0.1 to 0.7) (7)           | 1.6 (1.1 to 2.1) (40) <sup>e</sup>                       | 0.3 (0.2 to 0.5) (29)          |
| Adjudicated tuberculosis, IR (95% CI) (n)                                   | 0.2 (0.1 to 0.2) (38)              | 0.0 (0.0 to 0.2) (0)           | 0.0 (0.0 to 0.1) (0) <sup>e</sup>                        | 0.0 (0.0 to 0.1) (1)           |
| Adjudicated malignancies excluding all NMSC, IR (95% CI) (n) n1 (%)         | 0.7 (0.6 to 0.9) (179) 211 (2.6)   | 0.7 (0.4 to 1.2) (15) 18 (2.3) | 0.6 (0.3 to 1.0) (16) <sup>e</sup> 20 (1.8) <sup>e</sup> | 0.7 (0.5 to 0.8) (60) 74 (2.0) |
| Adjudicated NMSC, IR (95% CI) (n) n1 (%)                                    | 0.6 (0.5 to 0.7) (133) 135 (1.7)   | 0.8 (0.4 to 1.3) (16) 16 (2.0) | 0.7 (0.4 to 1.1) (19) <sup>e</sup> 19 (1.7) <sup>e</sup> | 0.7 (0.5 to 0.9) (63) 67 (1.8) |
| Adjudicated melanoma, IR (95% CI) (n) n1 (%)                                | 0.1 (0.0 to 0.1) (14) 14 (0.2)     | 0.0 (0.0 to 0.2) (0) 0 (0.0)   | 0.1 (0.0 to 0.3) (2) <sup>e</sup> 2 (0.2) <sup>e</sup>   | 0.1 (0.0 to 0.1) (5) 5 (0.1)   |
| Adjudicated lymphoma/lymphoproliferative disorders, IR (95% CI) (n), n1 (%) | 0.1 (0.0 to 0.1) (12) 19 (0.2)     | 0.1 (0.0 to 0.3) (1) 1 (0.1)   | 0.1 (0.0 to 0.3) (2) <sup>e</sup> 2 (0.2) <sup>e</sup>   | 0.02 (0.0 to 0.1) (2) 4 (0.1)  |
| Adjudicated gastrointestinal perforation, IR (95% CI) (n)                   | 0.1 (0.1 to 0.2) (27)              | 0.1 (0.0 to 0.3) (1)           | 0.2 (0.1 to 0.5) (6) <sup>e</sup>                        | 0.1 (0.0 to 0.2) (7)           |
| Adjudicated MACE, <sup>f</sup> IR (95% CI) (n)                              | 0.4 (0.3 to 0.5) (85) <sup>g</sup> | 0.3 (0.1 to 0.6) (6)           | 0.3 (0.1 to 0.5) (7) <sup>e</sup>                        | 0.3 (0.2 to 0.4) (23)          |
| DVT, <sup>h</sup> IR (95% CI) (n)                                           | 0.2 (0.1 to 0.2) (37)              | 0.1 (0.0 to 0.3) (1)           | 0.0 (0.0 to 0.2) (1)                                     | 0.1 (0.0 to 0.1) (6)           |
| PE, <sup>h</sup> IR (95% CI) (n)                                            | 0.1 (0.1 to 0.2) (31)              | 0.1 (0.0 to 0.3) (1)           | 0.2 (0.0 to 0.4) (4)                                     | 0.1 (0.0 to 0.2) (9)           |

The ISS and analysis of AEs of special interest include pooled data from patients exposed to ≥1 dose of XELJANZ in:

- Phase 1, 2, 3, or 3b/4 clinical trials and LTE studies in RA<sup>1,i</sup>
- Phase 3 clinical trials and LTE studies in PsA<sup>2,i</sup>
- Phase 2 and 3 clinical trials and LTE studies in UC<sup>2,i</sup>

XELJANZ 5 mg BID and 11 mg prolonged-release QD are the only approved dosages for the treatment of RA and PsA, which should not be exceeded. XELJANZ 10 mg BID is not licensed for RA or PsA. XELJANZ is not indicated for the treatment of PsO.<sup>3</sup>

<sup>a</sup>Final data for the RA and PsA cohorts are from 18 April 2019 and 31 July 2019, respectively.<sup>1</sup>

<sup>b</sup>All doses in RA included XELJANZ 1 mg, 3 mg, 5 mg, 10 mg, 15 mg, and 30 mg BID; 10 mg or 20 mg QD; or 11 mg MR QD.<sup>2</sup>

<sup>c</sup>All doses in PsA included XELJANZ 5 mg and 10 mg BID.<sup>2</sup>

<sup>d</sup>The LTE data cutoff was 27 May 2019 (interim analysis). All doses in UC included XELJANZ 0.5 mg, 3 mg, 5 mg, 10 mg and 15 mg BID.<sup>1</sup>

<sup>e</sup>N=1124.<sup>1</sup>

<sup>f</sup>Composite MACE defined as any myocardial infarction, stroke, or cardiovascular death.<sup>1</sup>

<sup>g</sup>N=7311.<sup>1</sup>

<sup>h</sup>Previously reported in Mease et al (excludes Study A3921133) and Sandborn et al.<sup>1</sup>

<sup>i</sup>In LTE studies, dose adjustments for XELJANZ or concomitant medications were allowed at the investigator's discretion for efficacy or safety reasons.<sup>1</sup>

Extracted from Burmester GR, et al. *RMD Open*. 2021.<sup>1</sup>

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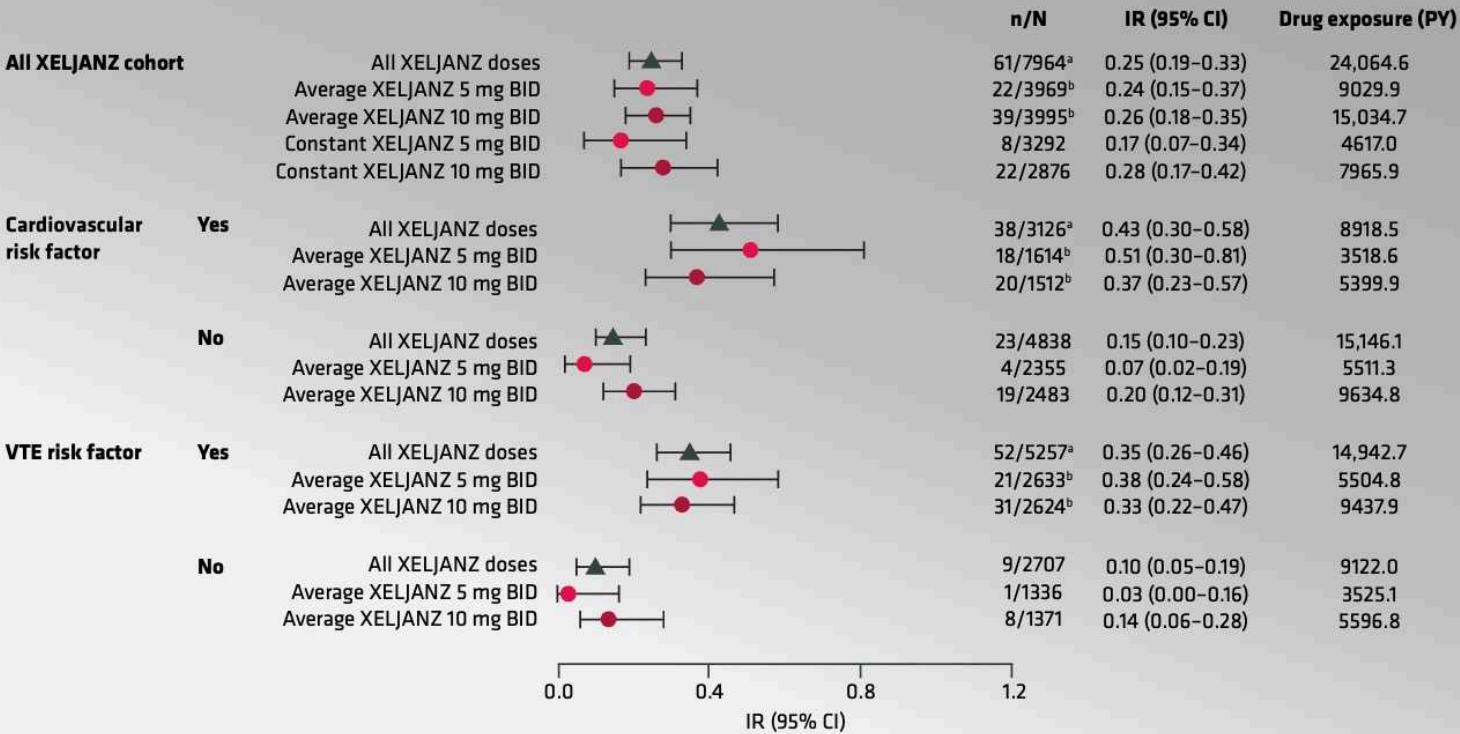
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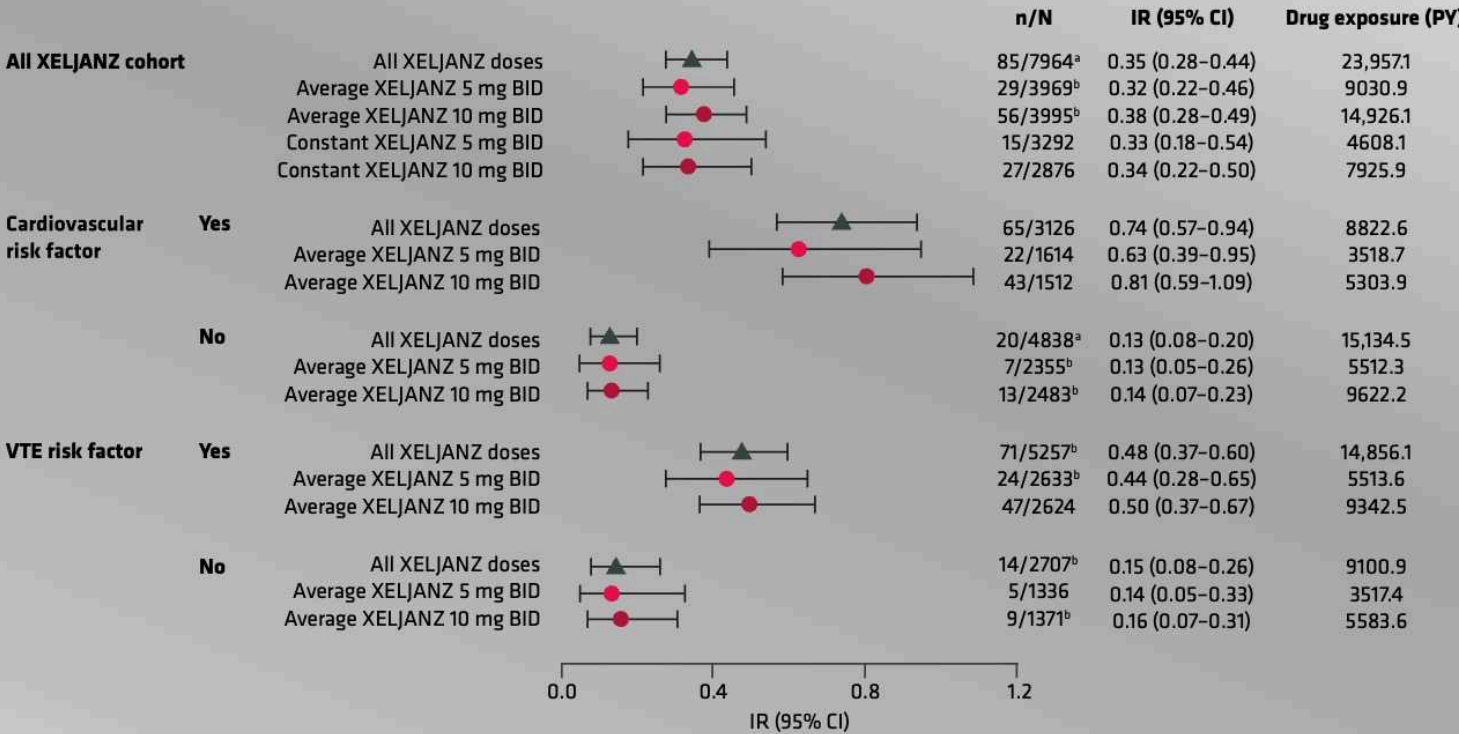
# AEs of special interest in the RA (excluding ORAL Surveillance) clinical trial programme

## All XELJANZ cohort: VTE (DVT or PE)



Extracted from Mease P, et al. *Ann Rheum Dis*. 2020.<sup>1</sup>

## All XELJANZ cohort: ATE



XELJANZ 5 mg BID and 11 mg prolonged-release QD are the only approved dosages for the treatment of RA, which should not be exceeded. XELJANZ 10 mg BID is not licensed for RA.<sup>2</sup>

<sup>a</sup>Two or <sup>b</sup>one patients were not counted in the numerator of the IR calculations because the events occurred outside the defined risk period.<sup>1</sup>

AE, adverse event; ATE, arterial thromboembolism; BID, twice daily; CI, confidence interval; DVT, deep vein thrombosis; IR, incidence rate; ORAL, Oral Rheumatoid Arthritis Trial; PE, pulmonary embolism; PY, patient-years; QD, once daily; RA, rheumatoid arthritis; VTE, venous thromboembolism.

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# AEs of special interest in the AS clinical trial programme

## Summary of safety up to Week 16 and up to Week 48<sup>1</sup>

| Patients with events, n (%)                                                                            | Up to Week 16<br>(double-blind phase) |                 | Up to Week 48<br>(double-blind and open-label phases) |                          |
|--------------------------------------------------------------------------------------------------------|---------------------------------------|-----------------|-------------------------------------------------------|--------------------------|
|                                                                                                        | XELJANZ (n=133)                       | Placebo (n=136) | XELJANZ (n=133)                                       | Placebo--XELJANZ (n=136) |
| Adverse events                                                                                         | 73 (54.9)                             | 70 (51.5)       | 103 (77.4)                                            | 93 (68.4)                |
| Serious adverse events <sup>a</sup>                                                                    | 2 (1.5)                               | 1 (0.7)         | 7 (5.3)                                               | 2 (1.5)                  |
| Severe adverse events <sup>b</sup>                                                                     | 2 (1.5)                               | 0               | 6 (4.5)                                               | 0                        |
| Discontinued study drug due to adverse events                                                          | 3 (2.3)                               | 1 (0.7)         | 8 (6.0)                                               | 3 (2.2)                  |
| Reduced dose or temporarily discontinued study drug due to adverse events                              | 9 (6.8)                               | 5 (3.7)         | 18 (13.5)                                             | 13 (9.6)                 |
| Deaths                                                                                                 | 0                                     | 0               | 0                                                     | 0                        |
| Most common adverse events by preferred term (>5% of any treatment group)                              |                                       |                 |                                                       |                          |
| Upper respiratory tract infection                                                                      | 14 (10.5)                             | 10 (7.4)        | 21 (15.8)                                             | 18 (13.2)                |
| Nasopharyngitis                                                                                        | 9 (6.8)                               | 10 (7.4)        | 11 (8.3)                                              | 17 (12.5)                |
| Diarrhoea                                                                                              | 6 (4.5)                               | 5 (3.7)         | 10 (7.5)                                              | 8 (5.9)                  |
| Arthralgia                                                                                             | 1 (0.8)                               | 8 (5.9)         | 2 (1.5)                                               | 9 (6.6)                  |
| ALT increased                                                                                          | 4 (3.0)                               | 1 (0.7)         | 8 (6.0)                                               | 2 (1.5)                  |
| Protein urine present                                                                                  | 5 (3.8)                               | 2 (1.5)         | 8 (6.0)                                               | 4 (2.9)                  |
| Headache                                                                                               | 2 (1.5)                               | 3 (2.2)         | 5 (3.8)                                               | 7 (5.1)                  |
| Abdominal pain upper                                                                                   | 0                                     | 4 (2.9)         | 2 (1.5)                                               | 7 (5.1)                  |
| Adverse events of special interest                                                                     |                                       |                 |                                                       |                          |
| Malignancies (including NMSC) <sup>c</sup>                                                             | 0                                     | 0               | 0                                                     | 0                        |
| MACE <sup>c</sup>                                                                                      | 0                                     | 0               | 0                                                     | 0                        |
| Thromboembolic events (DVT, PE, or ATE) <sup>c</sup>                                                   | 0                                     | 0               | 0                                                     | 0                        |
| GI perforation <sup>c</sup>                                                                            | 0                                     | 0               | 0                                                     | 0                        |
| Hepatic events <sup>c</sup>                                                                            | 1 (0.8) <sup>d</sup>                  | 0               | 3 (2.3) <sup>e</sup>                                  | 0                        |
| DILI <sup>c</sup>                                                                                      | 0                                     | 0               | 0                                                     | 0                        |
| HZ (serious and non-serious)                                                                           | 0                                     | 0               | 3 (2.3) <sup>f</sup>                                  | 2 (1.5) <sup>f</sup>     |
| Opportunistic infections <sup>c</sup>                                                                  | 0                                     | 0               | 0                                                     | 0                        |
| Serious infections                                                                                     | 1 (0.8) <sup>g</sup>                  | 0               | 1 (0.8) <sup>g</sup>                                  | 0                        |
| ILD <sup>c</sup>                                                                                       | 0                                     | 0               | 0                                                     | 0                        |
| Laboratory values meeting protocol criteria for monitoring <sup>h</sup>                                | 0                                     | 6 (4.4)         | 7 (5.3)                                               | 10 (7.4)                 |
| Haemoglobin drop >20 g/L below baseline                                                                | 0                                     | 4 (2.9)         | 3 (2.3)                                               | 5 (3.7)                  |
| Platelet count <100x10 <sup>9</sup> /L                                                                 | 0                                     | 1 (0.7)         | 0                                                     | 1 (0.7)                  |
| Serum creatinine increase >50% or increase 0.5 mg/dL over the average of screening and baseline values | 0                                     | 0               | 4 (3.0)                                               | 3 (2.2)                  |
| Creatine kinase >5xULN                                                                                 | 0                                     | 1 (0.7)         | 0                                                     | 1 (0.7)                  |
| Laboratory values meeting protocol criteria for discontinuation of study drug <sup>i</sup>             | 1 (0.8)                               | 0               | 2 (1.5)                                               | 0                        |
| Two sequential AST or ALT elevations >5xULN                                                            | 1 (0.8)                               | 0               | 2 (1.5)                                               | 0                        |

The analysis of AEs of special interest includes data from patients exposed to ≥1 dose of XELJANZ in a Phase 3 clinical trial in AS<sup>1</sup>

<sup>a</sup>SAEs were defined as any untoward medical occurrence at any dose that was life-threatening; resulted in hospitalisation, prolongation of existing hospitalisation, persistent or significant disability/incapacity, congenital anomaly/birth defect, or death; or was considered to be an important medical event.

<sup>b</sup>Investigators used the adjectives mild, moderate, or severe to describe the maximum intensity of the AE. Severe AEs were defined as those that interfered significantly with the patient's usual function.

<sup>c</sup>Adjudicated events.  
<sup>d</sup>Two sequential AST or ALT measurements ≥3 × ULN; unrelated DILI; patient did not meet criteria for potential Hy's law or definite Hy's law.

<sup>e</sup>One patient had 2 sequential AST or ALT measurements ≥3 × ULN, which was unrelated DILI; one patient had AST or ALT ≥5 × ULN, which was unlikely DILI; one patient had cholecystitis and recurrence of gallstones, which were unrelated DILIs. None of these patients met the criteria for potential Hy's law or definite Hy's law.

<sup>f</sup>All cases were non-serious.  
<sup>g</sup>Meningitis; did not meet OI adjudication criteria.

<sup>h</sup>Notably, no patients met the following protocol criteria for monitoring: absolute neutrophil count <1.2 × 10<sup>9</sup>/L; absolute lymphocyte count <0.5 × 10<sup>9</sup>/L.

<sup>i</sup>Notably, no patients met the following protocol criteria for discontinuation of study drug: 2 sequential absolute neutrophil counts <1.0 × 10<sup>9</sup>/L; 2 sequential absolute lymphocyte counts <0.5 × 10<sup>9</sup>/L.

Extracted from Deodhar A, et al. *Ann Rheum Dis*. 2021.<sup>1</sup>

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# Incidence of malignancy in RA and PsA in a real-world cohort study<sup>1</sup>

## Incidence rates of malignancy in PsA and RA per 100 PY

|                          | PsA   |                    |                   | RA    |                    |                   | PsA vs RA           |         |
|--------------------------|-------|--------------------|-------------------|-------|--------------------|-------------------|---------------------|---------|
|                          | Count | Total PY for event | IR (95% CI)       | Count | Total PY for event | IR (95% CI)       | IRR                 | P value |
| All cancers <sup>a</sup> | 40    | 7156.1             | 0.56 (0.40, 0.76) | 307   | 54709.7            | 0.56 (0.50, 0.63) | 1.00 (0.70, 1.36)   | 0.864   |
| NMSC                     | 15    | 7099.0             | 0.21 (0.12, 0.35) | 109   | 54136.8            | 0.20 (0.17, 0.24) | 1.05 (0.61, 1.80)   | 0.854   |
| Non-NMSC <sup>b</sup>    | 25    | 7121.9             | 0.35 (0.23, 0.52) | 198   | 54387.2            | 0.36 (0.32, 0.42) | 0.97 (0.61, 1.42)   | 0.725   |
| Solid                    | 20    | 7112.8             | 0.28 (0.17, 0.43) | 168   | 54294.0            | 0.31 (0.26, 0.36) | 0.90 (0.57, 1.45)   | 0.691   |
| Breast                   | 7     | 3580.0             | 0.20 (0.08, 0.40) | 55    | 41025.4            | 0.13 (0.10, 0.17) | 1.54 (0.67, 3.23)   | 0.338   |
| Prostate                 | 3     | 3477.4             | 0.09 (0.02, 0.25) | 20    | 12747.5            | 0.16 (0.10, 0.24) | 0.56 (0.16, 1.86)   | 0.338   |
| Colorectal               | 3     | 7073.9             | 0.04 (0.01, 0.12) | 14    | 53847.2            | 0.03 (0.01, 0.04) | 1.33 (0.47, 5.70)   | 0.438   |
| Melanoma                 | 3     | 7068.8             | 0.04 (0.01, 0.12) | 15    | 53850.4            | 0.03 (0.02, 0.05) | 1.33 (0.44, 5.28)   | 0.502   |
| Haematologic             | 5     | 7074.1             | 0.07 (0.02, 0.16) | 30    | 53907.6            | 0.06 (0.04, 0.08) | 1.17 (0.36, 2.89)   | 0.971   |
| Lymphoma                 | 3     | 7069.7             | 0.04 (0.01, 0.12) | 21    | 53874.8            | 0.04 (0.02, 0.06) | 1.00 (0.17, 3.11)   | 0.668   |
| Multiple myeloma         | 1     | 7067.1             | 0.01 (0.00, 0.08) | 1     | 53821.2            | 0.00 (0.00, 0.01) | 7.78 (0.48, 122.23) | 0.150   |
| Leukaemia                | 1     | 7067.1             | 0.01 (0.00, 0.08) | 8     | 53840.2            | 0.01 (0.01, 0.03) | 1.00 (0.12, 7.64)   | 0.966   |

This real-world study included patients with RA and PsA who had ≥2 study visits during the period August 2003 to October 2010:

- N=19,260 for RA
- N=2970 for PsA

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<sup>a</sup>All cancers = NMSC + non-NMSC.

<sup>b</sup>Non-NMSC = solid + haematologic.

Please see [limitations for RWE studies](#)

Extracted from Gross RL, et al. *Arthritis Rheum.* 2014.<sup>1</sup>

BID, twice daily; CI, confidence interval; IR, incidence rate; IRR, incidence rate ratio; NMSC, nonmelanoma skin cancer; PsA, psoriatic arthritis; PY, patient-year; QD, once daily; RA, rheumatoid arthritis; RWE, real-world evidence.

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# Safety data in Study JIA-I

## AEs from Study JIA-I<sup>1</sup>

|                                                                            | Part 1                       |                             | Part 2              |  | Entire XELJANZ exposure period <sup>a</sup> |
|----------------------------------------------------------------------------|------------------------------|-----------------------------|---------------------|--|---------------------------------------------|
|                                                                            | XELJANZ (n=225) <sup>b</sup> | XELJANZ (n=88) <sup>b</sup> | Placebo (n=85)      |  | XELJANZ (n=225) <sup>b</sup>                |
| Adverse events                                                             | 153 (68%)                    | 68 (77%)                    | 63 (74%)            |  | 189 (84%)                                   |
| Incidence rate per 100 patient-years (95% CI)                              | –                            | 371.7 (288.6–471.2)         | 417.8 (321.0–534.5) |  | 394.0 (339.9–454.4)                         |
| Serious adverse events                                                     | 7 (3%)                       | 1 (1%)                      | 2 (2%)              |  | 9 (4%)                                      |
| Incidence rate per 100 patient-years (95% CI)                              | –                            | 2.4 (0.1–13.4)              | 6.0 (0.7–21.8)      |  | 7.3 (3.4–13.9)                              |
| Severe adverse events                                                      | 5 (2%)                       | 0                           | 3 (4%)              |  | 5 (2%)                                      |
| Permanent discontinuation from study due to adverse events                 | 26 (12%)                     | 16 (18%)                    | 29 (34%)            |  | 49 (22%)                                    |
| Incidence rate per 100 patient-years (95% CI)                              | –                            | 39.6 (22.6–64.3)            | 94.2 (63.1–135.3)   |  | 40.9 (30.3–54.1)                            |
| Temporary dose reduction or temporary hold due to adverse events           | 20 (9%)                      | 9 (10%)                     | 8 (9%)              |  | 25 (11%)                                    |
| Most common adverse events by preferred term (≥10% in any treatment group) |                              |                             |                     |  |                                             |
| Upper respiratory tract infection                                          | 24 (11%)                     | 13 (15%)                    | 9 (11%)             |  | 34 (15%)                                    |
| Disease progression                                                        | 5 (2%)                       | 8 (9%)                      | 13 (15%)            |  | 13 (6%)                                     |
| JIA exacerbation                                                           | 6 (3%)                       | 3 (3%)                      | 12 (14%)            |  | 9 (4%)                                      |
| Adverse events of special interest <sup>c</sup>                            |                              |                             |                     |  |                                             |
| Deaths                                                                     | 0                            | 0                           | 0                   |  | 0                                           |
| Hepatic events <sup>d</sup>                                                | 3 (1%)                       | 0                           | 0                   |  | 3 (1%)                                      |
| Herpes zoster (non-serious and serious) <sup>d,e</sup>                     | 2 (1%)                       | 0                           | 0                   |  | 2 (1%)                                      |
| Incidence rate per 100 patient-years (95% CI)                              | –                            | –                           | –                   |  | 1.6 (0.2–5.9)                               |
| Serious infection                                                          | 3 (1%)                       | 1 (1%) <sup>f</sup>         | 1 (1%)              |  | 4 (2%) <sup>f</sup>                         |
| Incidence rate per 100 patient-years (95% CI)                              | –                            | –                           | 3.0 (0.1–16.8)      |  | 2.4 (0.5–7.1)                               |

- XELJANZ 5 mg tablets and XELJANZ Oral Solution were studied in 225 patients from 2 to <18 years of age in Study JIA-I, dosed according to study protocol<sup>1,2</sup>
- In Study JIA-I, adverse reactions included infections (influenza, pharyngitis, sinusitis, viral infection) and GI or general disorders (abdominal pain, nausea, vomiting, pyrexia, headache, cough). There were no cases of MACE, malignancies (including NMSC), mortality, or thrombotic events (DVT, PE, or ATE) in Study JIA-I<sup>1,2</sup>
- **Serious infections in Study JIA-I included appendicitis, epidural empyema (with sinusitis and subperiosteal abscess), pilonidal cyst, pneumonia, *Escherichia* pyelonephritis, abscess limb, and UTI<sup>1,2</sup>**

<sup>a</sup>Placebo exposure might have contributed a maximum of 28 days to the risk period for the following events: AEs, serious AEs, permanent discontinuations due to AEs, and AEs of special interest except hepatic events; for other events reported, those occurring during placebo exposure were excluded.

<sup>b</sup>Patients weighing ≥40 kg received 5 mg tablets or 5 mL of grape-flavoured oral solution (1 mg/mL) if unable to swallow tablets. Patients weighing <40 kg received equivalent weight-based lower dose via oral solution.<sup>2</sup>

<sup>c</sup>During the trial, there were no reports of the following AEs of special interest: gastrointestinal perforation, interstitial lung disease, MACE, macrophage activation syndrome, malignancies, opportunistic infection, thrombotic events, or tuberculosis.

<sup>d</sup>Adjudicated events.

<sup>e</sup>Both incidences were mild, monodermatomal, and non-serious, and neither met opportunistic infection criteria.

<sup>f</sup>One serious AE of pilonidal cyst repair was coded to surgical procedures instead of infections and was inadvertently not identified as a serious infection. The serious AE was adjudicated and was determined to not meet opportunistic infection criteria. It is presented in the table as a serious infection; however, it was not included in the incidence rate calculation.

Extracted from Ruperto N, et al. *Lancet*. 2021.<sup>1</sup>

AE, adverse event; ATE, arterial thromboembolism; CI, confidence interval; DVT, deep vein thrombosis; GI, gastrointestinal; JIA, juvenile idiopathic arthritis; MACE, major adverse cardiovascular events; NMSC, nonmelanoma skin cancer; PE, pulmonary embolism; UTI, urinary tract infection.

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# Safety data in Study JIA-I

## AEs from Study JIA-I<sup>1</sup>

|                            | Part 1                       |                             | Part 2         |                              | Entire XELJANZ exposure period <sup>a</sup> |
|----------------------------|------------------------------|-----------------------------|----------------|------------------------------|---------------------------------------------|
|                            | XELJANZ (n=225) <sup>b</sup> | XELJANZ (n=88) <sup>b</sup> | Placebo (n=85) | XELJANZ (n=225) <sup>b</sup> |                                             |
| Creatine kinase >2.0 x ULN | 12/224 (5%)                  | 2 (2%)                      | 2 (2%)         | 13/224 (6%)                  |                                             |
| Haemoglobin <0.8 x LLN     | 1/224 (<0.5%)                | 1/87 (1%)                   | 3 (4%)         | 2/224 (1%)                   |                                             |
| Lymphocytes >1.2 x ULN     | 2/224 (1%)                   | 1/87 (1%)                   | 0              | 3/224 (1%)                   |                                             |
| Neutrophils >1.2 x ULN     | 18/224 (8%)                  | 7/87 (8%)                   | 5 (6%)         | 19/224 (8%)                  |                                             |
| AST ≥1.0 x ULN             | 25 (11%)                     | 12 (14%)                    | 9 (11%)        | 35 (16%)                     |                                             |
| ALT ≥1.0 x ULN             | 33 (15%)                     | 14 (16%)                    | 11 (13%)       | 37 (16%)                     |                                             |
| HDL cholesterol <0.8 x LLN | 2/223 (1%)                   | 0 <sup>c</sup>              | 2/61 (3%)      | 2/223 (1%)                   |                                             |
| LDL cholesterol >1.2 x ULN | 4/87 (5%)                    | 0 <sup>d</sup>              | 0 <sup>e</sup> | 4/87 (5%)                    |                                             |
| Cholesterol >1.3 x ULN     | 2/223 (1%)                   | 0 <sup>f</sup>              | 0 <sup>g</sup> | 2/223 (1%)                   |                                             |

- XELJANZ 5 mg tablets and XELJANZ Oral Solution were studied in 225 patients from 2 to <18 years of age in Study JIA-I, dosed according to study protocol<sup>1,2</sup>
- In Study JIA-I, adverse reactions included infections (influenza, pharyngitis, sinusitis, viral infection) and GI or general disorders (abdominal pain, nausea, vomiting, pyrexia, headache, cough). There were no cases of MACE, malignancies (including NMSC), mortality, or thrombotic events (DVT, PE, or ATE) in Study JIA-I<sup>1,2</sup>
- **Serious infections in Study JIA-I included appendicitis, epidural empyema (with sinusitis and subperiosteal abscess), pilonidal cyst, pneumonia, *Escherichia* pyelonephritis, abscess limb, and UTI<sup>1,2</sup>**

<sup>a</sup>Placebo exposure might have contributed a maximum of 28 days to the risk period for the following events: AEs, serious AEs, permanent discontinuations due to AEs, and AEs of special interest except hepatic events; for other events reported, those occurring during placebo exposure were excluded.

<sup>b</sup>Patients weighing ≥40 kg received 5 mg tablets or 5 mL of grape-flavoured oral solution (1 mg/mL) if unable to swallow tablets. Patients weighing <40 kg received equivalent weight-based lower dose via oral solution.<sup>2</sup>

<sup>c</sup>Assessed in 70 patients.

<sup>d</sup>Assessed in 5 patients.

<sup>e</sup>Assessed in 4 patients.

<sup>f</sup>Assessed in 71 patients.

<sup>g</sup>Assessed in 61 patients.

Extracted from Ruperto N, et al. *Lancet*. 2021.<sup>1</sup>

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ATE, arterial thromboembolism; DVT, deep vein thrombosis; GI, gastrointestinal; HDL, high-density lipoprotein; JIA, juvenile idiopathic arthritis; LDL, low-density lipoprotein; LLN, lower limit of normal; MACE, major adverse cardiovascular events; NMSC, nonmelanoma skin cancer; PE, pulmonary embolism; ULN, upper limit of normal; UTI, urinary tract infection.

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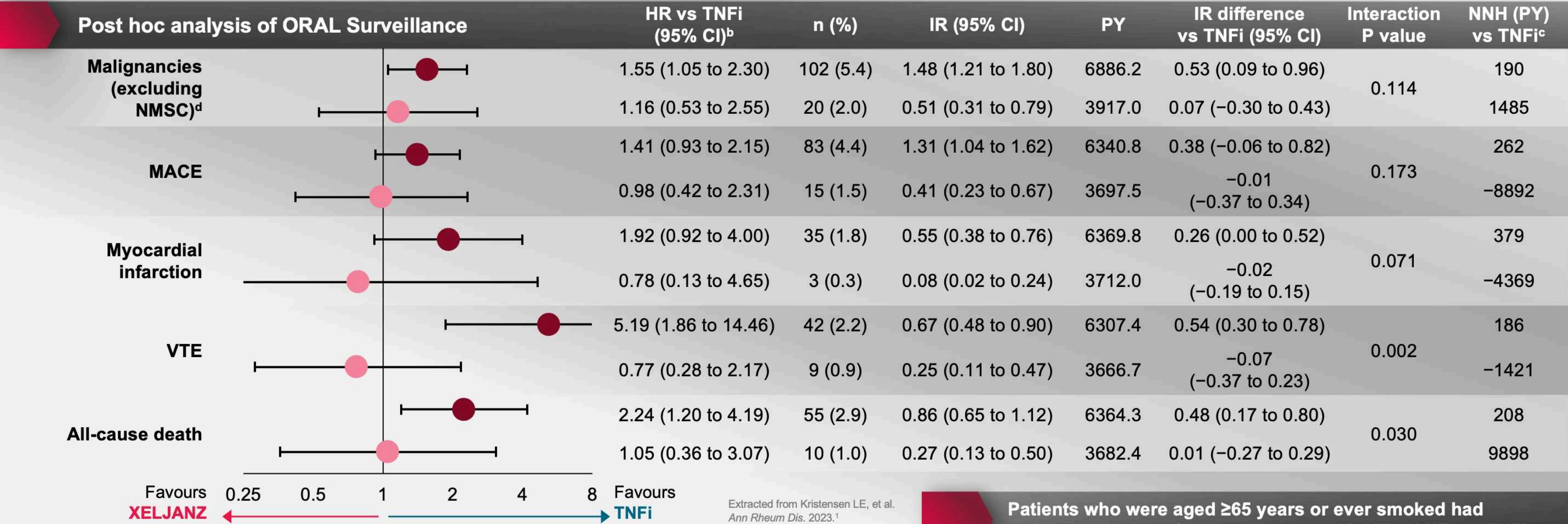




# Patients who were aged <65 years and never smoked showed no detectable risk increase for adverse events with XELJANZ<sup>a</sup> vs TNFi<sup>1</sup>

● Aged ≥65 years or ever smoked  
XELJANZ<sup>a</sup> (n=1895) vs TNFi (n=926)

● Aged <65 years and never smoked  
XELJANZ<sup>a</sup> (n=1016) vs TNFi (n=525)



XELJANZ 10 mg BID is not approved for the treatment of RA. The recommended dosage of XELJANZ is 5 mg BID or 11 mg QD.<sup>2</sup>  
<sup>a</sup>Combined doses.<sup>1</sup> <sup>b</sup>Based on a simple Cox proportional hazards model comparing combined XELJANZ doses vs TNFi.<sup>1</sup> <sup>c</sup>Interpreted as the number of PY of exposure to XELJANZ required to have 1 additional event vs TNFi.<sup>1</sup> <sup>d</sup>Results reported in Curtis JR, et al. *Ann Rheum Dis.* 2023;82:331–343.<sup>1</sup>  
BID, twice daily; CI, confidence interval; HR, hazard ratio; IR, incidence rate; MACE, major adverse cardiovascular events; NMSC, nonmelanoma skin cancer; NNH, number needed to harm; ORAL, Oral Rheumatoid Arthritis Trial; PY, patient-years; QD, once daily; RA, rheumatoid arthritis; TNFi, tumour necrosis factor inhibitor; VTE, venous thromboembolism.

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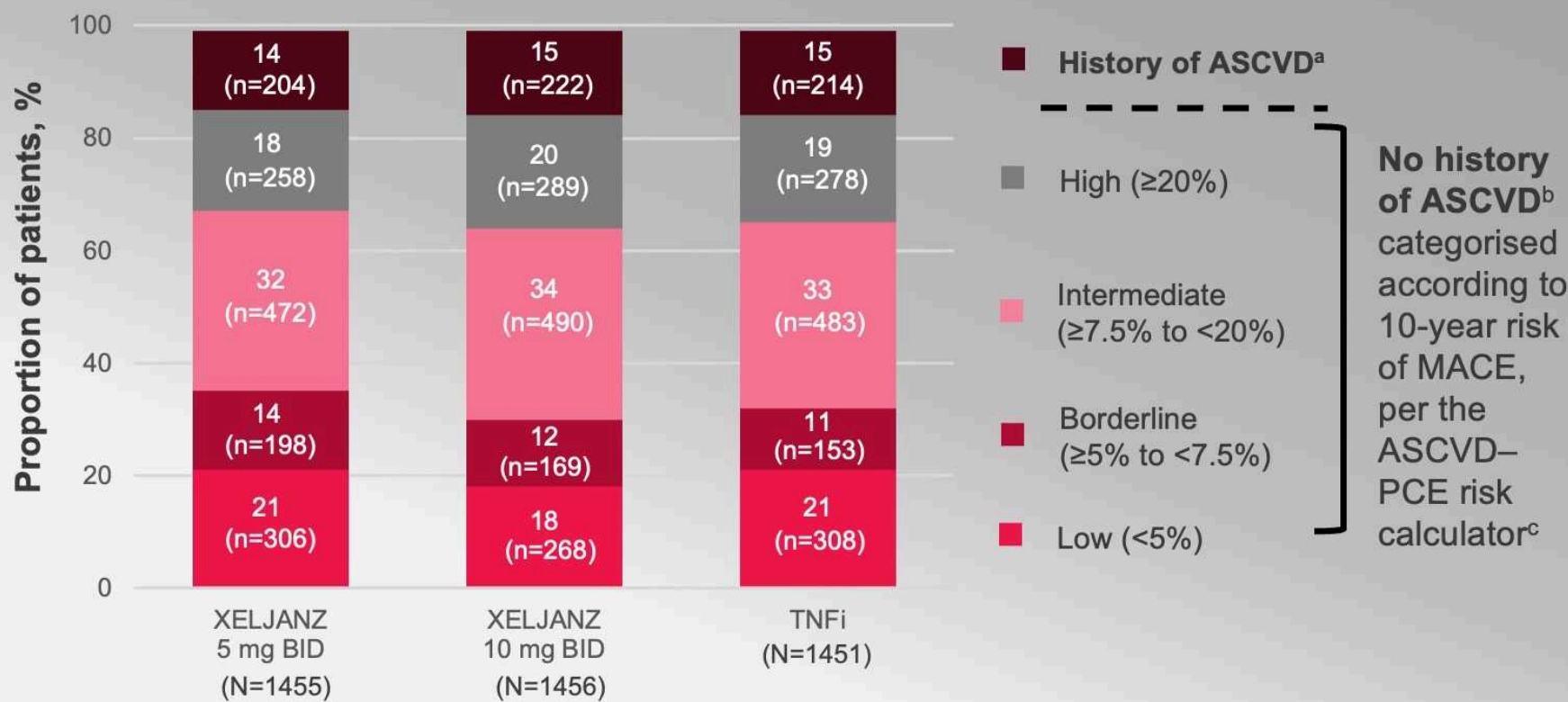
Malignancy

VTE



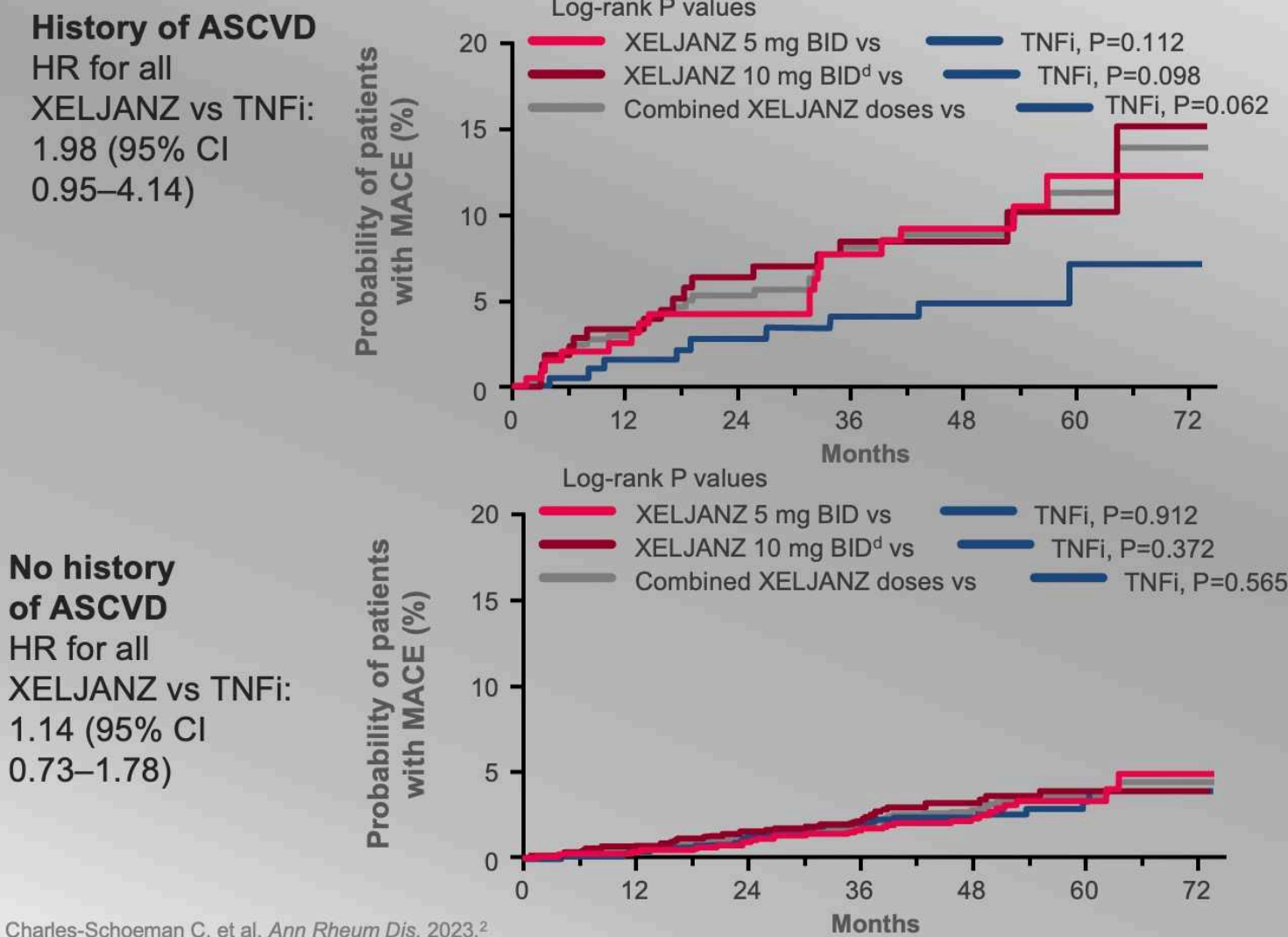
# A post hoc analysis of ORAL Surveillance showed that history of ASCVD is a risk factor accounting for higher relative risk of MACE between XELJANZ and TNFi<sup>1,2</sup>

Baseline history of ASCVD and 10-year risk of MACE<sup>2</sup>



Extracted from Charles-Schoeman C, et al. *Ann Rheum Dis.* 2023 and supplementary appendix.<sup>2</sup>

Risk of MACE with XELJANZ vs TNFi for patients with and without a history of ASCVD<sup>2,a</sup>



Extracted from Charles-Schoeman C, et al. *Ann Rheum Dis.* 2023.<sup>2</sup>

XELJANZ 10 mg BID is not approved for the treatment of RA. The recommended dosage of XELJANZ is 5 mg BID or 11 mg QD.<sup>3</sup>

<sup>a</sup>History of ASCVD defined as the composite of CAD, CeVD, or PAD.<sup>2</sup> <sup>b</sup>The proportions of patients who had no history of ASCVD and were missing ASCVD–PCE risk category data are not shown (XELJANZ 5 mg BID, n=17 [1.2%]; XELJANZ 10 mg BID, n=18 [1.2%]; TNFi, n=15 [1.0%]).<sup>2</sup> <sup>c</sup>A 10-year risk of MACE was calculated with the ASCVD–PCE calculator, and a 1.5 multiplier was applied for RA, as recommended by EULAR.<sup>2</sup> <sup>d</sup>For patients randomised to the XELJANZ 10 mg BID group who had their dose of XELJANZ reduced to 5 mg BID, the data collected after patients were switched to XELJANZ 5 mg BID were counted in the XELJANZ 10 mg BID group.<sup>2</sup> ASCVD, atherosclerotic cardiovascular disease; BID, twice daily; CAD, coronary artery disease; CeVD, cerebrovascular disease; CI, confidence interval; EULAR, European Alliance of Associations for Rheumatology; HR, hazard ratio; MACE, major adverse cardiovascular events; ORAL, Oral Rheumatoid Arthritis Trial; PAD, peripheral artery disease; PCE, pooled cohort equations; QD, once daily; RA, rheumatoid arthritis; TNFi, tumour necrosis factor inhibitor.

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# Analysing the safety profile of XELJANZ: risk visualisation overview

The following pages depict visualisations of the risk of certain adverse events of special interest (MACE, malignancy [excluding NMSC], and VTE) in different RA patient populations.

The visualisations show incidence rates per 1000 PY, i.e., filled people represent the number of events that occurred for every 1000 patients with RA for 1 year.

Please note, these pages include data from several different sources. Data from different studies should not be directly compared because of differences in trial design, populations, and methodology.

Not all possible adverse events are visualised; please refer to the SmPC for full safety information.

Some patients may not be suitable for XELJANZ treatment. For full information on adverse events, contraindications, warnings and precautions, please ensure you consult the Prescribing Information, SmPC and adverse event reporting information before prescribing. Clinical decision-making should be informed by discussions between the physician and the patient, and based on a range of factors including disease activity, patient characteristics, and the benefit–risk profile of the drug.

**Example:**

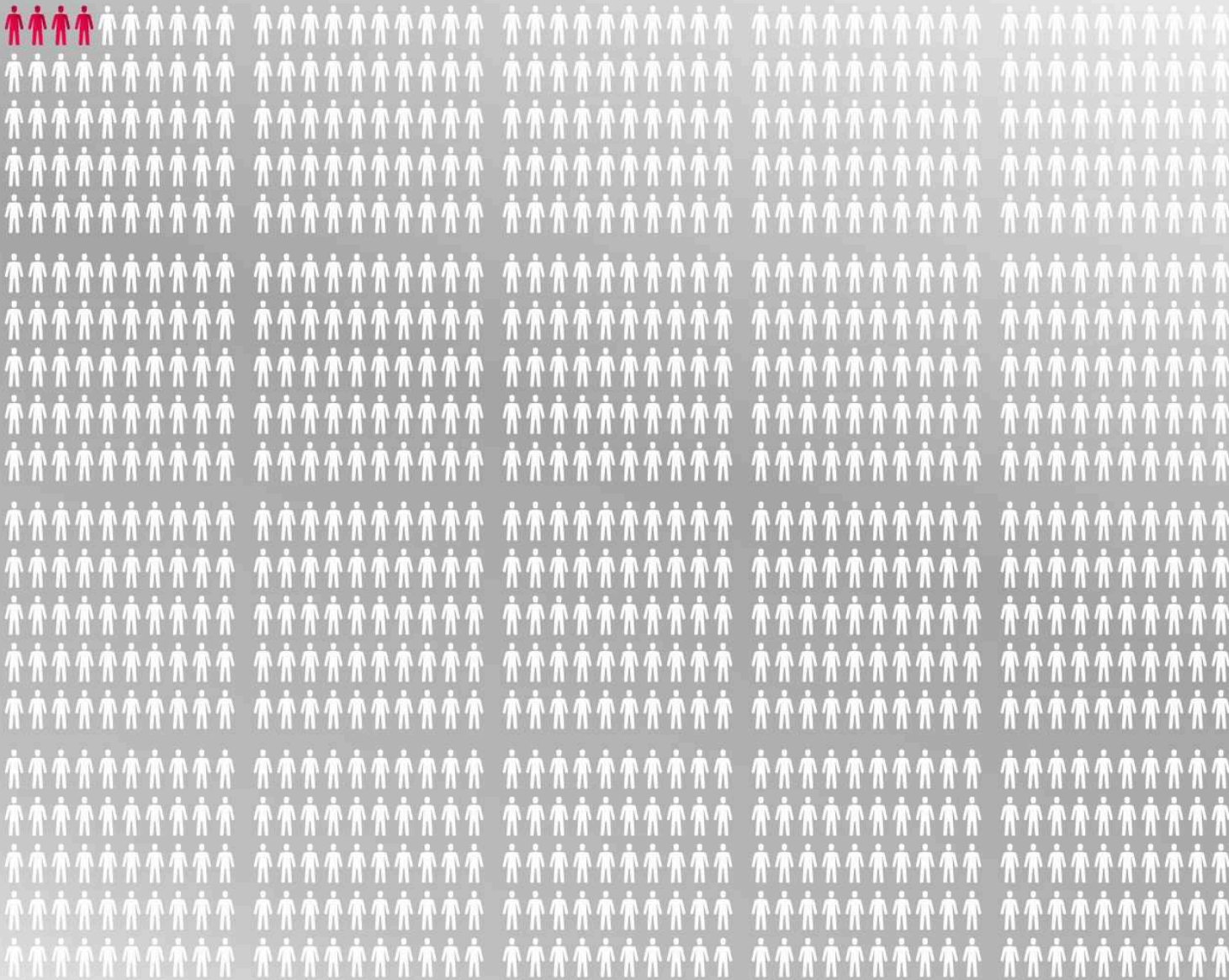
**4 out of 1000 people filled**

**=**

**Incidence rate of 4 per 1000 PY**

**=**

**4 events in 1000 patients in 1 year**



MACE, major adverse cardiovascular events; NMSC, nonmelanoma skin cancer; PY, patient-years; RA, rheumatoid arthritis; SmPC, summary of product characteristics; VTE, venous thromboembolism.

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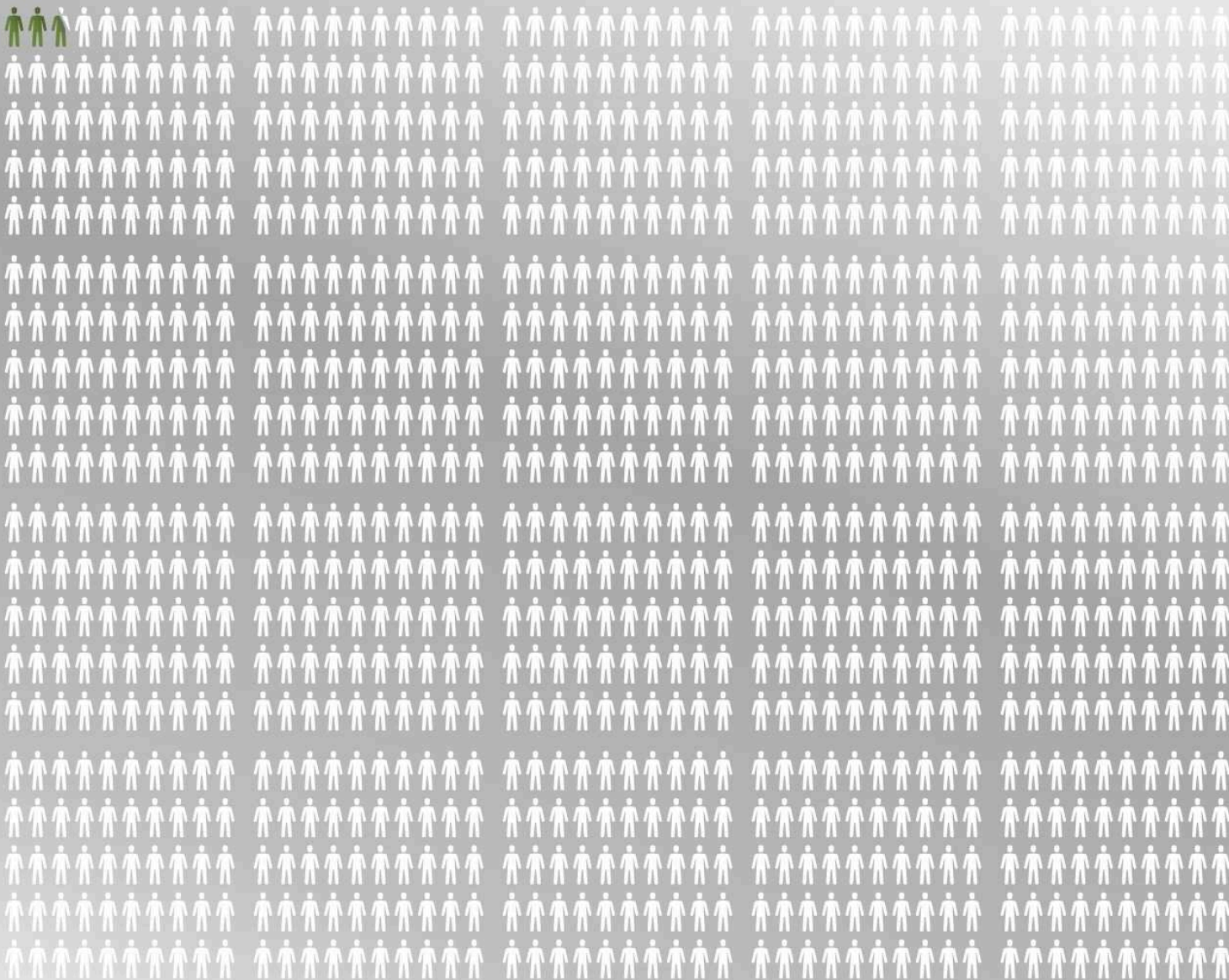


# Analysing the safety profile of XELJANZ: incidence rate of MACE in different patient populations

**Incidence rate of MACE<sup>a</sup>**  
Filled people represent the number  
of events for every 1000 patients  
with RA for 1 year.

General RA  
population:  
2.67 per  
1000 PY<sup>1,a</sup>

From a mixed  
retrospective  
and prospective  
cohort study of  
the SCQM  
registry<sup>1</sup>



Data from different studies should not be directly compared because  
of differences in trial design, populations, and methodology.

For more information, see the limitations of the SCQM registry.

Created from Lauper K, et al. *Arthritis Care Res.* 2018.<sup>1</sup>

XELJANZ 10 mg BID is not approved for the treatment of RA. The recommended dosage of XELJANZ is 5 mg BID or 11 mg QD.<sup>2</sup>  
<sup>a</sup>MACE were defined as myocardial infarction, a transient or permanent cerebrovascular event, or CV-associated death. For the calculation of an incidence rate of MACE, the year of occurrence from the time of disease onset until the last visit before the end of the study was recorded. The exposure time was defined as the time in years between the onset of the rheumatic disease until either the first MACE or the end of follow-up, whichever occurred first. Incidence rates reported as unadjusted incidence per 1000 PY.<sup>1</sup>  
BID, twice daily; CV, cardiovascular; MACE, major adverse cardiovascular events; PY, patient-year; QD, once daily; RA, rheumatoid arthritis; SCQM, Swiss Clinical Quality Management in Rheumatic Diseases.



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# Analysing the safety profile of XELJANZ: incidence rate of MACE in different patient populations

## Incidence rate of MACE<sup>a,b</sup>

Filled people represent the number of events for every 1000 patients with RA for 1 year.

For more information on the:

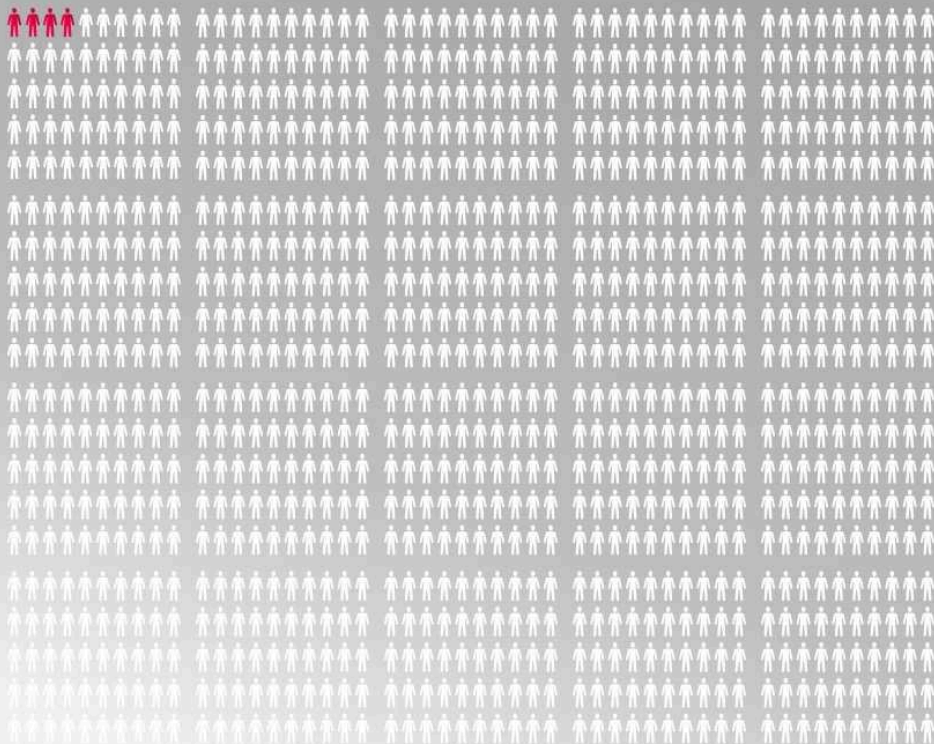
[XELJANZ pooled clinical trial programme](#)

[ORAL Surveillance trial](#)

[Can the higher-risk patient population be further characterised?](#)

From the XELJANZ pooled clinical trial programme (excluding ORAL Surveillance)<sup>a</sup>

RA population receiving XELJANZ  
all doses: 4.0 per 1000 PY<sup>1,a</sup>

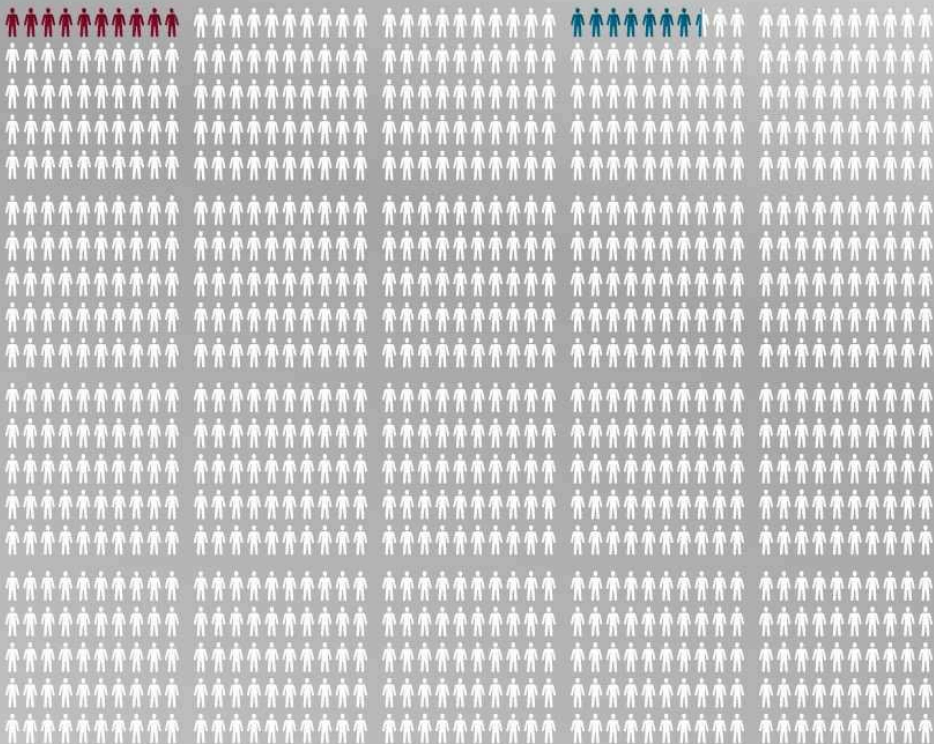


Created from Burmester GR, et al. *RMD Open*. 2021.<sup>1</sup>

[Please see the full table here.](#)

From ORAL Surveillance, patients with moderate-to-severe RA who were aged ≥50 years with ≥1 additional CV risk factor<sup>2,c</sup>

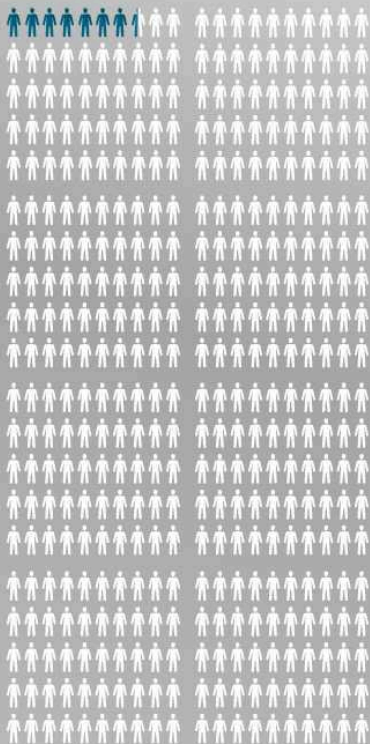
Higher-risk RA population  
receiving XELJANZ  
combined doses:  
9.8 per 1000 PY<sup>2,b</sup>



Created from Ytterberg SR, et al. *N Engl J Med*. 2022.<sup>2</sup>

[Please see the full table here.](#)

Higher-risk  
RA population  
receiving TNFi:  
7.3 per 1000 PY<sup>2,b</sup>



XELJANZ 10 mg BID is not approved for the treatment of RA. The recommended dosage of XELJANZ is 5 mg BID or 11 mg QD.<sup>3</sup>

<sup>a</sup>Adjudicated composite MACE were defined as any myocardial infarction, stroke, or CV death. Incidence rate was calculated as unique patients with events per 100 PY. The ISS and analysis of adverse events of special interest include pooled data from patients exposed to ≥1 dose of XELJANZ in phase 1, 2, 3, or 3b/4 clinical trials and LTE studies in RA.<sup>1</sup> <sup>b</sup>Adjudicated MACE were defined as death from CV causes, nonfatal myocardial infarction, or nonfatal stroke. Crude incidence rates were expressed in patients with first events per 100 PY.<sup>2</sup> <sup>c</sup>CV risk factors included current cigarette smoker, hypertension, HDL-C level of <40 mg/dL, diabetes mellitus, family history of premature CHD, extra-articular RA, or history of CAD.<sup>2</sup>

BID, twice daily; CAD, coronary artery disease; CHD, coronary heart disease; CV, cardiovascular; HDL-C, high-density lipoprotein-cholesterol; ISS, integrated safety summary; LTE, long-term extension; MACE, major adverse cardiovascular events; ORAL, Oral Rheumatoid Arthritis Trial; PY, patient-year; QD, once daily; RA, rheumatoid arthritis; TNFi, tumour necrosis factor inhibitor.

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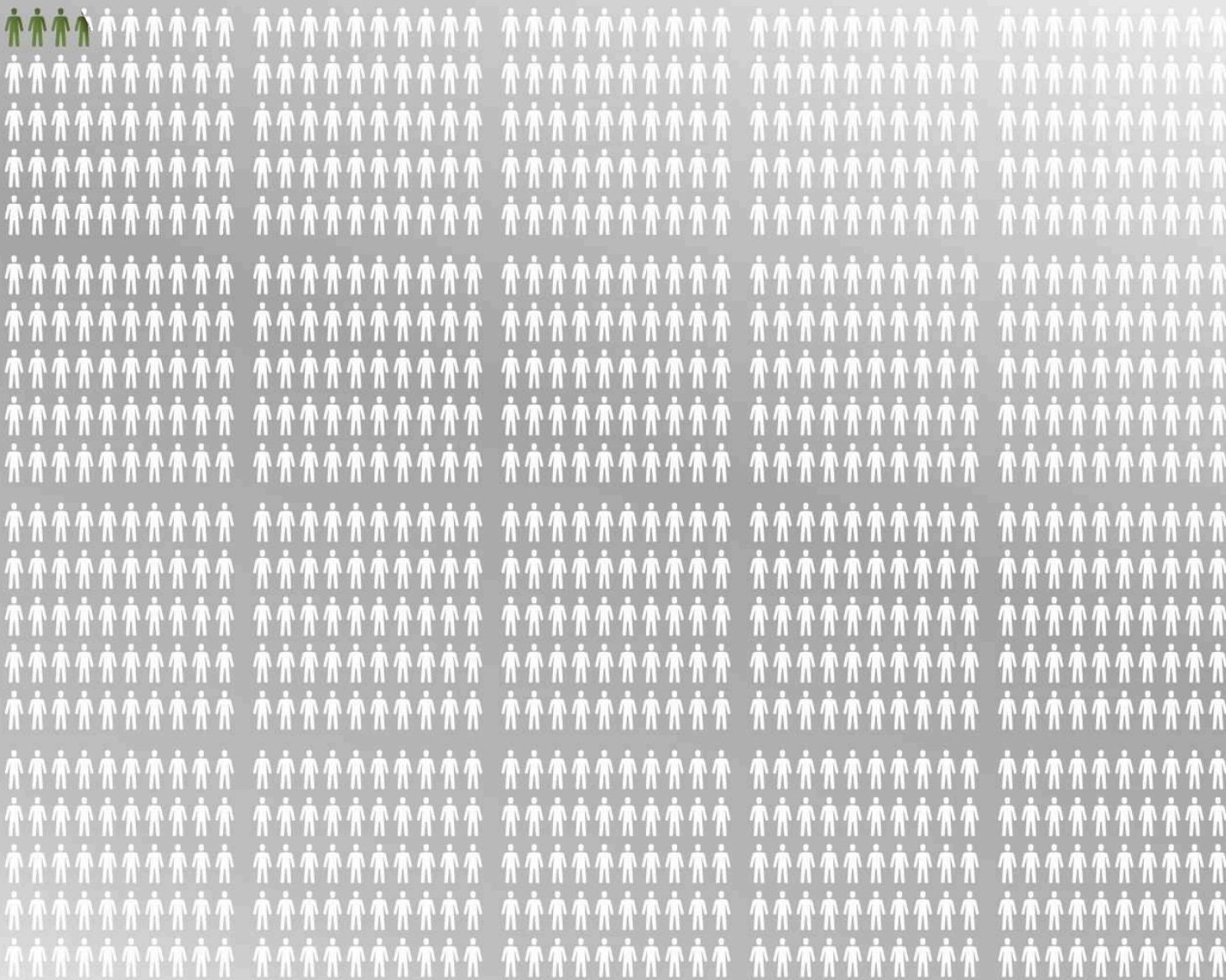
# Analysing the safety profile of XELJANZ: incidence rate of malignancy in different patient populations

## Incidence rate of malignancy (excluding NMSC)<sup>a</sup>

Filled people represent the number  
of events for every 1000 patients  
with RA for 1 year.

General RA  
population:  
3.6 per  
1000 PY<sup>1,a</sup>

From the  
prospective,  
longitudinal  
US CorEvitas  
registry<sup>1,b</sup>



Data from different studies should not be directly compared because  
of differences in trial design, populations, and methodology.

[For information on the limitations of the CorEvitas registry](#)

Created from Gross RL, et al. *Arthritis Rheumatol.* 2014.<sup>1</sup>

[Please see the full table here.](#)

XELJANZ 10 mg BID is not approved for the treatment of RA. The recommended dosage of XELJANZ is 5 mg BID or 11 mg QD.<sup>2</sup>  
<sup>a</sup>Adjudicated malignancy excluding NMSC. Incidence rates were calculated per 100 PY. For patients with more than one malignancy reported during the follow-up period, only the first event was used in the analysis.<sup>1</sup> <sup>b</sup>Previously known as the Corona Registry.<sup>3</sup>  
BID, twice daily; NMSC, nonmelanoma skin cancer; PY, patient-year; QD, once daily; RA, rheumatoid arthritis.



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# Analysing the safety profile of XELJANZ: incidence rate of malignancy in different patient populations

## Incidence rate of malignancy (excluding NMSC)<sup>a,b</sup>

Filled people represent the number of events for every 1000 patients with RA for 1 year.

For more information on the:

[XELJANZ pooled clinical trial programme](#)

[ORAL Surveillance trial](#)

[Can the higher-risk patient population be further characterised?](#)

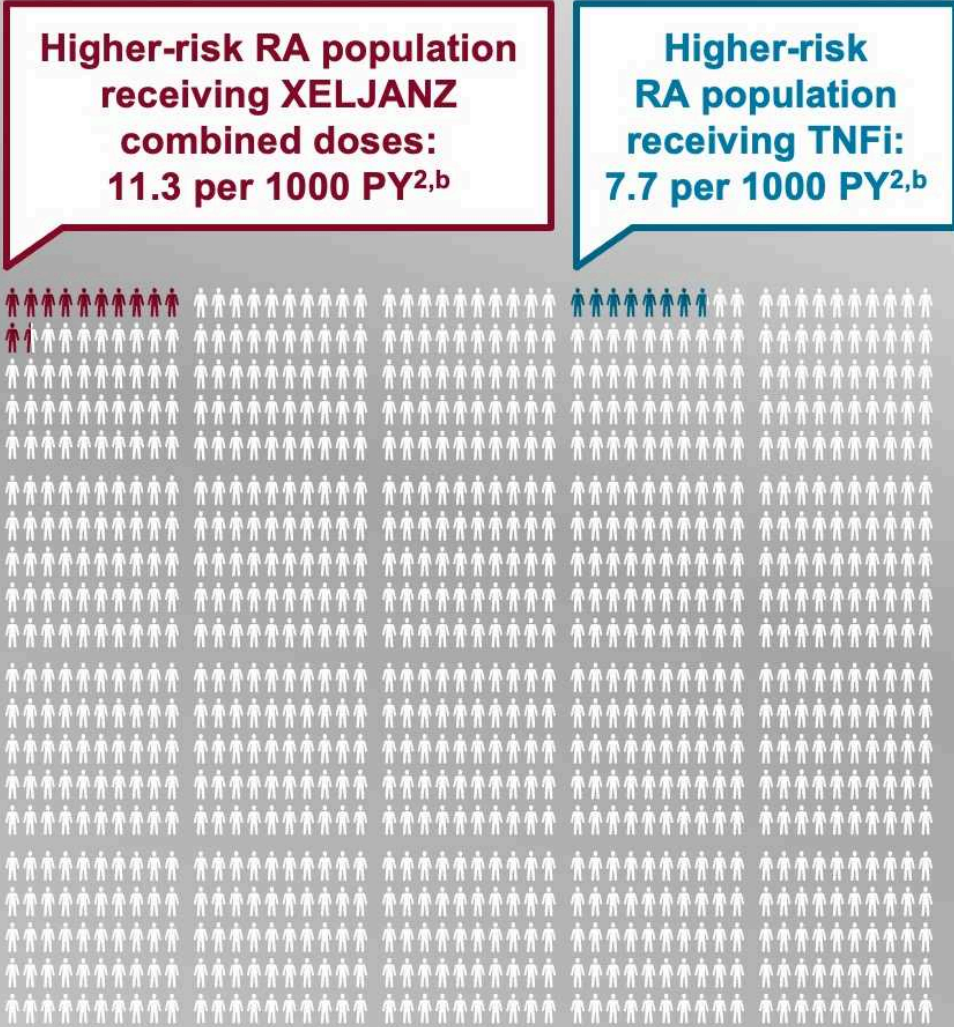
From the XELJANZ pooled clinical trial programme  
(excluding ORAL Surveillance)<sup>1</sup>



Created from Burmester GR, et al. *RMD Open*. 2021.<sup>1</sup>

[Please see the full table here.](#)

From ORAL Surveillance, patients with moderate-to-severe RA  
who were aged ≥50 years with ≥1 additional CV risk factor<sup>2,c</sup>



Created from Ytterberg SR, et al. *N Engl J Med*. 2022.<sup>2</sup>

[Please see the full table here.](#)

XELJANZ 10 mg BID is not approved for the treatment of RA. The recommended dosage of XELJANZ is 5 mg BID or 11 mg QD.<sup>3</sup>

<sup>a</sup>Adjudicated malignancy defined as cancers excluding NMSC. Incidence rate was calculated as unique patients with events per 100 PY. The ISS and analysis of adverse events of special interest include pooled data from patients exposed to ≥1 dose of XELJANZ in phase 1, 2, 3, or 3b/4 clinical trials and LTE studies in RA.<sup>1</sup> <sup>b</sup>Adjudicated malignancy defined as cancers excluding NMSC. Crude incidence rates were expressed in patients with first events per 100 PY.<sup>2</sup> <sup>c</sup>CV risk factors included current cigarette smoker, hypertension, HDL-C level of <40 mg/dL, diabetes mellitus, family history of premature CHD, extra-articular RA, or history of CAD.<sup>2</sup>  
BID, twice daily; CAD, coronary artery disease; CHD, coronary heart disease; CV, cardiovascular; HDL-C, high-density lipoprotein-cholesterol; ISS, integrated safety summary; LTE, long-term extension; NMSC, nonmelanoma skin cancer; ORAL, Oral Rheumatoid Arthritis Trial; PY, patient-year; QD, once daily; RA, rheumatoid arthritis; TNFi, tumour necrosis factor inhibitor.

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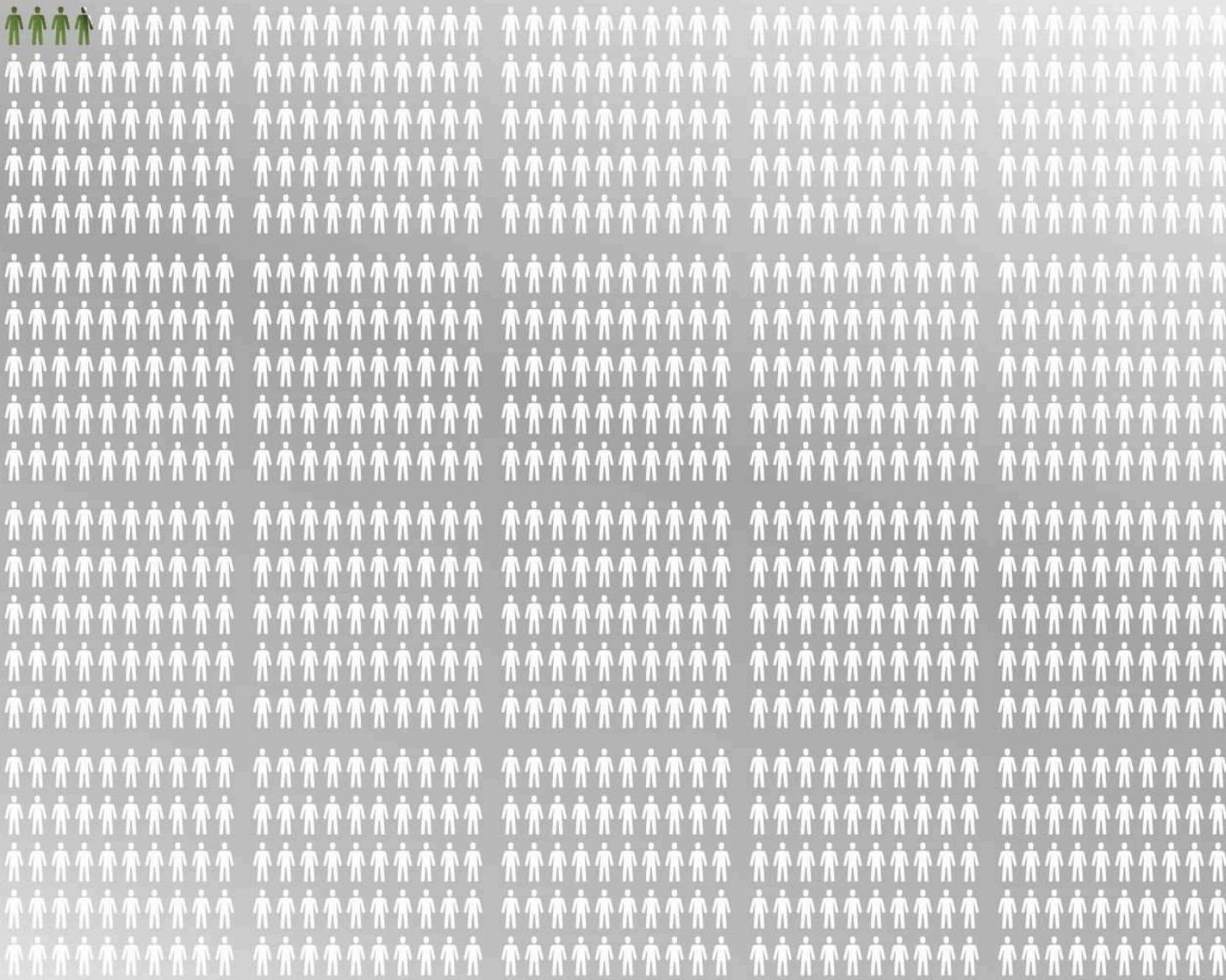
# Analysing the safety profile of XELJANZ: incidence rate of VTE in different patient populations

## Incidence rate of VTE<sup>a</sup>

Filled people represent the number of events that occurred for every 1000 patients with RA for 1 year.

General RA  
population:  
3.79 per  
1000 PY<sup>1,a</sup>

From a matched  
cohort study  
of a Canadian,  
population-based  
administrative  
health database<sup>1</sup>



Data from different studies should not be directly compared because of differences in trial design, populations, and methodology

For information on the limitations of the Canadian observational study

Created from Li L, et al. *Rheumatology (Oxford)*. 2021.<sup>1</sup>

<sup>a</sup>VTE included deep vein thrombosis and pulmonary embolism. Incidence rates were calculated per 1000 PY.<sup>1</sup> PY, patient-year; RA, rheumatoid arthritis; VTE, venous thromboembolism.

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# Analysing the safety profile of XELJANZ: incidence rate of VTE in different patient populations

## Incidence rate of VTE<sup>a,b</sup>

Filled people represent the number of events that occurred for every 1000 patients with RA for 1 year.

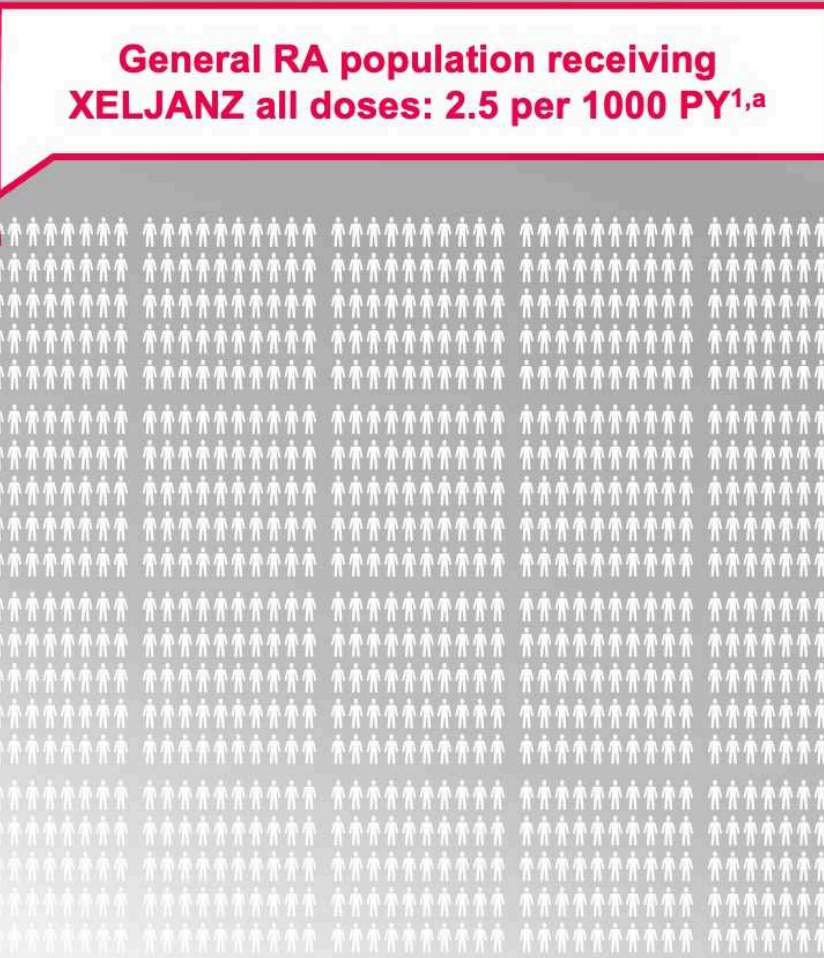
For more information on the:

[XELJANZ pooled clinical trial programme](#)

[ORAL Surveillance trial](#)

[Can the higher-risk patient population be further characterised?](#)

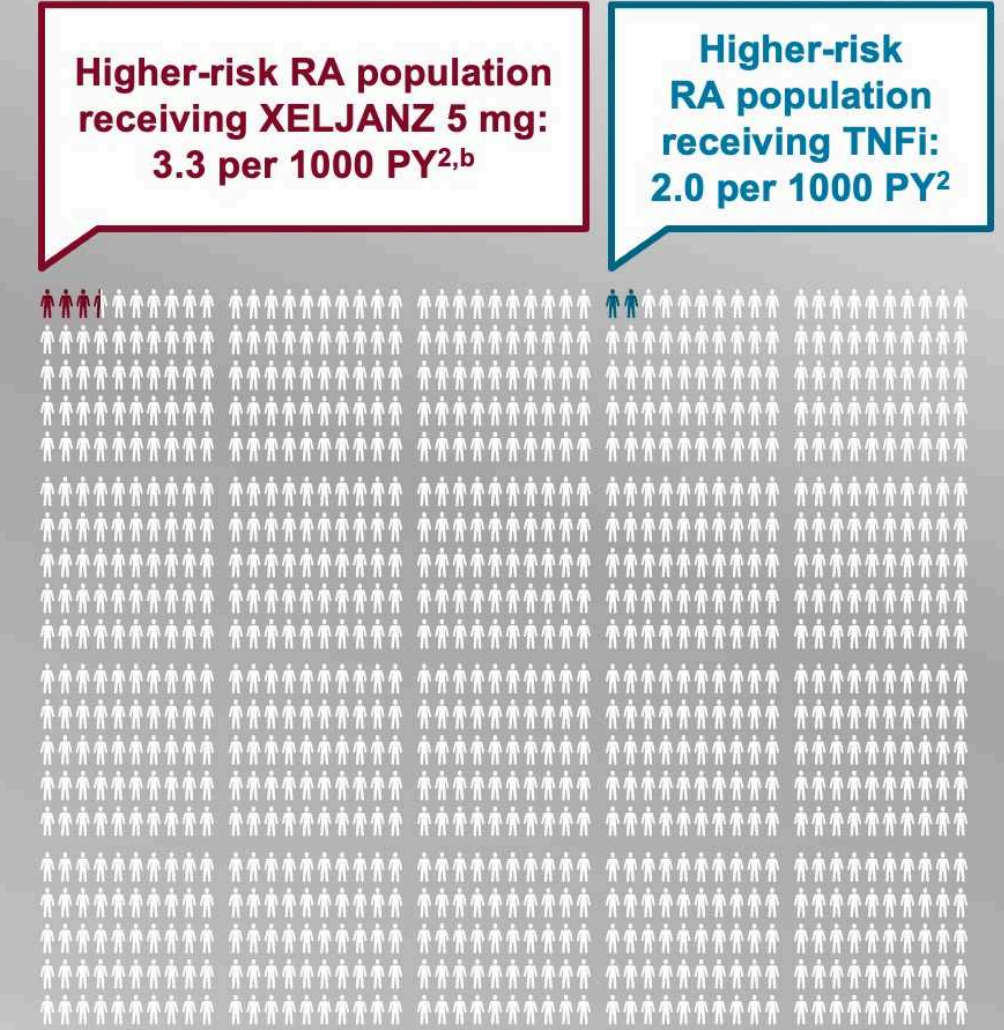
From the XELJANZ pooled clinical trial programme  
(excluding ORAL Surveillance)<sup>1</sup>



Created from Mease P, et al. *Ann Rheum Dis*. 2020.<sup>1</sup>

[Please see the full table here.](#)

From ORAL Surveillance, patients with moderate-to-severe RA  
who were aged ≥50 years with ≥1 additional CV risk factor<sup>2,c</sup>



Created from Ytterberg SR, et al. *N Engl J Med*. 2022.<sup>2</sup>

[Please see the full table here.](#)

XELJANZ 10 mg BID is not approved for the treatment of RA. The recommended dosage of XELJANZ is 5 mg BID or 11 mg QD.<sup>3</sup>

<sup>a</sup>VTE included deep vein thrombosis and pulmonary embolism. Incidence rate was calculated as number of patients with an event per 100 PY. The ISS and analysis of adverse events of special interest include pooled data from patients exposed to ≥1 dose of XELJANZ in phase 1, 2, 3, or 3b/4 clinical trials and LTE studies in RA.<sup>1</sup> <sup>b</sup>Adjudicated VTE. Crude incidence rates were expressed in patients with first events per 100 PY.<sup>2</sup> <sup>c</sup>CV risk factors included current cigarette smoker, hypertension, HDL-C level of <40 mg/dL, diabetes mellitus, family history of premature CHD, extra-articular RA, or history of CAD.<sup>2</sup>

BID, twice daily; CAD, coronary artery disease; CHD, congenital heart disease; CV, cardiovascular; HDL-C, high-density lipoprotein-cholesterol; ISS, integrated safety summary; LTE, long-term extension; ORAL, Oral Rheumatoid Arthritis Trial; QD, once daily; RA, rheumatoid arthritis; TNFi, tumour necrosis factor inhibitor; VTE, venous thromboembolism.

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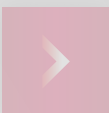
HIGHER-RISK  
PATIENT POPULATION

Post hoc analysis of ORAL Surveillance

MACE

Malignancy

VTE





XELJANZ demonstrated efficacy, with a well-characterised safety profile across 5 indications



 The **only oral JAK inhibitor to be evaluated** in a CV risk-enriched population<sup>7</sup>

 **Long-term safety** evaluated in RA, PsA, and UC<sup>8</sup>

 XELJANZ offers **robust clinical and market experience** established over time<sup>1,5-7,9,10</sup>

 The **FIRST oral JAK inhibitor approved for 5 indications: RA, PsA, AS, UC, and JIA<sup>7,11-15</sup>**

AS, ankylosing spondylitis; CV, cardiovascular; JAK, Janus kinase; JIA, juvenile idiopathic arthritis; PsA, psoriatic arthritis; RA, rheumatoid arthritis; UC, ulcerative colitis.

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# Limitations

**Limitations of the UC induction study post hoc analysis:** These analyses were post hoc, and data were based on daily telephone diary entries. Onset of XELJANZ efficacy in the wider population of patients with UC may differ. XELJANZ plasma concentration may not be at steady state until 24 to 48 hours after initial dosing. Therefore, these analyses should be interpreted with caution.<sup>1,2</sup>

**Limitations of the RA LTE study:** Limitations include lack of a placebo-control arm, data representing an enriched population of patients with continued efficacy and tolerability, and the potential for responder (or other) bias in patients who remain in open-label studies for longer periods.<sup>3,4</sup>

**Limitations of the PsA LTE study:** Limitations include lack of a placebo-control arm, limiting the estimate of treatment effect; data representing an enriched population of patients (n=680) who had responded to and tolerated XELJANZ in qualifying studies; the potential for responder (or other) bias in patients who remain in open-label studies for longer periods; observed data that were not designed to look at differences between doses, as patients could change dose during the study; dose groups that were assessed post hoc; and limitations in the algorithms used to assess the doses.<sup>5</sup>

**Limitations of the UC LTE study:** This is a post hoc analysis of data from an OLE study of XELJANZ in a subpopulation of patients with moderate to severe UC meeting remission criteria following completion of the 52-week OCTAVE Sustain study. Open-label studies have inherent biases. For this analysis from the OLE study, treatment and dose were known to investigator and patient, there was no comparator arm, and the sample size was small. This analysis should be interpreted with caution while taking these considerations into account.<sup>6</sup>

**Limitations of the SCQM registry:** Limitations include missing baseline covariates; however, multiple imputations were performed and confirmed that there was no bias to the results. As expected with observational studies, the data may be confounded by unmeasured factors. Specific geographical population may not be representative of the worldwide population (e.g., patient characteristics, healthcare access). Reduced proportion of patients having CDAI assessment at 1 year to assess effectiveness. Long-term efficacy and safety of XELJANZ was not explored.<sup>7</sup>

**Limitations of the CorEvitas registry:** Limitations include nonrandomised, prospective comparison, and potential for unmeasured confounders despite propensity score matching and controlling for measured differences. Results from the CorEvitas Registry study do not necessarily apply to the worldwide RA patient population.<sup>8</sup>

**Limitations of the Canadian observational study:** Uncertainty in the accuracy of RA case definitions cannot be completely ruled out, laboratory test data were not available, there was potential for unmeasured confounders, and results from the study do not necessarily apply to the worldwide RA patient population.<sup>9</sup>

CDAI, Clinical Disease Activity Index; LTE, long-term extension; OLE, open-label extension; PsA, psoriatic arthritis; RA, rheumatoid arthritis; SCQM, Swiss Clinical Quality Management in Rheumatic Diseases; UC, ulcerative colitis.

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**Efficacy: PsA, AS, and JIA**

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**ORAL Surveillance 3**  
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Limitations

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