

XELJANZ Safety Data

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XELJANZ® XR
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Q1

5 Safety Questions Remaining

The ORAL Surveillance study was a long-term noninferiority trial conducted to evaluate safety with XELJANZ at 2 doses, 5 mg twice daily and 10 mg twice daily,* versus a TNF blocker control in adult patients with **moderately to severely active RA** who were 50 years of age and older with at least 1 cardiovascular risk factor.

## Which 1 of the following items is not included as a CV risk factor as part of the ORAL Surveillance key eligibility criteria?

Select 1 option

- ☐ Current cigarette smoker
- ☐ Consumption of 2 or more sugary soft drinks per day
- ☐ High-density lipoprotein <40 mg/L
- ☐ Diabetes mellitus
- ☐ History of coronary artery disease
- ☐ History of premature coronary heart disease or sudden death documented in a first-degree relative
- ☐ Presence of extra-articular disease
- ☐ Diagnosis of hypertension

*NOTE: XELJANZ 10 mg twice daily was discontinued by the Data Monitoring Committee due to safety concerns, and ongoing patients were switched from XELJANZ 10 mg to XELJANZ 5 mg. The column “XELJANZ 10 mg BID” includes all events and follow-up for patients randomized to XELJANZ 10 mg twice daily. XELJANZ/XELJANZ Oral Solution 10 mg twice daily (or a XELJANZ XR 22 mg once daily) dosage is not recommended for the treatment of RA, PsA, AS, or pcJIA.[1]

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## IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

**Patients treated with XELJANZ* are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.**

**If a serious infection develops, interrupt XELJANZ until the infection is controlled.**

**Reported infections include:**

- **Active tuberculosis, which may present with pulmonary or extrapulmonary disease. Patients should be tested for latent tuberculosis before XELJANZ use and during therapy. Treatment for latent infection should be initiated prior to XELJANZ use.**
- **Invasive fungal infections, including cryptococcosis and pneumocystosis. Patients with invasive fungal infections may present with disseminated, rather than localized, disease.**
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In the UC population, XELJANZ 10 mg twice daily was associated with greater risk of serious infections compared to 5 mg twice daily. Opportunistic herpes zoster infections (including meningoencephalitis, ophthalmologic, and disseminated cutaneous) were seen in patients who were treated with XELJANZ 10 mg



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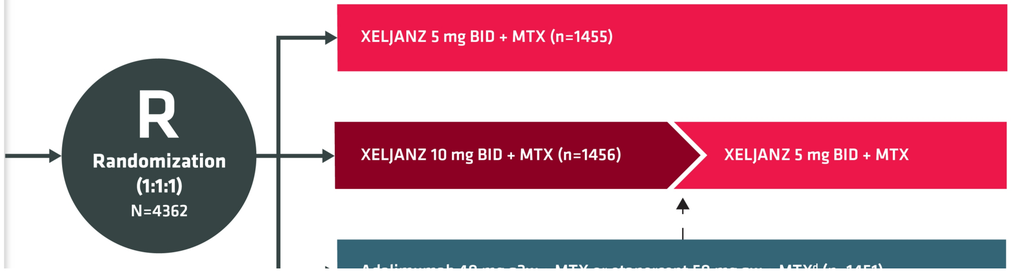
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# ORAL Surveillance Study Design: A Long-Term Safety Study in RA

| | |
|---|---|
| DESIGN | Phase 3b/4 randomized, parallel-arm, open-label, safety endpoint–driven study (N=4362[a]) |
| PRIMARY OBJECTIVE | Evaluate the safety of XELJANZ at 2 doses vs a TNF blocker in RA patients who were ≥50 years old with at least 1 CV risk factor |
| COPRIMARY ENDPOINTS | Adjudicated MACE[b] and adjudicated malignancies (excluding NMSC)[c] |
| OTHER ENDPOINTS | Mortality, serious infections, and thromboembolic events |
| STATISTICAL PLAN | Assess noninferiority of XELJANZ combined doses vs TNF blocker; determine whether the upper bound of the 95% CI for the hazard ratio for the primary comparison of XELJANZ (combined doses) vs TNF blocker met prespecified noninferiority criterion (ie, upper limit of 95% CI <1.8 for analyses of MACE and malignancy [excluding NMSC]) |
| PROTOCOL AMENDMENT FEBRUARY 2019 | Amendment was based on an ad hoc safety analysis in which the DSMB observed an increased occurrence of pulmonary embolism and overall mortality in the XELJANZ 10 mg BID arm vs the 2 other arms. The 10 mg BID dose was discontinued, and patients in this arm were allowed to switch to 5 mg BID dosing |
| STUDY COMPLETION REQUIREMENTS | The study was event driven, requiring at least 1500 patients to be followed for 3 years, with 103 cases of adjudicated MACE and 138 cases of adjudicated malignancies (excluding NMSC) |

### KEY ELIGIBILITY CRITERIA

- Moderate to severe RA, including ≥6 tender or painful joints and ≥6 swollen joints (28-joint count)
- Taking MTX without adequate control of symptoms
- ≥50 years of age
- ≥1 CV risk factor
  - Current cigarette smoker
  - Diagnosis of hypertension
  - High-density lipoprotein <40 mg/dL




NEXT QUESTION

## IMPORTANT SAFETY INFORMATION

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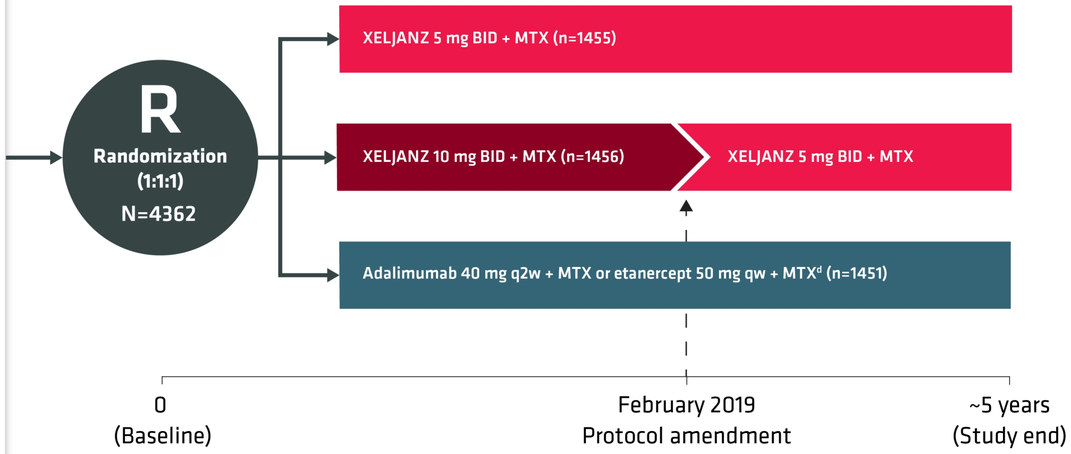
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  - Diabetes mellitus
  - History of coronary artery disease
  - History of premature coronary heart disease or sudden death documented in first-degree relative
  - Presence of extra-articular disease associated with RA[e]




## Baseline Patient Characteristics[1,2]

| CV RISK–ENRICHED POPULATION: RA patients with ≥1 CV risk factor | XELJANZ 5 mg BID (N=1455) | XELJANZ 10 mg BID (N=1456) (includes patients switched to 5 mg BID dose per Feb 2019 protocol amendment) | TNF Blocker (N=1451) |
|---|---|---|---|
| Female (%) | 80.3 | 77.2 | 77.0 |
| Age, median (years) | 60 | 61 | 60 |
| ≥65 years of age (%) | 28.4 | 32.8 | 31.8 |

NEXT QUESTION

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| BMI,[f] mean (kg/m$^2$) ± SD | 29.7 ± 6.5 | 29.7 ± 6.3 | 29.8 ± 6.6 |
| BMI[f] ≥30 kg/m$^2$ (%) | 41.6 | 40.8 | 42.5 |
| Disease duration, mean (years) | 10.44 | 10.21 | 10.61 |
| HAQ-DI, mean (score) ± SD | 1.6 ± 0.6 | 1.6 ± 0.6 | 1.6 ± 0.6 |
| **Cardiovascular Risk Factors (%)** | | | |
| Smoking, current or past | 49.5 | 48.4 | 46.8 |
| Hypertension | 65.6 | 65.5 | 66.8 |
| HDL <40 mg/dL | 11.8 | 13.4 | 11.9 |
| Diabetes mellitus | 16.7 | 17.9 | 17.6 |
| Family history of premature coronary heart disease | | | |
| First-degree male relative aged <55 years | 10.6 | 9.1 | 10.4 |

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| First-degree male relative aged <55 years | 10.6 | 9.1 | 10.4 |
| First-degree female relative aged <65 years | 7.9 | 7.3 | 6.9 |
| Extra-articular disease associated with RA | 36.6 | 35.8 | 38.0 |
| Coronary artery disease | 11.1 | 11.8 | 11.3 |

**XELJANZ 10 mg twice daily dosage is not recommended for the treatment of RA, PsA, AS, or pcJIA.[1,g]**

**XELJANZ is approved for use in patients with inadequate response or intolerance to TNF blockers.[1]**

[a]Randomized patients who received study drug.[4] [b]MACE includes CV death, nonfatal myocardial infarction, and nonfatal stroke of any classification.[1] [c]An independent committee conducted a blinded evaluation of the coprimary endpoints according to predefined criteria (adjudication).[1] [d]Patients randomized to TNF blocker in the United States, Puerto Rico, and Canada received adalimumab 40 mg q2w; in all other countries, those randomized to TNF blockers received etanercept 50 mg qw.[4] [e]Extra-articular diseases may include nodules, Sjögren's syndrome, anemia of chronic disease, and pulmonary manifestations.[4] [f]For BMI, N=4345; BMI data not available for 17 patients at baseline.[2] [g]Study pcJIA-I included patients with active polyarthritis including RF negative, RF positive, extended oligoarthritis, systemic JIA without system manifestations, as well as jPsA and ERA patients.[1]

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| PRIMARY OBJECTIVE | Evaluate the safety of XELJANZ at 2 doses vs a TNF blocker in RA patients who were ≥50 years old with at least 1 CV risk factor |
| COPRIMARY ENDPOINTS | Adjudicated MACE[b] and adjudicated malignancies (excluding NMSC)[c] |
| OTHER ENDPOINTS | Mortality, serious infections, and thromboembolic events |
| STATISTICAL PLAN | Assess noninferiority of XELJANZ combined doses vs TNF blocker; determine whether the upper bound of the 95% CI for the hazard ratio for the primary comparison of XELJANZ (combined doses) vs TNF blocker met prespecified noninferiority criterion (ie, upper limit of 95% CI <1.8 for analyses of MACE and malignancy [excluding NMSC]) |
| PROTOCOL AMENDMENT FEBRUARY 2019 | Amendment was based on an ad hoc safety analysis in which the DSMB observed an increased occurrence of pulmonary embolism and overall mortality in the XELJANZ 10 mg BID arm vs the 2 other arms. The 10 mg BID dose was discontinued, and patients in this arm were allowed to switch to 5 mg BID dosing |
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**KEY ELIGIBILITY CRITERIA**

- Moderate to severe RA, including ≥6 tender or painful joints and ≥6 swollen joints (28-joint count)
- Taking MTX without adequate control of symptoms
- ≥50 years of age
- ≥1 CV risk factor
  - Current cigarette smoker
  - Diagnosis of hypertension
  - High-density lipoprotein <40 mg/dL




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**IMPORTANT SAFETY INFORMATION**

**SERIOUS INFECTIONS**

**Patients treated with XELJANZ* are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.**

**If a serious infection develops, interrupt XELJANZ until the infection is controlled.**

**Reported infections include:**

- **Active tuberculosis, which may present with pulmonary or extrapulmonary disease. Patients should be tested for latent tuberculosis before XELJANZ use and during therapy. Treatment for latent infection should be initiated prior to XELJANZ use.**
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# Baseline Patient Characteristics[1,2]

| CV RISK-ENRICHED POPULATION: RA patients with ≥1 CV risk factor | XELJANZ 5 mg BID (N=1455) | XELJANZ 10 mg BID (N=1456) (includes patients switched to 5 mg BID dose per Feb 2019 protocol amendment) | TNF Blocker (N=1451) |
|---|---|---|---|
| Female (%) | 80.3 | 77.2 | 77.0 |
| Age, median (years) | 60 | 61 | 60 |
| ≥65 years of age (%) | 28.4 | 32.8 | 31.8 |
| BMI,[f] mean (kg/m$^2$) ± SD | 29.7 ± 6.5 | 29.7 ± 6.3 | 29.8 ± 6.6 |
| BMI[f] ≥30 kg/m$^2$ (%) | 41.6 | 40.8 | 42.5 |
| Disease duration, mean (years) | 10.44 | 10.21 | 10.61 |
| HAQ-DI, mean (score) ± SD | 1.6 ± 0.6 | 1.6 ± 0.6 | 1.6 ± 0.6 |
| **Cardiovascular Risk Factors (%)** | | | |
| Smoking, current or past | 49.5 | 48.4 | 46.8 |
| Hypertension | 65.6 | 65.5 | 66.8 |
| HDL <40 mg/dL | 11.8 | 13.4 | 11.9 |
| Diabetes mellitus | 16.7 | 17.9 | 17.6 |
| Family history of premature coronary heart disease | | | |
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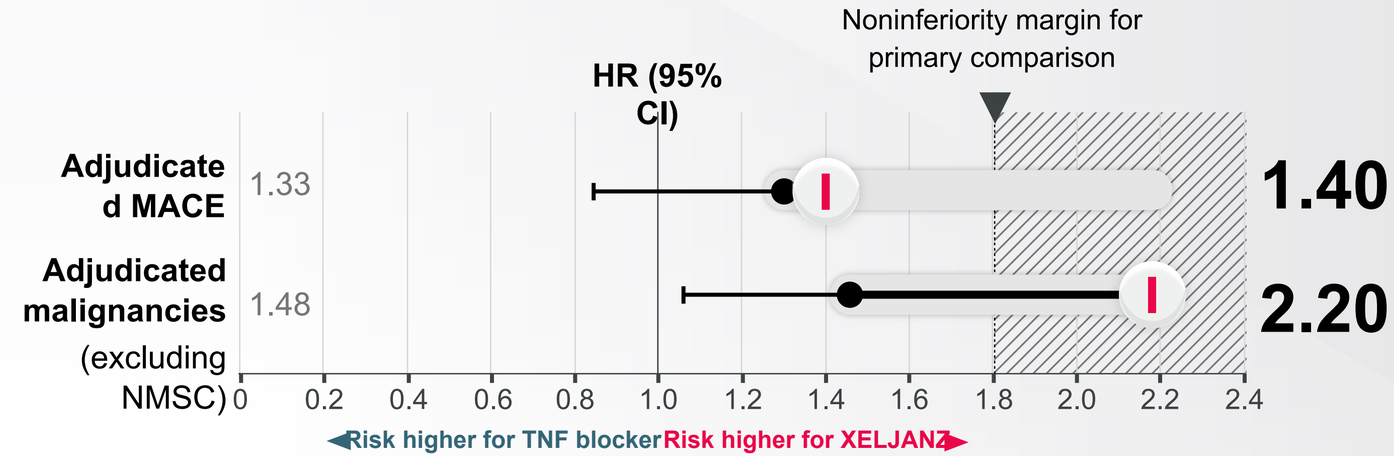
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PRIMARY COMPARISON

XELJANZ DOSES COMBINED[a] (N=2911)

VS

TNF BLOCKER (N=1451)




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RESET VIEW ANSWER

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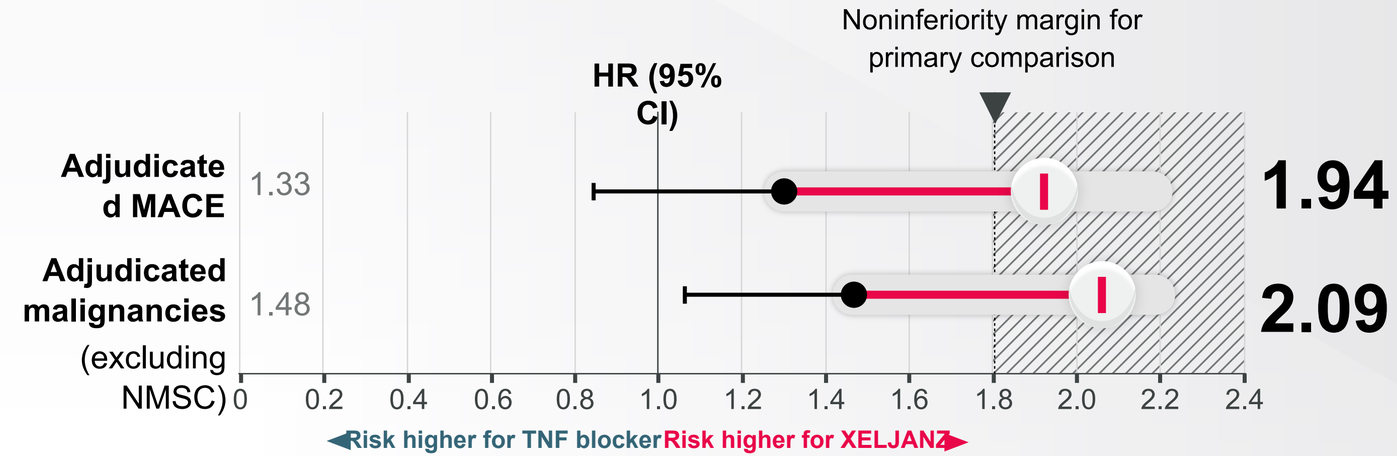
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RESET

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Q1 Q2

4 Safety Questions Remaining

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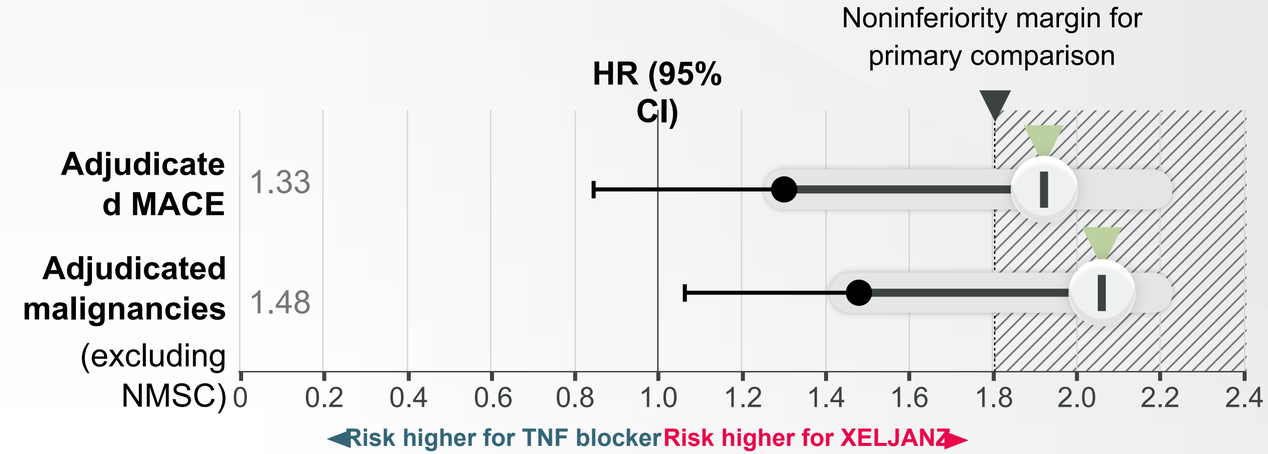
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PRIMARY COMPARISON

XELJANZ DOSES COMBINED[a] (N=2911)

VS

TNF BLOCKER (N=1451)




Correct answer **1.94** | Your answer 1.94

Correct answer **2.09** | Your answer 2.09

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ADDITIONAL INFORMATION

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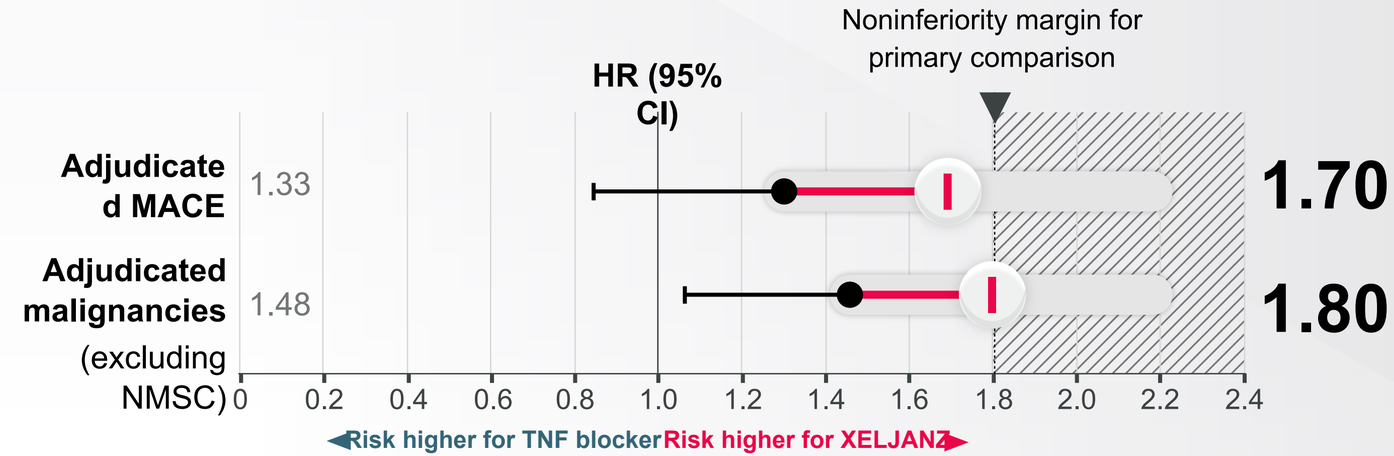
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RESET VIEW ANSWER

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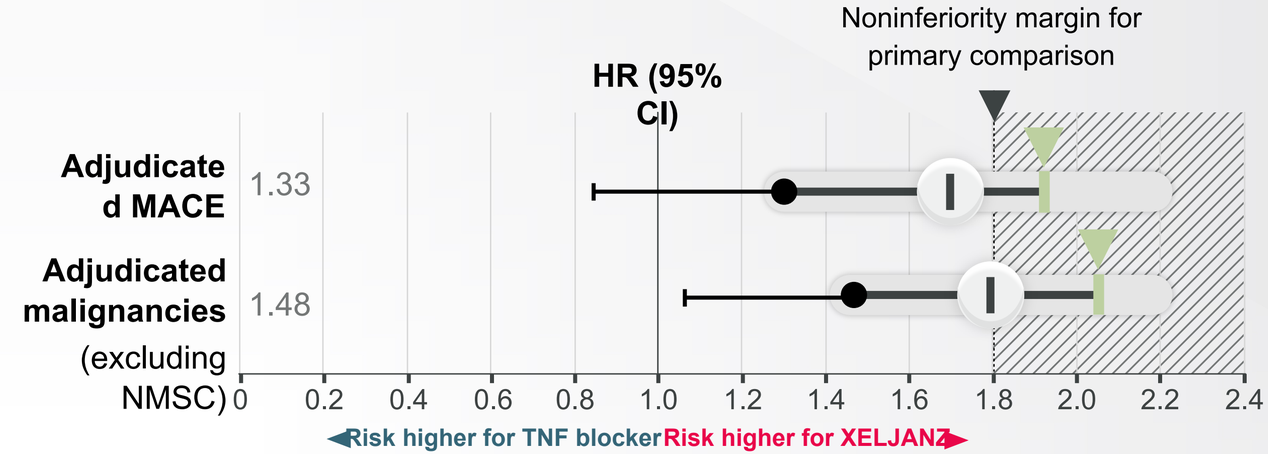
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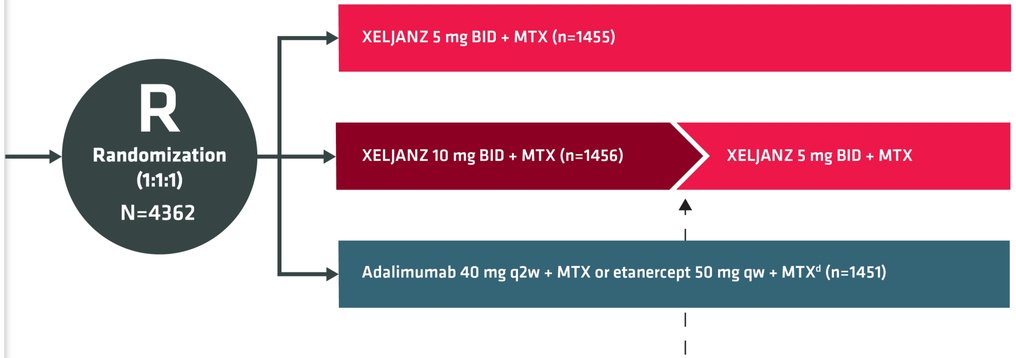
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# ORAL Surveillance Study Design[1,2]

| | |
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- Taking MTX without adequate control of symptoms
- ≥50 years of age
- ≥1 CV risk factor
  - Current cigarette smoker
  - Diagnosis of hypertension
  - High-density lipoprotein <40 mg/dL
  - Diabetes mellitus
  - History of coronary artery disease
  - History of premature coronary heart disease




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| HAQ-DI, mean (score) ± SD | 1.6 ± 0.6 | 1.6 ± 0.6 | 1.6 ± 0.6 |
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IMPORTANT SAFETY INFORMATION

SERIOUS INFECTIONS

**Patients treated with XELJANZ* are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.**

**If a serious infection develops, interrupt XELJANZ until the infection is controlled.**

**Reported infections include:**

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

The most common serious infections reported with XELJANZ included pneumonia, cellulitis, herpes zoster, urinary tract infection, diverticulitis, and appendicitis. Avoid use of XELJANZ in patients with an active, serious infection, including localized infections.

In the UC† population, XELJANZ 10 mg twice daily was associated with greater risk of serious infections compared to 5 mg twice daily. Opportunistic herpes zoster infections (including meningoencephalitis, ophthalmologic,

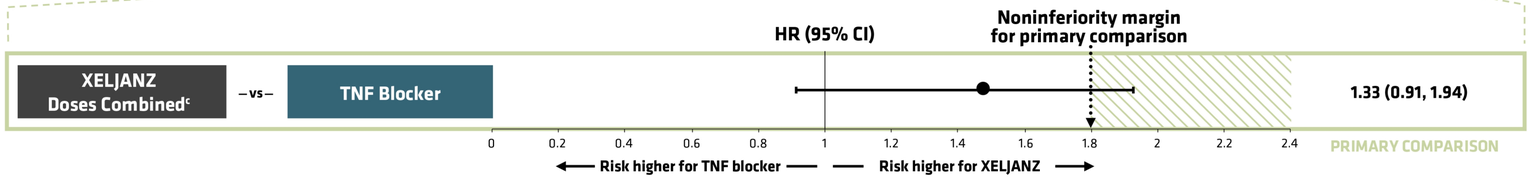
# ORAL Surveillance Coprimary Endpoint Data: Adjudicated MACE (60-Day Analysis)[1,2,a]

**Noninferiority was not met for the primary comparison of the combined XELJANZ doses to TNF blockers, as the upper limit of the 95% CI exceeded the prespecified noninferiority criterion of 1.8.[1]**

- 60 days after last dose analysis, per protocol[2,b]
- The primary analyses included 135 patients with MACE[2]
- The most frequently reported MACE with XELJANZ was myocardial infarction[2]

| | XELJANZ 5 mg BID (N=1455) | XELJANZ 10 mg BID (N=1456) (includes patients switched to 5 mg BID dose per Feb 2019 protocol amendment) | XELJANZ Doses Combined[c] (N=2911) | TNF Blocker (N=1451) |
|---|---|---|---|---|
| Patient with first event within risk period, n (%)[b] | 47 (3.23) | 51 (3.50) | 98 (3.37) | 37 (2.55) |
| Total exposure, PY | 5166.32 | 4871.96 | 10,038.28 | 5045.27 |
| Incidence rate (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) |
| HR (95% CI) for XELJANZ vs TNF blocker | 1.24 (0.81, 1.91) | 1.43 (0.94, 2.18) | **1.33 (0.91, 1.94)** | – |

PRIMARY COMPARISON UPPER LIMIT >1.8




**XELJANZ is approved for use in patients with inadequate response or intolerance to TNF blockers.[1]**

**XELJANZ 10 mg twice daily dosage is not recommended for the treatment of RA, PsA, AS, or pcJIA.[1]**

[a]Based on Cox proportional hazard model.[2]
[b]The risk period was from start of therapy up to 60 days past last dose.[2]
[c]XELJANZ doses combined included XELJANZ 5 mg twice daily and XELJANZ 10 mg twice daily groups.

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## IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

**Patients treated with XELJANZ* are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.**

**If a serious infection develops, interrupt XELJANZ until the infection is controlled.**

**Reported infections include:**

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

The most common serious infections reported with XELJANZ included pneumonia, cellulitis, herpes zoster, urinary tract infection, diverticulitis, and appendicitis. Avoid use of XELJANZ in patients with an active, serious infection, including localized infections.

In the UC† population, XELJANZ 10 mg twice daily was associated with greater risk of serious infections compared to 5 mg twice daily. Opportunistic herpes zoster infections (including meningoencephalitis, ophthalmologic,

# ORAL Surveillance Coprimary Endpoint Data: Coprimary And Other Endpoints (Total Time Analysis)[1,2,a]

| CV RISK-ENRICHED POPULATION: RA patients with ≥1 CV risk factor<br>n [incidence rate per 100 PY]<br>HR (95% CI)[b] | XELJANZ 5 mg BID (N=1455; PY=5490) | XELJANZ 10 mg BID (N=1456; PY=5298) | TNF Blocker (N=1451; PY=5468) |
|---|---|---|---|
| MACE | 50 [0.91]<br>1.16 (0.77, 1.74) | 59 [1.11]<br>1.41 (0.95, 2.10) | 43 [0.79] |
| Myocardial infarction[c] | 20 [0.36]<br>1.81 (0.87, 3.79) | 21 [0.39]<br>1.97 (0.95, 4.09) | 11 [0.20] |
| Stroke[c] | 18 [0.33]<br>0.89 (0.47, 1.69) | 21 [0.39]<br>1.08 (0.59, 2.00) | 20 [0.36] |
| Cardiovascular death | 18 [0.32]<br>1.20 (0.60, 2.37) | 25 [0.47]<br>1.71 (0.90, 3.24) | 15 [0.27] |
| Malignancies (excluding NMSC) | 62 [1.13]<br>1.47 (1.00, 2.18) | 60 [1.13]<br>1.48 (1.00, 2.19) | 42 [0.77] |
| Among current and past smokers[d] | 41 [1.53]<br>1.55 (0.94, 2.55) | 48 [1.91]<br>1.94 (1.19, 3.14) | 25 [0.99] |
| All death | 49 [0.88]<br>1.29 (0.84, 1.96) | 66 [1.23]<br>1.79 (1.20, 2.66) | 38 [0.69] |
| Serious infections | 155 [2.95]<br>1.17 (0.93, 1.47) | 184 [3.65]<br>1.44 (1.15, 1.80) | 133 [2.52] |
| Deep vein thrombosis | 12 [0.22]<br>1.33 (0.56, 3.15) | 15 [0.28]<br>1.72 (0.75, 3.92) | 9 [0.16] |
| Pulmonary embolism | 10 [0.18]<br>3.32 (0.91, 12.08) | 26 [0.49]<br>8.95 (2.71, 29.56) | 3 [0.05] |
| Venous thromboembolism | 18 [0.33]<br>1.50 (0.72, 3.10) | 36 [0.68]<br>3.10 (1.61, 5.96) | 12 [0.22] |
| Arterial thromboembolism | 51 [0.93]<br>1.13 (0.76, 1.69) | 55 [1.04]<br>1.26 (0.85, 1.87) | 45 [0.83] |
| Thromboembolism | 67 [1.23]<br>1.19 (0.84, 1.70) | 86 [1.65]<br>1.60 (1.14, 2.23) | 56 [1.03] |

**NOTE:** XELJANZ 10 mg twice daily was discontinued by the Data Monitoring Committee due to safety concerns, and ongoing patients switched from XELJANZ 10 mg to XELJANZ 5 mg. The column "XELJANZ 10 mg BID" includes all events and follow-up for patients randomized to XELJANZ 10 mg twice daily. **A XELJANZ/XELJANZ Oral Solution 10 mg twice daily (or a XELJANZ XR 22 mg once daily) dosage is not recommended for the treatment of RA or PsA.**

N indicates number of patients; n indicates number of patients with events.[1]

[a]The risk period included all available follow-up regardless of time since last treatment exposure. The median on-study follow-up time was 4 years.[1,2]

[b]HR (95% CI) for XELJANZ vs TNF blocker (univariate Cox proportional hazard model).[1]

[c]Myocardial infarction and stroke include fatal and nonfatal events.[1]

[d]Data and analyses for malignancies (excluding NMSC) for current and ex-smokers are included. There were 720 current and ex-smokers randomized to XELJANZ 5 mg, 704 to XELJANZ 10 mg, and 679 to TNF blockers.[1]

**XELJANZ is approved for use in patients with inadequate response or intolerance to TNF blockers.[1]**

NEXT QUESTION

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## IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

**Patients treated with XELJANZ* are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.**

**If a serious infection develops, interrupt XELJANZ until the infection is controlled.**

**Reported infections include:**

- **Active tuberculosis, which may present with pulmonary or extrapulmonary disease. Patients should be tested for latent tuberculosis before XELJANZ use and during therapy. Treatment for latent infection should be initiated prior to XELJANZ use.**
- **Invasive fungal infections, including cryptococcosis and pneumocystosis. Patients with invasive fungal infections may present with disseminated, rather than localized, disease.**
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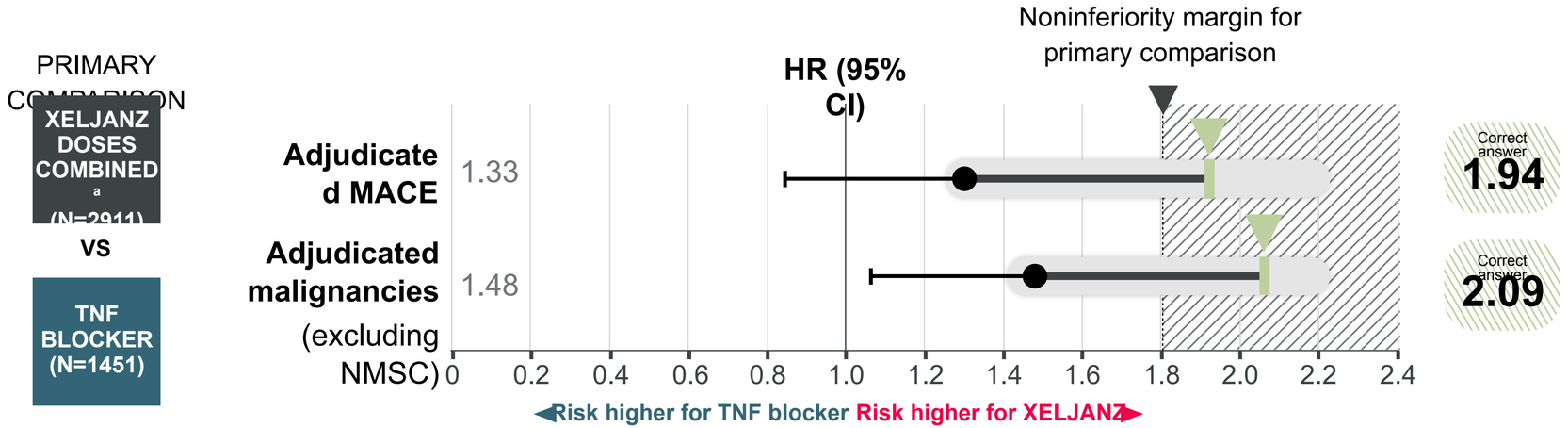
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# SAFETY DATA QUESTION 2 – Correct Answer

The ORAL Surveillance study was a long-term noninferiority trial conducted to evaluate safety with XELJANZ at 2 doses, 5 mg twice daily and 10 mg twice daily,* versus a TNF blocker control in adult patients with **moderately to severely active RA** who were 50 years of age and older with at least 1 cardiovascular risk factor. The study was designed to assess noninferiority of XELJANZ combined doses vs TNF blocker by determining whether the upper bound of the 95% CI for the hazard ratio for the primary comparison of XELJANZ (doses combined) vs TNF blocker met the prespecified noninferiority criterion (ie, upper limit of 95% CI <1.8 for analyses of adjudicated MACE and

## What are the upper limits of the 95% CI for the HRs for both adjudicated MACE (60-day analysis) and adjudicated malignancies (excluding NMSC) (total time analysis)?




[a]XELJANZ doses combined included XELJANZ 5 mg twice daily and XELJANZ 10 mg twice daily groups.
*NOTE: XELJANZ 10 mg twice daily was discontinued by the Data Monitoring Committee due to safety concerns, and ongoing patients were switched from XELJANZ 10 mg to XELJANZ 5 mg. The column "XELJANZ 10 mg BID" includes all events and follow-up for patients randomized to XELJANZ 10 mg twice

**XELJANZ is approved for use in patients with inadequate response or intolerance to TNF blockers.**[1]

ADDITIONAL INFORMATION

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The most common serious infections reported with XELJANZ included pneumonia, cellulitis, herpes zoster, urinary tract infection, diverticulitis, and appendicitis. Avoid use of XELJANZ in patients with an active, serious infection, including localized infections.

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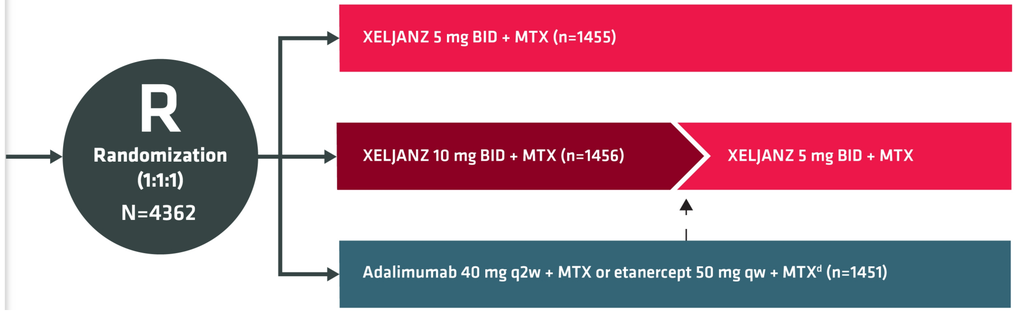
# SAFETY DATA QUESTION 2 – Additional Information

## ORAL Surveillance Study Design[1,2]

| | |
|---|---|
| DESIGN | Phase 3b/4 randomized, parallel-arm, open-label, safety endpoint–driven study (N=4362[a]) |
| PRIMARY OBJECTIVE | Evaluate the safety of XELJANZ at 2 doses vs a TNF blocker in RA patients who were ≥50 years old with at least 1 CV risk factor |
| COPRIMARY ENDPOINTS | Adjudicated MACE[b] and adjudicated malignancies (excluding NMSC)[c] |
| OTHER ENDPOINTS | Mortality, serious infections, and thromboembolic events |
| STATISTICAL PLAN | Assess noninferiority of XELJANZ combined doses vs TNF blocker; determine whether the upper bound of the 95% CI for the hazard ratio for the primary comparison of XELJANZ (combined doses) vs TNF blocker met prespecified noninferiority criterion (ie, upper limit of 95% CI <1.8 for analyses of MACE and malignancy [excluding NMSC]) |
| PROTOCOL AMENDMENT FEBRUARY 2019 | Amendment was based on an ad hoc safety analysis in which the DSMB observed an increased occurrence of pulmonary embolism and overall mortality in the XELJANZ 10 mg BID arm vs the 2 other arms. The 10 mg BID dose was discontinued, and patients in this arm were allowed to switch to 5 mg BID dosing |
| STUDY COMPLETION REQUIREMENTS | The study was event driven, requiring at least 1500 patients to be followed for 3 years, with 103 cases of adjudicated MACE and 138 cases of adjudicated malignancies (excluding NMSC) |

### KEY ELIGIBILITY CRITERIA

- Moderate to severe RA, including ≥6 tender or painful joints and ≥6 swollen joints (28-joint count)
- Taking MTX without adequate control of symptoms
- ≥50 years of age
- ≥1 CV risk factor
  - Current cigarette smoker
  - Diagnosis of hypertension
  - High-density lipoprotein <40 mg/dL
  - Diabetes mellitus




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STUDY DESIGNS, DEFINITIONS & ABBREVIATIONS
INDICATIONS & IMPORTANT SAFETY INFORMATION
REFERENCES
PRESCRIBING INFORMATION & MEDICATION GUIDE

# Baseline Patient Characteristics[1,2]

| CV RISK-ENRICHED POPULATION: RA patients with ≥1 CV risk factor | XELJANZ 5 mg BID (N=1455) | XELJANZ 10 mg BID (N=1456) (includes patients switched to 5 mg BID dose per Feb 2019 protocol amendment) | TNF Blocker (N=1451) |
|---|---|---|---|
| Female (%) | 80.3 | 77.2 | 77.0 |
| Age, median (years) | 60 | 61 | 60 |
| ≥65 years of age (%) | 28.4 | 32.8 | 31.8 |
| BMI,[f] mean (kg/m$^2$) ± SD | 29.7 ± 6.5 | 29.7 ± 6.3 | 29.8 ± 6.6 |
| BMI[f] ≥30 kg/m$^2$ (%) | 41.6 | 40.8 | 42.5 |
| Disease duration, mean (years) | 10.44 | 10.21 | 10.61 |
| HAQ-DI, mean (score) ± SD | 1.6 ± 0.6 | 1.6 ± 0.6 | 1.6 ± 0.6 |
| **Cardiovascular Risk Factors (%)** | | | |
| Smoking, current or past | 49.5 | 48.4 | 46.8 |
| Hypertension | 65.6 | 65.5 | 66.8 |
| HDL <40 mg/dL | 11.8 | 13.4 | 11.9 |
| Diabetes mellitus | 16.7 | 17.9 | 17.6 |
| Family history of premature coronary heart disease | | | |
| First-degree male relative aged <55 years | 10.6 | 9.1 | 10.4 |

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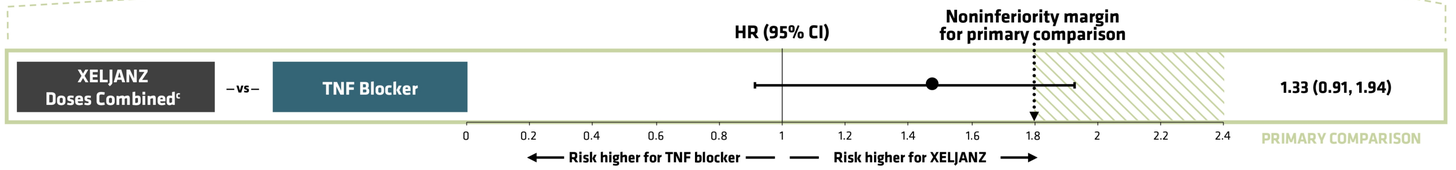
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- 60 days after last dose analysis, per protocol[2,b]
- The primary analyses included 135 patients with MACE[2]
- The most frequently reported MACE with XELJANZ was myocardial infarction[2]

| | XELJANZ 5 mg BID (N=1455) | XELJANZ 10 mg BID (N=1456) (includes patients switched to 5 mg BID dose per Feb 2019 protocol amendment) | XELJANZ Doses Combined[c] (N=2911) | TNF Blocker (N=1451) |
|---|---|---|---|---|
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| Total exposure, PY | 5166.32 | 4871.96 | 10,038.28 | 5045.27 |
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| HR (95% CI) for XELJANZ vs TNF blocker | 1.24 (0.81, 1.91) | 1.43 (0.94, 2.18) | **1.33 (0.91, 1.94)** | – |

PRIMARY COMPARISON UPPER LIMIT >1.8




**XELJANZ is approved for use in patients with inadequate response or intolerance to TNF blockers.[1]**

**XELJANZ 10 mg twice daily dosage is not recommended for the treatment of RA, PsA, AS, or pcJIA.[1]**

[a]Based on Cox proportional hazard model.[2]
[b]The risk period was from start of therapy up to 60 days past last dose.[2]
[c]XELJANZ doses combined included XELJANZ 5 mg twice daily and XELJANZ 10 mg twice daily groups.

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**If a serious infection develops, interrupt XELJANZ until the infection is controlled.**

**Reported infections include:**

- **Active tuberculosis, which may present with pulmonary or extrapulmonary disease. Patients should be tested for latent tuberculosis before XELJANZ use and during therapy. Treatment for latent infection should be initiated prior to XELJANZ use.**
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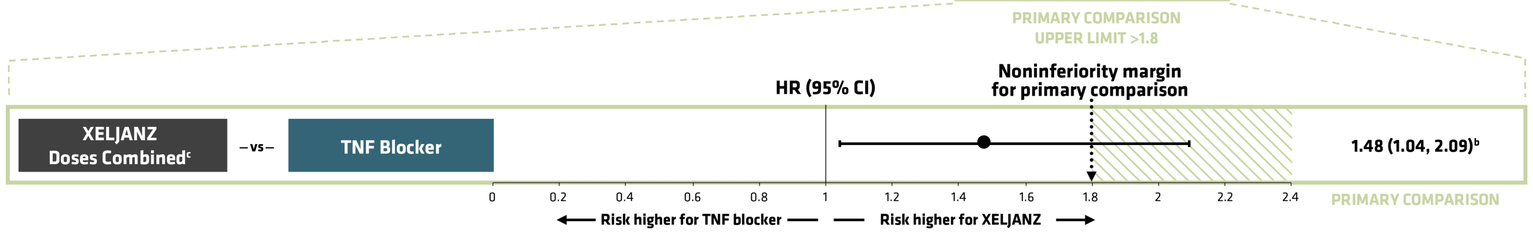
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# ORAL Surveillance Coprimary Endpoint Data: Adjudicated Malignancies (Excluding NMSC) (Total Time Analysis)[1,2,a]

**Noninferiority was not met for the primary comparison of the combined XELJANZ doses to TNF blockers, as the upper limit of the 95% CI exceeded the prespecified noninferiority criterion of 1.8.[1]**

- Total time analysis, per protocol, included all available follow-up regardless of time since last treatment exposure[2,b]
- The primary analyses included 164 patients with malignancies (excluding NMSC)[1,2]
- The most frequently reported malignancy (excluding NMSC) with XELJANZ was lung cancer[2]

| | XELJANZ 5 mg BID (N=1455) | XELJANZ 10 mg BID (N=1456) (includes patients switched to 5 mg BID dose per Feb 2019 protocol amendment) | XELJANZ Doses Combined[c] (N=2911) | TNF Blocker (N=1451) |
|---|---|---|---|---|
| Patient with first event within risk period, n (%)[b] | 62 (4.26) | 60 (4.12) | 122 (4.19) | 42 (2.89) |
| Total exposure, PY | 5491.48 | 5311.71 | 10,803.19 | 5482.30 |
| Incidence rate (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) |
| HR (95% CI) for XELJANZ vs TNF blocker | 1.47 (1.00, 2.18) | 1.48 (1.00, 2.19) | **1.48 (1.04, 2.09)[b]** | – |




- Lymphoma was reported for 4 patients receiving XELJANZ 5 mg BID, 6 patients receiving XELJANZ 10 mg BID, and 1 patient receiving TNF blockers (incidence rate of 0.07, 0.11, and 0.02 per 100 PY, respectively)[1]
- Among current and past smokers, lung cancer was reported for 13 patients receiving XELJANZ 5 mg BID, 15 patients receiving XELJANZ 10 mg BID, and 7 patients receiving TNF blockers (incidence rate of 0.48, 0.59, and 0.27 per 100 PY, respectively)[1]

**XELJANZ is approved for use in patients with inadequate response or intolerance to TNF blockers.[1]**

**XELJANZ 10 mg twice daily dosage is not recommended for the treatment of RA, PsA, AS, or pcJIA.[1]**

[a]Based on Cox proportional hazard model.[2]
[b]The risk period included all available follow-up regardless of time since last treatment exposure.[2]
[c]XELJANZ doses combined included XELJANZ 5 mg twice daily and XELJANZ 10 mg twice daily groups.

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# ORAL Surveillance Coprimary Endpoint Data: Coprimary And Other Endpoints (Total Time Analysis)[1,2,a]

| CV RISK-ENRICHED POPULATION: RA patients with ≥1 CV risk factor<br>n [incidence rate per 100 PY]<br>HR (95% CI)[b] | XELJANZ 5 mg BID (N=1455; PY=5490) | XELJANZ 10 mg BID (N=1456; PY=5298) | TNF Blocker (N=1451; PY=5468) |
|---|---|---|---|
| MACE | 50 [0.91]<br>1.16 (0.77, 1.74) | 59 [1.11]<br>1.41 (0.95, 2.10) | 43 [0.79] |
| Myocardial infarction[c] | 20 [0.36]<br>1.81 (0.87, 3.79) | 21 [0.39]<br>1.97 (0.95, 4.09) | 11 [0.20] |
| Stroke[c] | 18 [0.33]<br>0.89 (0.47, 1.69) | 21 [0.39]<br>1.08 (0.59, 2.00) | 20 [0.36] |
| Cardiovascular death | 18 [0.32]<br>1.20 (0.60, 2.37) | 25 [0.47]<br>1.71 (0.90, 3.24) | 15 [0.27] |
| Malignancies (excluding NMSC) | 62 [1.13]<br>1.47 (1.00, 2.18) | 60 [1.13]<br>1.48 (1.00, 2.19) | 42 [0.77] |
| Among current and past smokers[d] | 41 [1.53]<br>1.55 (0.94, 2.55) | 48 [1.91]<br>1.94 (1.19, 3.14) | 25 [0.99] |
| All death | 49 [0.88]<br>1.29 (0.84, 1.96) | 66 [1.23]<br>1.79 (1.20, 2.66) | 38 [0.69] |
| Serious infections | 155 [2.95]<br>1.17 (0.93, 1.47) | 184 [3.65]<br>1.44 (1.15, 1.80) | 133 [2.52] |
| Deep vein thrombosis | 12 [0.22]<br>1.33 (0.56, 3.15) | 15 [0.28]<br>1.72 (0.75, 3.92) | 9 [0.16] |
| Pulmonary embolism | 10 [0.18]<br>3.32 (0.91, 12.08) | 26 [0.49]<br>8.95 (2.71, 29.56) | 3 [0.05] |
| Venous thromboembolism | 18 [0.33]<br>1.50 (0.72, 3.10) | 36 [0.68]<br>3.10 (1.61, 5.96) | 12 [0.22] |
| Arterial thromboembolism | 51 [0.93]<br>1.13 (0.76, 1.69) | 55 [1.04]<br>1.26 (0.85, 1.87) | 45 [0.83] |
| Thromboembolism | 67 [1.23]<br>1.19 (0.84, 1.70) | 86 [1.65]<br>1.60 (1.14, 2.23) | 56 [1.03] |

**NOTE:** XELJANZ 10 mg twice daily was discontinued by the Data Monitoring Committee due to safety concerns, and ongoing patients switched from XELJANZ 10 mg to XELJANZ 5 mg. The column "XELJANZ 10 mg BID" includes all events and follow-up for patients randomized to XELJANZ 10 mg twice daily. **A XELJANZ/XELJANZ Oral Solution 10 mg twice daily (or a XELJANZ XR 22 mg once daily) dosage is not recommended for the treatment of RA or PsA.**

N indicates number of patients; n indicates number of patients with events.[1]

[a]The risk period included all available follow-up regardless of time since last treatment exposure. The median on-study follow-up time was 4 years.[1,2]

[b]HR (95% CI) for XELJANZ vs TNF blocker (univariate Cox proportional hazard model).[1]

[c]Myocardial infarction and stroke include fatal and nonfatal events.[1]

[d]Data and analyses for malignancies (excluding NMSC) for current and ex-smokers are included. There were 720 current and ex-smokers randomized to XELJANZ 5 mg, 704 to XELJANZ 10 mg, and 679 to TNF blockers.[1]

**XELJANZ is approved for use in patients with inadequate response or intolerance to TNF blockers.[1]**

CLOSE

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## IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

**Patients treated with XELJANZ* are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.**

**If a serious infection develops, interrupt XELJANZ until the infection is controlled.**

**Reported infections include:**

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

The most common serious infections reported with XELJANZ included pneumonia, cellulitis, herpes zoster, urinary tract infection, diverticulitis, and appendicitis. Avoid use of XELJANZ in patients with an active, serious infection, including localized infections.

In the UC† population, XELJANZ 10 mg twice daily was associated with greater risk of serious infections compared to 5 mg twice daily. Opportunistic herpes zoster infections (including meningoencephalitis, ophthalmologic,



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Q1 Q2 Q3

3 Safety Questions Remaining

The safety events described in the BOXED WARNING for XELJANZ only include Serious Infections and Malignancies.

Select true or false

☐ TRUE ☐ FALSE

RESET VIEW ANSWER

Help Go to Efficacy

## IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

**Patients treated with XELJANZ* are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.**

**If a serious infection develops, interrupt XELJANZ until the infection is controlled.**

**Reported infections include:**

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

The most common serious infections reported with XELJANZ included pneumonia, cellulitis, herpes zoster, urinary tract infection, diverticulitis, and appendicitis. Avoid use of XELJANZ in patients with an active, serious infection, including localized infections.

In the UC population, XELJANZ 10 mg twice daily was associated with greater risk of serious infections compared to 5 mg twice daily. Opportunistic herpes zoster infections (including meningoencephalitis, ophthalmologic, and disseminated cutaneous) were seen in patients who were treated with XELJANZ 10 mg



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Q1 Q2 Q3

3 Safety Questions Remaining

The safety events described in the BOXED WARNING for XELJANZ only include Serious Infections and Malignancies.

Select true or false

☐ TRUE

☑ FALSE

RESET

VIEW ANSWER

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## IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

**Patients treated with XELJANZ* are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.**

**If a serious infection develops, interrupt XELJANZ until the infection is controlled.**

**Reported infections include:**

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

The most common serious infections reported with XELJANZ included pneumonia, cellulitis, herpes zoster, urinary tract infection, diverticulitis, and appendicitis. Avoid use of XELJANZ in patients with an active, serious infection, including localized infections.

In the UC population, XELJANZ 10 mg twice daily was associated with greater risk of serious infections compared to 5 mg twice daily. Opportunistic herpes zoster infections (including meningoencephalitis, ophthalmologic, and disseminated cutaneous) were seen in patients who were treated with XELJANZ 10 mg



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Q1 Q2 Q3

3 Safety Questions Remaining

The safety events described in the BOXED WARNING for XELJANZ only include Serious Infections and Malignancies.

☐ TRUE

☑ FALSE Correct answer

**The BOXED WARNING for XELJANZ includes Important Safety Information for Serious Infections, Mortality, Malignancies, Major Adverse Cardiovascular Events, and Thrombosis.**

**XELJANZ is approved for use in patients with inadequate response or intolerance to TNF blockers.[1]**

ADDITIONAL INFORMATION

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## IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

**Patients treated with XELJANZ* are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.**

**If a serious infection develops, interrupt XELJANZ until the infection is controlled.**

**Reported infections include:**

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

The most common serious infections reported with XELJANZ included pneumonia, cellulitis, herpes zoster, urinary tract infection, diverticulitis, and appendicitis. Avoid use of XELJANZ in patients with an active, serious infection, including localized infections.

In the UC population, XELJANZ 10 mg twice daily was associated with greater risk of serious infections compared to 5 mg twice daily. Opportunistic herpes zoster infections (including meningoencephalitis, ophthalmologic, and disseminated cutaneous) were seen in patients who were treated with XELJANZ 10 mg



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Q1 Q2 Q3

3 Safety Questions Remaining

The safety events described in the BOXED WARNING for XELJANZ only include Serious Infections and Malignancies.

Select true or false

☑ TRUE ☐ FALSE

RESET VIEW ANSWER

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## IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

**Patients treated with XELJANZ* are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.**

**If a serious infection develops, interrupt XELJANZ until the infection is controlled.**

**Reported infections include:**

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

The most common serious infections reported with XELJANZ included pneumonia, cellulitis, herpes zoster, urinary tract infection, diverticulitis, and appendicitis. Avoid use of XELJANZ in patients with an active, serious infection, including localized infections.

In the UC population, XELJANZ 10 mg twice daily was associated with greater risk of serious infections compared to 5 mg twice daily. Opportunistic herpes zoster infections (including meningoencephalitis, ophthalmologic, and disseminated cutaneous) were seen in patients who were treated with XELJANZ 10 mg

STUDY DESIGNS, DEFINITIONS & ABBREVIATIONS | INDICATIONS & IMPORTANT SAFETY INFORMATION
REFERENCES | PRESCRIBING INFORMATION & MEDICATION GUIDE



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Q1 Q2 Q3

3 Safety Questions Remaining

The safety events described in the BOXED WARNING for XELJANZ only include Serious Infections and Malignancies.

☑ TRUE

☐ FALSE Correct answer

**The BOXED WARNING for XELJANZ includes Important Safety Information for Serious Infections, Mortality, Malignancies, Major Adverse Cardiovascular Events, and Thrombosis.**

**XELJANZ is approved for use in patients with inadequate response or intolerance to TNF blockers.[1]**

ADDITIONAL INFORMATION

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## IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

**Patients treated with XELJANZ* are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.**

**If a serious infection develops, interrupt XELJANZ until the infection is controlled.**

**Reported infections include:**

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

The most common serious infections reported with XELJANZ included pneumonia, cellulitis, herpes zoster, urinary tract infection, diverticulitis, and appendicitis. Avoid use of XELJANZ in patients with an active, serious infection, including localized infections.

In the UC population, XELJANZ 10 mg twice daily was associated with greater risk of serious infections compared to 5 mg twice daily. Opportunistic herpes zoster infections (including meningoencephalitis, ophthalmologic, and disseminated cutaneous) were seen in patients who were treated with XELJANZ 10 mg

**WARNING: SERIOUS INFECTIONS, MORTALITY, MALIGNANCY, MAJOR ADVERSE CARDIOVASCULAR EVENTS, AND THROMBOSIS**

**SERIOUS INFECTIONS**

**Patients treated with XELJANZ/XELJANZ XR/XELJANZ Oral Solution are at increased risk for developing serious infections that may lead to hospitalization or death** [see Warnings and Precautions (5.1), Adverse Reactions (6.1)]**. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.**

- **Active tuberculosis, which may present with pulmonary or extrapulmonary disease. Patients should be tested for latent tuberculosis before XELJANZ/XELJANZ XR/XELJANZ Oral Solution use and during therapy. Treatment for latent infection should be initiated prior to XELJANZ/XELJANZ XR/XELJANZ Oral Solution use.**
- **Invasive fungal infections, including cryptococcosis and pneumocystosis. Patients with invasive fungal infections may present with disseminated, rather than localized, disease.**
- **Bacterial, viral, including herpes zoster, and other infections due to opportunistic pathogens.**

**The risks and benefits of treatment with XELJANZ/XELJANZ XR/XELJANZ Oral Solution should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection. Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with XELJANZ/XELJANZ XR/XELJANZ Oral Solution, including the possible development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to initiating therapy** [see Warnings and Precautions (5.1)]**.**

**MORTALITY**

**In a large, randomized, postmarketing safety study in rheumatoid arthritis (RA) patients 50 years of age and older with at least one cardiovascular risk factor comparing XELJANZ 5 mg twice a day or XELJANZ 10 mg twice a day**

**XELJANZ is approved for use in patients with inadequate response or intolerance to TNF blockers.[1]**

NEXT QUESTION

## IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

**Patients treated with XELJANZ* are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.**

**If a serious infection develops, interrupt XELJANZ until the infection is controlled.**

**Reported infections include:**

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

The most common serious infections reported with XELJANZ included pneumonia, cellulitis, herpes zoster, urinary tract infection, diverticulitis, and appendicitis. Avoid use of XELJANZ in patients with an active, serious infection, including localized infections.

In the UC population, XELJANZ 10 mg twice daily was associated with greater risk of serious infections compared to 5 mg twice daily. Opportunistic herpes zoster infections (including meningoencephalitis, ophthalmologic, and disseminated cutaneous) were seen in patients who were treated with XELJANZ 10 mg

# SAFETY QUESTION 3 – Correct Answer

The safety events described in the BOXED WARNING for XELJANZ only include Serious Infections and Malignancies.

☐ TRUE

☒ FALSE Correct answer

**The BOXED WARNING for XELJANZ includes Important Safety Information for Serious Infections, Mortality, Malignancies, Major Adverse Cardiovascular Events, and Thrombosis.**

**XELJANZ is approved for use in patients with inadequate response or intolerance to TNF blockers.[1]**

ADDITIONAL INFORMATION



## IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

**Patients treated with XELJANZ* are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.**

**If a serious infection develops, interrupt XELJANZ until the infection is controlled.**

**Reported infections include:**

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

The most common serious infections reported with XELJANZ included pneumonia, cellulitis, herpes zoster, urinary tract infection, diverticulitis, and appendicitis. Avoid use of XELJANZ in patients with an active, serious infection, including localized infections.

In the UC population, XELJANZ 10 mg twice daily was associated with greater risk of serious infections compared to 5 mg twice daily. Opportunistic herpes zoster infections (including meningoencephalitis, ophthalmologic, and disseminated cutaneous) were seen in patients who were treated with XELJANZ 10 mg

# SAFETY QUESTION 3 – Additional Information

**WARNING: SERIOUS INFECTIONS, MORTALITY, MALIGNANCY, MAJOR ADVERSE CARDIOVASCULAR EVENTS, AND THROMBOSIS**

**SERIOUS INFECTIONS**

**Patients treated with XELJANZ/XELJANZ XR/XELJANZ Oral Solution are at increased risk for developing serious infections that may lead to hospitalization or death** [see Warnings and Precautions (5.1), Adverse Reactions (6.1)]**. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.**

- **Active tuberculosis, which may present with pulmonary or extrapulmonary disease. Patients should be tested for latent tuberculosis before XELJANZ/XELJANZ XR/XELJANZ Oral Solution use and during therapy. Treatment for latent infection should be initiated prior to XELJANZ/XELJANZ XR/XELJANZ Oral Solution use.**
- **Invasive fungal infections, including cryptococcosis and pneumocystosis. Patients with invasive fungal infections may present with disseminated, rather than localized, disease.**
- **Bacterial, viral, including herpes zoster, and other infections due to opportunistic pathogens.**

**The risks and benefits of treatment with XELJANZ/XELJANZ XR/XELJANZ Oral Solution should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection. Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with XELJANZ/ XELJANZ XR/XELJANZ Oral Solution, including the possible development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to initiating therapy** [see Warnings and Precautions (5.1)]**.**

**MORTALITY**

**In a large, randomized, postmarketing safety study in rheumatoid arthritis (RA) patients 50 years of age and older with at least one cardiovascular risk factor comparing XELJANZ 5 mg twice a day or XELJANZ 10 mg twice a day**

**XELJANZ is approved for use in patients with inadequate response or intolerance to TNF blockers.[1]**

CLOSE

## IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

**Patients treated with XELJANZ* are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.**

**If a serious infection develops, interrupt XELJANZ until the infection is controlled.**

**Reported infections include:**

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

The most common serious infections reported with XELJANZ included pneumonia, cellulitis, herpes zoster, urinary tract infection, diverticulitis, and appendicitis. Avoid use of XELJANZ in patients with an active, serious infection, including localized infections.

In the UC population, XELJANZ 10 mg twice daily was associated with greater risk of serious infections compared to 5 mg twice daily. Opportunistic herpes zoster infections (including meningoencephalitis, ophthalmologic, and disseminated cutaneous) were seen in patients who were treated with XELJANZ 10 mg



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Q1 | Q2 | Q3 | Q4

2 Safety Questions Remaining

Check when each of the following monitoring recommendations should be performed, based on observations during the XELJANZ clinical program.

Select all that apply

| | AT BASELINE | AFTER 4 TO 8 WEEKS | EVERY 3 MONTHS THEREAFTER |
|---|---|---|---|
| LYMPHOCYTES | ☐ | ☐ | ☐ |
| NEUTROPHILS | ☐ | ☐ | ☐ |
| HEMOGLOBIN | ☐ | ☐ | ☐ |
| LIPIDS | ☐ | ☐ | ☐ |
| LIVER ENZYMES | Routine monitoring and prompt investigation of the causes of liver enzyme elevations are recommended | | |

**XELJANZ is approved for use in patients with inadequate response or intolerance to TNF blockers.**[1]

RESET

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## IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

**Patients treated with XELJANZ* are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.**

**If a serious infection develops, interrupt XELJANZ until the infection is controlled.**

**Reported infections include:**

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

The most common serious infections reported with XELJANZ included pneumonia, cellulitis, herpes zoster, urinary tract infection, diverticulitis, and appendicitis. Avoid use of XELJANZ in patients with an active, serious infection, including localized infections.

In the UC population, XELJANZ 10 mg twice daily was associated with greater risk of serious infections compared to 5 mg twice daily. Opportunistic herpes zoster infections (including meningoencephalitis, ophthalmologic, and disseminated cutaneous) were seen in patients who were treated with XELJANZ 10 mg



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Q1 | Q2 | Q3 | Q4

2 Safety Questions Remaining

Check when each of the following monitoring recommendations should be performed, based on observations during the XELJANZ clinical program.

Select all that apply

| | AT BASELINE | AFTER 4 TO 8 WEEKS | EVERY 3 MONTHS THEREAFTER |
|---|---|---|---|
| LYMPHOCYTES | ☑ | ☐ | ☑ |
| NEUTROPHILS | ☑ | ☑ | ☑ |
| HEMOGLOBIN | ☑ | ☑ | ☑ |
| LIPIDS | ☐ | ☑ | ☐ |
| LIVER ENZYMES | Routine monitoring and prompt investigation of the causes of liver enzyme elevations are recommended | | |

**XELJANZ is approved for use in patients with inadequate response or intolerance to TNF blockers.**[1]

RESET

VIEW ANSWER

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Go to Efficacy

### IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

**Patients treated with XELJANZ* are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.**

**If a serious infection develops, interrupt XELJANZ until the infection is controlled.**

**Reported infections include:**

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

The most common serious infections reported with XELJANZ included pneumonia, cellulitis, herpes zoster, urinary tract infection, diverticulitis, and appendicitis. Avoid use of XELJANZ in patients with an active, serious infection, including localized infections.

In the UC population, XELJANZ 10 mg twice daily was associated with greater risk of serious infections compared to 5 mg twice daily. Opportunistic herpes zoster infections (including meningoencephalitis, ophthalmologic, and disseminated cutaneous) were seen in patients who were treated with XELJANZ 10 mg



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Q1 | Q2 | Q3 | Q4

2 Safety Questions Remaining

Check when each of the following monitoring recommendations should be performed, based on observations during the XELJANZ clinical program.

## Lab monitoring recommendations for patients taking XELJANZ/XELJANZ XR[1]

| | AT BASELINE | AFTER 4 TO 8 WEEKS | EVERY 3 MONTHS THEREAFTER |
|---|---|---|---|
| LYMPHOCYTES[a] | ☑ Correct answer | ☐ | ☑ Correct answer |
| NEUTROPHILS | ☑ Correct answer | ☑ Correct answer | ☑ Correct answer |
| HEMOGLOBIN | ☑ Correct answer | ☑ Correct answer | ☑ Correct answer |
| LIPIDS[b] | ☐ | ☑ Correct answer | ☐ |

## LIVER ENZYMES

Routine monitoring and prompt investigation of the causes of liver enzyme elevations are recommended

Screening for viral hepatitis should be performed in accordance with clinical guidelines before starting therapy with XELJANZ/XELJANZ XR

Patients should be evaluated and tested for latent or active tuberculosis prior to and per applicable guidelines during administration of XELJANZ/XELJANZ XR

**XELJANZ is approved for use in patients with inadequate response or intolerance to TNF blockers.**[1]

[a]Risk of infection may be higher with increasing degrees of lymphopenia, and consideration should be given to lymphocyte counts when assessing individual patient risk of infection.

[b]Assessment of lipid parameters should be performed approximately 4-8 weeks following initiation of XELJANZ/XELJANZ XR therapy. Manage patients according to clinical guidelines [eg., National Cholesterol Educational Program (NCEP) for the management of hyperlipidemia].

ADDITIONAL INFORMATION

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## IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

**Patients treated with XELJANZ* are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.**

**If a serious infection develops, interrupt XELJANZ until the infection is controlled.**

**Reported infections include:**

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

The most common serious infections reported with XELJANZ included pneumonia, cellulitis, herpes zoster, urinary tract infection, diverticulitis, and appendicitis. Avoid use of XELJANZ in patients with an active, serious infection, including localized infections.

In the UC population, XELJANZ 10 mg twice daily was associated with greater risk of serious infections compared to 5 mg twice daily. Opportunistic herpes zoster infections (including meningoencephalitis, ophthalmologic, and disseminated cutaneous) were seen in patients who were treated with XELJANZ 10 mg



## XELJANZ Safety Data

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Q1 | Q2 | Q3 | Q4

2 Safety Questions Remaining

Check when each of the following monitoring recommendations should be performed, based on observations during the XELJANZ clinical program.

Select all that apply

| | AT BASELINE | AFTER 4 TO 8 WEEKS | EVERY 3 MONTHS THEREAFTER |
|---|---|---|---|
| LYMPHOCYTES | ☑ | ☑ | ☐ |
| NEUTROPHILS | ☑ | ☑ | ☐ |
| HEMOGLOBIN | ☑ | ☐ | ☐ |
| LIPIDS | ☐ | ☑ | ☑ |

LIVER ENZYMES Routine monitoring and prompt investigation of the causes of liver enzyme elevations are recommended

**XELJANZ is approved for use in patients with inadequate response or intolerance to TNF blockers.**[1]

RESET

VIEW ANSWER

Help

Go to Efficacy

### IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

**Patients treated with XELJANZ* are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.**

**If a serious infection develops, interrupt XELJANZ until the infection is controlled.**

**Reported infections include:**

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

The most common serious infections reported with XELJANZ included pneumonia, cellulitis, herpes zoster, urinary tract infection, diverticulitis, and appendicitis. Avoid use of XELJANZ in patients with an active, serious infection, including localized infections.

In the UC population, XELJANZ 10 mg twice daily was associated with greater risk of serious infections compared to 5 mg twice daily. Opportunistic herpes zoster infections (including meningoencephalitis, ophthalmologic, and disseminated cutaneous) were seen in patients who were treated with XELJANZ 10 mg



XELJANZ Safety Data

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2 Safety Questions Remaining

Check when each of the following monitoring recommendations should be performed, based on observations during the XELJANZ clinical program.

## Lab monitoring recommendations for patients taking XELJANZ/XELJANZ XR[1]

| | AT BASELINE | AFTER 4 TO 8 WEEKS | EVERY 3 MONTHS THEREAFTER |
|---|---|---|---|
| LYMPHOCYTES[a] | ☑ Correct answer | ☑ | ☐ Correct answer |
| NEUTROPHILS | ☑ Correct answer | ☑ Correct answer | ☐ Correct answer |
| HEMOGLOBIN | ☑ Correct answer | ☐ Correct answer | ☐ Correct answer |
| LIPIDS[b] | ☐ | ☑ Correct answer | ☑ |

## LIVER ENZYMES

Routine monitoring and prompt investigation of the causes of liver enzyme elevations are recommended

Screening for viral hepatitis should be performed in accordance with clinical guidelines before starting therapy with XELJANZ/XELJANZ XR

Patients should be evaluated and tested for latent or active tuberculosis prior to and per applicable guidelines during administration of XELJANZ/XELJANZ XR

**XELJANZ is approved for use in patients with inadequate response or intolerance to TNF blockers.**[1]

[a]Risk of infection may be higher with increasing degrees of lymphopenia, and consideration should be given to lymphocyte counts when assessing individual patient risk of infection.

[b]Assessment of lipid parameters should be performed approximately 4-8 weeks following initiation of XELJANZ/XELJANZ XR therapy. Manage patients according to clinical guidelines [eg., National Cholesterol Educational Program (NCEP) for the management of hyperlipidemia].

ADDITIONAL INFORMATION

Help

Go to Efficacy

### IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

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**If a serious infection develops, interrupt XELJANZ until the infection is controlled.**

**Reported infections include:**

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- **Invasive fungal infections, including cryptococcosis and pneumocystosis. Patients with invasive fungal infections may present with disseminated, rather than localized, disease.**
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The most common serious infections reported with XELJANZ included pneumonia, cellulitis, herpes zoster, urinary tract infection, diverticulitis, and appendicitis. Avoid use of XELJANZ in patients with an active, serious infection, including localized infections.

In the UC population, XELJANZ 10 mg twice daily was associated with greater risk of serious infections compared to 5 mg twice daily. Opportunistic herpes zoster infections (including meningoencephalitis, ophthalmologic, and disseminated cutaneous) were seen in patients who were treated with XELJANZ 10 mg

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# XELJANZ/XELJANZ XR Laboratory Monitoring Recommendations[1]

| | AT BASELINE | AFTER 4 TO 8 WEEKS | EVERY 3 MONTHS THEREAFTER |
|---|---|---|---|
| LYMPHOCYTES[a] | ✓ | | ✓ |
| NEUTROPHILS | ✓ | ✓ | ✓ |
| HEMOGLOBIN | ✓ | ✓ | ✓ |
| LIPIDS[b] | | ✓ | |
| LIVER ENZYMES | Routine monitoring of liver tests and prompt investigation of the causes of liver enzyme elevations are recommended | | |
| AVOID INITIATION OF XELJANZ/ XELJANZ XR TREATMENT IN PATIENTS WITH: | **Lymphocyte count <500 cells/mm³** | **Absolute neutrophil count <1000 cells/mm³** | **Hemoglobin level <9 g/dL** |

NEXT QUESTION

## IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

**Patients treated with XELJANZ* are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.**

**If a serious infection develops, interrupt XELJANZ until the infection is controlled.**

**Reported infections include:**

- **Active tuberculosis, which may present with pulmonary or extrapulmonary disease. Patients should be tested for latent tuberculosis before XELJANZ use and during therapy. Treatment for latent infection should be initiated prior to XELJANZ use.**
- **Invasive fungal infections, including cryptococcosis and pneumocystosis. Patients with invasive fungal infections may present with disseminated, rather than localized, disease.**
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In the UC population, XELJANZ 10 mg twice daily was associated with greater risk of serious infections compared to 5 mg twice daily. Opportunistic herpes zoster infections (including meningoencephalitis, ophthalmologic, and disseminated cutaneous) were seen in patients who were treated with XELJANZ 10 mg

## XELJANZ/XELJANZ XR Laboratory Monitoring Recommendations[1]

| AVOID INITIATION OF XELJANZ/ XELJANZ XR TREATMENT IN PATIENTS WITH: | Lymphocyte count <500 cells/mm³ | Absolute neutrophil count <1000 cells/mm³ | Hemoglobin level <9 g/dL |
|---|---|---|---|

- Screening for viral hepatitis should be performed in accordance with clinical guidelines before starting therapy with XELJANZ/XELJANZ XR
- Patients should be evaluated and tested for latent or active tuberculosis prior to and per applicable guidelines during administration of XELJANZ/XELJANZ XR

**XELJANZ is approved for use in patients with inadequate response or intolerance to TNF blockers.[1]**

[a]Risk of infection may be higher with increasing degrees of lymphopenia, and consideration should be given to lymphocyte counts when assessing individual patient risk of infection.

[b]Assessment of lipid parameters should be performed approximately 4-8 weeks following initiation of XELJANZ/XELJANZ XR therapy. Manage patients according to clinical guidelines
[eg., National Cholesterol Educational Program (NCEP) for the management of hyperlipidemia].

## XELJANZ/XELJANZ XR Dosage and Administration Considerations[1]

### IMPORTANT ADMINISTRATION INSTRUCTIONS

- XELJANZ XR is not interchangeable or subsitutable with XELJANZ Oral Solution
- Changes between XELJANZ and XELJANZ XR should be made by the healthcare provider
- Dose interruption is recommended for management of lymphopenia, neutropenia, anemia, and if a patient develops a serious infection
- Take XELJANZ/XELJANZ XR with or without food
- Swallow XELJANZ XR tablets whole and intact. Do not crush, split, or chew

NEXT QUESTION

### IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

**Patients treated with XELJANZ* are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.**

**If a serious infection develops, interrupt XELJANZ until the infection is controlled.**

**Reported infections include:**

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

The most common serious infections reported with XELJANZ included pneumonia, cellulitis, herpes zoster, urinary tract infection, diverticulitis, and appendicitis. Avoid use of XELJANZ in patients with an active, serious infection, including localized infections.

In the UC population, XELJANZ 10 mg twice daily was associated with greater risk of serious infections compared to 5 mg twice daily. Opportunistic herpes zoster infections (including meningoencephalitis, ophthalmologic, and disseminated cutaneous) were seen in patients who were treated with XELJANZ 10 mg

# XELJANZ/XELJANZ XR Laboratory Monitoring Recommendations[1]

## Warning and Precaution:

### Risk of Gastrointestinal Obstruction With a Non-deformable Extended-Release Formulation Such as XELJANZ XR

As with any other non-deformable material, caution should be used when administering XELJANZ XR to patients with pre-existing severe gastrointestinal narrowing (pathologic or iatrogenic).

There have been rare reports of obstructive symptoms in patients with known strictures in association with the ingestion of other drugs utilizing a non-deformable extended-release formulation.

## Patient Counseling Information:

### Residual Tablet Shell

Patients receiving XELJANZ XR may notice an inert tablet shell passing in the stool or via colostomy. Patients should be informed that the active medication has already been absorbed by the time the patient sees the inert tablet shell.

## AVOID INITIATION IN PATIENTS WITH:

- ALC <500 cells/mm$^3$
- ANC <1000 cells/mm$^3$
- Active, serious infection
- Risk of thrombosis
- Hemoglobin levels <9 g/dL
- Severe hepatic impairment
- Concurrent live vaccine use

NEXT QUESTION

## IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

**Patients treated with XELJANZ* are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.**

**If a serious infection develops, interrupt XELJANZ until the infection is controlled.**

**Reported infections include:**

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

The most common serious infections reported with XELJANZ included pneumonia, cellulitis, herpes zoster, urinary tract infection, diverticulitis, and appendicitis. Avoid use of XELJANZ in patients with an active, serious infection, including localized infections.

In the UC population, XELJANZ 10 mg twice daily was associated with greater risk of serious infections compared to 5 mg twice daily. Opportunistic herpes zoster infections (including meningoencephalitis, ophthalmologic, and disseminated cutaneous) were seen in patients who were treated with XELJANZ 10 mg

# SAFETY QUESTION 4 – Correct Answer

Check when each of the following monitoring recommendations should be performed, based on observations during the XELJANZ clinical program.

## Lab monitoring recommendations for patients taking XELJANZ/XELJANZ XR[1]

| | AT BASELINE | AFTER 4 TO 8 WEEKS | EVERY 3 MONTHS THEREAFTER |
|---|---|---|---|
| LYMPHOCYTES[a] | ☒ Correct answer | ☐ | ☒ Correct answer |
| NEUTROPHILS | ☒ Correct answer | ☒ Correct answer | ☒ Correct answer |
| HEMOGLOBIN | ☒ Correct answer | ☒ Correct answer | ☒ Correct answer |
| LIPIDS[b] | ☐ | ☒ Correct answer | ☐ |
| LIVER ENZYMES | Routine monitoring and prompt investigation of the causes of liver enzyme elevations are recommended | | |

Screening for viral hepatitis should be performed in accordance with clinical guidelines before starting therapy with XELJANZ/XELJANZ XR
Patients should be evaluated and tested for latent or active tuberculosis prior to and per applicable guidelines during administration of XELJANZ/XELJANZ XR

ADDITIONAL INFORMATION

## IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

**Patients treated with XELJANZ* are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.**

**If a serious infection develops, interrupt XELJANZ until the infection is controlled.**

**Reported infections include:**

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

The most common serious infections reported with XELJANZ included pneumonia, cellulitis, herpes zoster, urinary tract infection, diverticulitis, and appendicitis. Avoid use of XELJANZ in patients with an active, serious infection, including localized infections.

In the UC population, XELJANZ 10 mg twice daily was associated with greater risk of serious infections compared to 5 mg twice daily. Opportunistic herpes zoster infections (including meningoencephalitis, ophthalmologic, and disseminated cutaneous) were seen in patients who were treated with XELJANZ 10 mg

# SAFETY QUESTION 4 – Additional Information

## XELJANZ/XELJANZ XR Laboratory Monitoring Recommendations[1]

| | AT BASELINE | AFTER 4 TO 8 WEEKS | EVERY 3 MONTHS THEREAFTER |
|---|---|---|---|
| LYMPHOCYTES[a] | ✓ | | ✓ |
| NEUTROPHILS | ✓ | ✓ | ✓ |
| HEMOGLOBIN | ✓ | ✓ | ✓ |
| LIPIDS[b] | | ✓ | |
| LIVER ENZYMES | Routine monitoring of liver tests and prompt investigation of the causes of liver enzyme elevations are recommended | | |
| AVOID INITIATION OF XELJANZ/ XELJANZ XR TREATMENT IN PATIENTS WITH: | **Lymphocyte count <500 cells/mm³** | **Absolute neutrophil count <1000 cells/mm³** | **Hemoglobin level <9 g/dL** |

CLOSE



### IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

**Patients treated with XELJANZ* are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.**

**If a serious infection develops, interrupt XELJANZ until the infection is controlled.**

**Reported infections include:**

- **Active tuberculosis, which may present with pulmonary or extrapulmonary disease. Patients should be tested for latent tuberculosis before XELJANZ use and during therapy. Treatment for latent infection should be initiated prior to XELJANZ use.**
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- **Bacterial, viral, including herpes zoster, and other infections due to opportunistic pathogens.**

The most common serious infections reported with XELJANZ included pneumonia, cellulitis, herpes zoster, urinary tract infection, diverticulitis, and appendicitis. Avoid use of XELJANZ in patients with an active, serious infection, including localized infections.

In the UC population, XELJANZ 10 mg twice daily was associated with greater risk of serious infections compared to 5 mg twice daily. Opportunistic herpes zoster infections (including meningoencephalitis, ophthalmologic, and disseminated cutaneous) were seen in patients who were treated with XELJANZ 10 mg

# XELJANZ/XELJANZ XR Laboratory Monitoring Recommendations[1]

| AVOID INITIATION OF XELJANZ/ XELJANZ XR TREATMENT IN PATIENTS WITH: | Lymphocyte count <500 cells/mm$^3$ | Absolute neutrophil count <1000 cells/mm$^3$ | Hemoglobin level <9 g/dL |
|---|---|---|---|

- Screening for viral hepatitis should be performed in accordance with clinical guidelines before starting therapy with XELJANZ/XELJANZ XR
- Patients should be evaluated and tested for latent or active tuberculosis prior to and per applicable guidelines during administration of XELJANZ/XELJANZ XR

**XELJANZ is approved for use in patients with inadequate response or intolerance to TNF blockers.[1]**

[a]Risk of infection may be higher with increasing degrees of lymphopenia, and consideration should be given to lymphocyte counts when assessing individual patient risk of infection.

[b]Assessment of lipid parameters should be performed approximately 4-8 weeks following initiation of XELJANZ/XELJANZ XR therapy. Manage patients according to clinical guidelines
[eg., National Cholesterol Educational Program (NCEP) for the management of hyperlipidemia].

# XELJANZ/XELJANZ XR Dosage and Administration Considerations[1]

## IMPORTANT ADMINISTRATION INSTRUCTIONS

- XELJANZ XR is not interchangeable or subsitutable with XELJANZ Oral Solution
- Changes between XELJANZ and XELJANZ XR should be made by the healthcare provider
- Dose interruption is recommended for management of lymphopenia, neutropenia, anemia, and if a patient develops a serious infection
- Take XELJANZ/XELJANZ XR with or without food
- Swallow XELJANZ XR tablets whole and intact. Do not crush, split, or chew

CLOSE

## IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

**Patients treated with XELJANZ* are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.**

**If a serious infection develops, interrupt XELJANZ until the infection is controlled.**

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- **Invasive fungal infections, including cryptococcosis and pneumocystosis. Patients with invasive fungal infections may present with disseminated, rather than localized, disease.**
- **Bacterial, viral, including herpes zoster, and other infections due to opportunistic pathogens.**

The most common serious infections reported with XELJANZ included pneumonia, cellulitis, herpes zoster, urinary tract infection, diverticulitis, and appendicitis. Avoid use of XELJANZ in patients with an active, serious infection, including localized infections.

In the UC population, XELJANZ 10 mg twice daily was associated with greater risk of serious infections compared to 5 mg twice daily. Opportunistic herpes zoster infections (including meningoencephalitis, ophthalmologic, and disseminated cutaneous) were seen in patients who were treated with XELJANZ 10 mg

# XELJANZ/XELJANZ XR Laboratory Monitoring Recommendations[1]

## Warning and Precaution:

### Risk of Gastrointestinal Obstruction With a Non-deformable Extended-Release Formulation Such as XELJANZ XR

As with any other non-deformable material, caution should be used when administering XELJANZ XR to patients with pre-existing severe gastrointestinal narrowing (pathologic or iatrogenic).

There have been rare reports of obstructive symptoms in patients with known strictures in association with the ingestion of other drugs utilizing a non-deformable extended-release formulation.

## Patient Counseling Information:

### Residual Tablet Shell

Patients receiving XELJANZ XR may notice an inert tablet shell passing in the stool or via colostomy. Patients should be informed that the active medication has already been absorbed by the time the patient sees the inert tablet shell.

## AVOID INITIATION IN PATIENTS WITH:

- ALC <500 cells/mm$^3$
- ANC <1000 cells/mm$^3$
- Active, serious infection
- Risk of thrombosis
- Hemoglobin levels <9 g/dL
- Severe hepatic impairment
- Concurrent live vaccine use

CLOSE

## IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

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1 Safety Question Remaining

Common adverse reactions shown here were reported in ≥2% of patients treated with XELJANZ 10 mg twice daily and reported in ≥1% of patients receiving placebo in the induction clinical trials.

## Select the most common adverse reactions in patients with UC during the 3 XELJANZ induction clinical trials (Study UC-I, UC-II, and UC-V).[1,2]

Select all that apply

- ☐ Headache
- ☐ Pyrexia
- ☐ Gastroenteritis
- ☐ Nasopharyngitis
- ☐ Rash
- ☐ Elevated cholesterol levels
- ☐ Nausea
- ☐ Diarrhea
- ☐ Acne
- ☐ Anemia
- ☐ Herpes zoster
- ☐ Increased blood creatine phosphokinase

**XELJANZ is approved for use in patients with inadequate response or intolerance to TNF blockers.[1]**

RESET

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### IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

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Select all that apply

- [x] Headache
- [x] Pyrexia
- [ ] Gastroenteritis
- [x] Nasopharyngitis
- [ ] Rash
- [x] Elevated cholesterol levels
- [ ] Nausea
- [ ] Diarrhea
- [x] Acne
- [ ] Anemia
- [ ] Herpes zoster
- [x] Increased blood creatine phosphokinase

**XELJANZ is approved for use in patients with inadequate response or intolerance to TNF blockers.[1]**

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### IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

**Patients treated with XELJANZ* are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.**

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- **Active tuberculosis, which may present with pulmonary or extrapulmonary disease. Patients should be tested for latent tuberculosis before XELJANZ use and during therapy. Treatment for latent infection should be initiated prior to XELJANZ use.**
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## Select the most common adverse reactions in patients with UC during the 3 XELJANZ induction clinical trials (Study UC-I, UC-II, and UC-V).[1,2]

- [x] Headache — Correct answer
- [x] Pyrexia — Correct answer
- [ ] Gastroenteritis
- [x] Nasopharyngitis — Correct answer
- [ ] Rash
- [x] Elevated cholesterol levels — Correct answer
- [ ] Nausea
- [ ] Diarrhea
- [x] Acne — Correct answer
- [ ] Anemia
- [ ] Herpes zoster
- [x] Increased blood creatine phosphokinase — Correct answer

**XELJANZ is approved for use in patients with inadequate response or intolerance to TNF blockers.[1]**

NEXT QUESTION

Help

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## IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

**Patients treated with XELJANZ* are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.**

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The most common serious infections reported with XELJANZ included pneumonia, cellulitis, herpes zoster, urinary tract infection, diverticulitis, and appendicitis. Avoid use of XELJANZ in patients with an active, serious infection, including localized infections.

In the UC population, XELJANZ 10 mg twice daily was associated with greater risk of serious infections compared to 5 mg twice daily. Opportunistic herpes zoster infections (including meningoencephalitis, ophthalmologic, and disseminated cutaneous) were seen in patients who were treated with XELJANZ 10 mg



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Q1 | Q2 | Q3 | Q4 | Q5

1 Safety Question Remaining

Common adverse reactions shown here were reported in ≥2% of patients treated with XELJANZ 10 mg twice daily and reported in ≥1% of patients receiving placebo in the induction clinical trials.

## Select the most common adverse reactions in patients with UC during the 3 XELJANZ induction clinical trials (Study UC-I, UC-II, and UC-V).[1,2]

Select all that apply

- [x] Headache
- [x] Pyrexia
- [x] Gastroenteritis
- [ ] Nasopharyngitis
- [ ] Rash
- [x] Elevated cholesterol levels
- [x] Nausea
- [ ] Diarrhea
- [ ] Acne
- [x] Anemia
- [x] Herpes zoster
- [ ] Increased blood creatine phosphokinase

**XELJANZ is approved for use in patients with inadequate response or intolerance to TNF blockers.[1]**

RESET

VIEW ANSWER

Help

Go to Efficacy

### IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

**Patients treated with XELJANZ* are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.**

**If a serious infection develops, interrupt XELJANZ until the infection is controlled.**

**Reported infections include:**

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

The most common serious infections reported with XELJANZ included pneumonia, cellulitis, herpes zoster, urinary tract infection, diverticulitis, and appendicitis. Avoid use of XELJANZ in patients with an active, serious infection, including localized infections.

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Q1 | Q2 | Q3 | Q4 | Q5

1 Safety Question Remaining

Common adverse reactions shown here were reported in ≥2% of patients treated with XELJANZ 10 mg twice daily and reported in ≥1% of patients receiving placebo in the induction clinical trials.

## Select the most common adverse reactions in patients with UC during the 3 XELJANZ induction clinical trials (Study UC-I, UC-II, and UC-V).[1,2]

- [x] Headache — Correct answer
- [x] Pyrexia — Correct answer
- [x] Gastroenteritis
- [x] Nasopharyngitis — Correct answer
- [ ] Rash
- [x] Elevated cholesterol levels — Correct answer
- [x] Nausea
- [ ] Diarrhea
- [x] Acne — Correct answer
- [x] Anemia
- [x] Herpes zoster
- [x] Increased blood creatine phosphokinase — Correct answer

**XELJANZ is approved for use in patients with inadequate response or intolerance to TNF blockers.[1]**

NEXT QUESTION

Help

Go to Efficacy

### IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

**Patients treated with XELJANZ* are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.**

**If a serious infection develops, interrupt XELJANZ until the infection is controlled.**

**Reported infections include:**

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The most common serious infections reported with XELJANZ included pneumonia, cellulitis, herpes zoster, urinary tract infection, diverticulitis, and appendicitis. Avoid use of XELJANZ in patients with an active, serious infection, including localized infections.

In the UC population, XELJANZ 10 mg twice daily was associated with greater risk of serious infections compared to 5 mg twice daily. Opportunistic herpes zoster infections (including meningoencephalitis, ophthalmologic, and disseminated cutaneous) were seen in patients who were treated with XELJANZ 10 mg

# SAFETY QUESTION 5 – Correct Answer

Common adverse reactions shown here were reported in ≥2% of patients treated with XELJANZ 10 mg twice daily and reported in ≥1% of patients receiving placebo in the induction clinical trials.

## Select the most common adverse reactions in patients with UC during the 3 XELJANZ induction clinical trials (Study UC-I, UC-II, and UC-V).[1,2]

| | | |
|---|---|---|
| ☒ Headache — Correct answer | ☒ Pyrexia — Correct answer | ☐ Gastroenteritis |
| ☒ Nasopharyngitis — Correct answer | ☐ Rash | ☒ Elevated cholesterol levels — Correct answer |
| ☐ Nausea | ☐ Diarrhea | ☒ Acne — Correct answer |
| ☐ Anemia | ☐ Herpes zoster | ☒ Increased blood creatine phosphokinase — Correct answer |

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IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

**Patients treated with XELJANZ* are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.**

**If a serious infection develops, interrupt XELJANZ until the infection is controlled.**

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Q1 | Q2 | Q3 | Q4 | Q5 | Q6

0 Safety Questions Remaining

Common adverse reactions shown here were reported in ≥4% of patients treated with either dose of XELJANZ and reported in ≥1% of patients receiving placebo in the maintenance clinical trials.

## The table below shows the percentages of common adverse reactions in patients with UC during the maintenance trial (Study UC-III). What are the missing percentages for the adverse reactions in patients on XELJANZ 5 mg twice daily?[1,2]

SELECT 1 COLUMN TO FILL IN THE BLANKS

| PREFERRED TERM | PLACEBO N=198 (%) | XELJANZ 5 mg twice daily N=198 (%) | | | | |
|---|---|---|---|---|---|---|
| **Nasopharyngitis** | 6 | | 18 | 12 | 6 | 10 |
| **Elevated cholesterol levels**[a] | 1 | | 4 | 1 | 7 | 5 |
| Headache | 6 | 9 | | | | |
| **Upper respiratory tract infection** | 4 | | 4 | 3 | 2 | 7 |
| Increased blood creatine phosphokinase | 2 | 3 | | | | |
| Rash | 4 | 3 | | | | |
| Diarrhea | 3 | 2 | | | | |
| **Herpes zoster** | 1 | | 1 | 1 | 9 | 1 |
| **Gastroenteritis** | 3 | | 1 | 4 | 3 | 3 |
| Anemia | 2 | 4 | | | | |
| Nausea | 3 | 1 | | | | |

**XELJANZ is approved for use in patients with inadequate response or intolerance to TNF blockers.**[1]

[a]Includes hypercholesterolemia, hyperlipidemia, blood cholesterol increased, dyslipidemia, blood triglycerides increased, low-density lipoprotein increased, low-density lipoprotein abnormal, or lipids increased.[1]

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### IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

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Q1 | Q2 | Q3 | Q4 | Q5 | Q6

0 Safety Questions Remaining

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SELECT 1 COLUMN TO FILL IN THE BLANKS

| PREFERRED TERM | PLACEBO N=198 (%) | XELJANZ 5 mg twice daily N=198 (%) | ☐ | ☐ | ☐ | ✓ |
|---|---|---|---|---|---|---|
| **Nasopharyngitis** | 6 | 10 | 18 | 12 | 6 | 10 |
| **Elevated cholesterol levels[a]** | 1 | 5 | 4 | 1 | 7 | 5 |
| Headache | 6 | 9 | | | | |
| **Upper respiratory tract infection** | 4 | 7 | 4 | 3 | 2 | 7 |
| Increased blood creatine phosphokinase | 2 | 3 | | | | |
| Rash | 4 | 3 | | | | |
| Diarrhea | 3 | 2 | | | | |
| **Herpes zoster** | 1 | 1 | 1 | 1 | 9 | 1 |
| **Gastroenteritis** | 3 | 3 | 1 | 4 | 3 | 3 |
| Anemia | 2 | 4 | | | | |
| Nausea | 3 | 1 | | | | |

**XELJANZ is approved for use in patients with inadequate response or intolerance to TNF blockers.**[1]

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### IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

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Q1 | Q2 | Q3 | Q4 | Q5 | Q6

0 Safety Questions Remaining

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SELECT 1 COLUMN TO FILL IN THE BLANKS

| PREFERRED TERM | PLACEBO N=198 (%) | XELJANZ 5 mg twice daily N=198 (%) | | | | | |
|---|---|---|---|---|---|---|---|
| **Nasopharyngitis** | 6 | 10 | ✓ | 18 | 12 | 6 | 10 |
| **Elevated cholesterol levels**[a] | 1 | 5 | ✓ | 4 | 1 | 7 | 5 |
| Headache | 6 | 9 | | | | | |
| **Upper respiratory tract infection** | 4 | 7 | ✓ | 4 | 3 | 2 | 7 |
| Increased blood creatine phosphokinase | 2 | 3 | | | | | |
| Rash | 4 | 3 | | | | | |
| Diarrhea | 3 | 2 | | | | | |
| **Herpes zoster** | 1 | 1 | ✓ | 1 | 1 | 9 | 1 |
| **Gastroenteritis** | 3 | 3 | ✓ | 1 | 4 | 3 | 3 |
| Anemia | 2 | 4 | | | | | |
| Nausea | 3 | 1 | | | | | |

Correct answer

**XELJANZ is approved for use in patients with inadequate response or intolerance to TNF blockers.**[1]

[a]Includes hypercholesterolemia, hyperlipidemia, blood cholesterol increased, dyslipidemia, blood triglycerides increased, low-density lipoprotein increased, low-density lipoprotein abnormal, or lipids increased.[1]

COMPLETE

Help

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### IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

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Q1 | Q2 | Q3 | Q4 | Q5 | Q6

0 Safety Questions Remaining

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SELECT 1 COLUMN TO FILL IN THE BLANKS

| PREFERRED TERM | PLACEBO N=198 (%) | XELJANZ 5 mg twice daily N=198 (%) | ✓ | | | |
|---|---|---|---|---|---|---|
| **Nasopharyngitis** | 6 | 18 | 18 | 12 | 6 | 10 |
| **Elevated cholesterol levels**[a] | 1 | 4 | 4 | 1 | 7 | 5 |
| Headache | 6 | 9 | | | | |
| **Upper respiratory tract infection** | 4 | 4 | 4 | 3 | 2 | 7 |
| Increased blood creatine phosphokinase | 2 | 3 | | | | |
| Rash | 4 | 3 | | | | |
| Diarrhea | 3 | 2 | | | | |
| **Herpes zoster** | 1 | 1 | 1 | 1 | 9 | 1 |
| **Gastroenteritis** | 3 | 1 | 1 | 4 | 3 | 3 |
| Anemia | 2 | 4 | | | | |
| Nausea | 3 | 1 | | | | |

**XELJANZ is approved for use in patients with inadequate response or intolerance to TNF blockers.**[1]

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VIEW ANSWER

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### IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

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**Reported infections include:**

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0 Safety Questions Remaining

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## The table below shows the percentages of common adverse reactions in patients with UC during the maintenance trial (Study UC-III). What are the missing percentages for the adverse reactions in patients on XELJANZ 5 mg twice daily?[1,2]

SELECT 1 COLUMN TO FILL IN THE BLANKS

| PREFERRED TERM | PLACEBO N=198 (%) | XELJANZ 5 mg twice daily N=198 (%) | ✓ | | | |
|---|---|---|---|---|---|---|
| **Nasopharyngitis** | 6 | 18 | 18 | 12 | 6 | 10 |
| **Elevated cholesterol levels**[a] | 1 | 4 | 4 | 1 | 7 | 5 |
| Headache | 6 | 9 | | | | |
| **Upper respiratory tract infection** | 4 | 4 | 4 | 3 | 2 | 7 |
| Increased blood creatine phosphokinase | 2 | 3 | | | | |
| Rash | 4 | 3 | | | | |
| Diarrhea | 3 | 2 | | | | |
| **Herpes zoster** | 1 | 1 | 1 | 1 | 9 | 1 |
| **Gastroenteritis** | 3 | 1 | 1 | 4 | 3 | 3 |
| Anemia | 2 | 4 | | | | |
| Nausea | 3 | 1 | | | | |

Correct answer

**XELJANZ is approved for use in patients with inadequate response or intolerance to TNF blockers.**[1]

[a]Includes hypercholesterolemia, hyperlipidemia, blood cholesterol increased, dyslipidemia, blood triglycerides increased, low-density lipoprotein increased, low-density lipoprotein abnormal, or lipids increased.[1]

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### IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

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**If a serious infection develops, interrupt XELJANZ until the infection is controlled.**

**Reported infections include:**

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# SAFETY QUESTION 6 – Correct Answer

Common adverse reactions shown here were reported in ≥4% of patients treated with either dose of XELJANZ and reported in ≥1% of patients receiving placebo in the maintenance clinical trials.

The table below shows the percentages of common adverse reactions in patients with UC during the maintenance trial (Study UC-III). What are the missing percentages for the adverse reactions in patients on XELJANZ 5 mg twice daily?[1,2]

| PREFERRED TERM | PLACEBO N=198 (%) | XELJANZ 5 mg twice daily N=198 (%) | SELECT 1 COLUMN TO FILL IN THE BLANKS | | | |
|---|---|---|---|---|---|---|
| | | | | | | |
| **Nasopharyngitis** | 6 | 10 | 18 | 12 | 6 | 10 |
| **Elevated cholesterol levels**[a] | 1 | 5 | 4 | 1 | 7 | 5 |
| Headache | 6 | 9 | | | | |
| **Upper respiratory tract infection** | 4 | 7 | 4 | 3 | 2 | 7 |
| Increased blood creatine phosphokinase | 2 | 3 | | | | |
| Rash | 4 | 3 | | | | |
| Diarrhea | 3 | 2 | | | | |
| **Herpes zoster** | 1 | 1 | 1 | 1 | 9 | 1 |
| **Gastroenteritis** | 3 | 3 | 1 | 4 | 3 | 3 |
| Anemia | 2 | 4 | | | | |
| Nausea | 3 | 1 | | | | |

Correct answer

**XELJANZ is approved for use in patients with inadequate response or intolerance to TNF blockers.**[1]

[a]Includes hypercholesterolemia, hyperlipidemia, blood cholesterol increased, dyslipidemia, blood triglycerides increased, low-density lipoprotein increased, low-density lipoprotein abnormal, or lipids increased.[1]

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IMPORTANT SAFETY INFORMATION

SERIOUS INFECTIONS

**Patients treated with XELJANZ* are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.**

**If a serious infection develops, interrupt XELJANZ until the infection is controlled.**

**Reported infections include:**

- **Active tuberculosis, which may present with pulmonary or extrapulmonary disease. Patients should be tested for latent tuberculosis before XELJANZ use and during therapy. Treatment for latent infection should be initiated prior to XELJANZ use.**
- **Invasive fungal infections, including cryptococcosis and pneumocystosis. Patients with invasive fungal infections may present with disseminated, rather than localized, disease.**
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# COMPLETE!

You have successfully tested your knowledge of select XELJANZ Safety and Efficacy Data.

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## IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

**Patients treated with XELJANZ* are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.**

**If a serious infection develops, interrupt XELJANZ until the infection is controlled.**

**Reported infections include:**

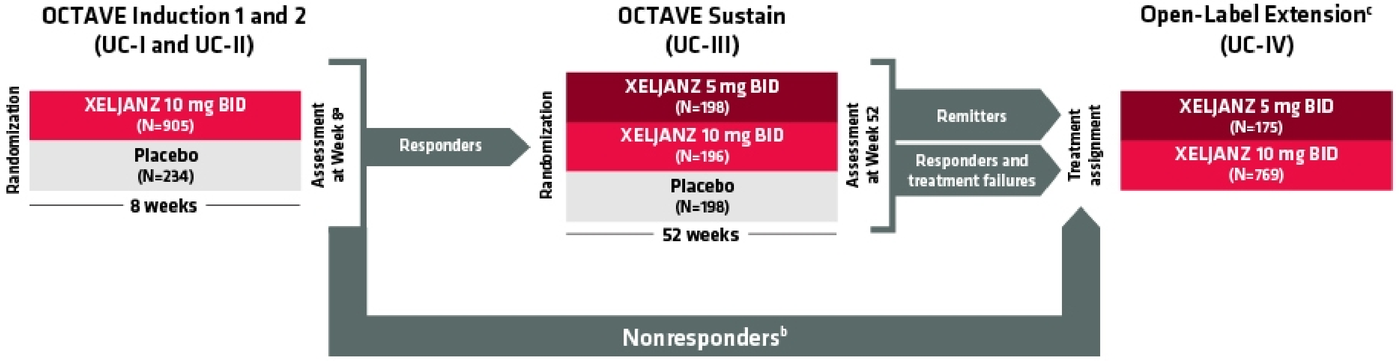
- **Active tuberculosis, which may present with pulmonary or extrapulmonary disease. Patients should be tested for latent tuberculosis before XELJANZ use and during therapy. Treatment for latent infection should be initiated prior to XELJANZ use.**
- **Invasive fungal infections, including cryptococcosis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

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# OCTAVE Clinical Trial Program for XELJANZ in UC[2-5]




- Remission (primary endpoint at week 8 [UC-I and UC-II], and primary endpoint at week 52 [UC-III]) was defined as Mayo score ≤2 with no individual subscore >1 **and** rectal bleeding subscore = 0[1]
- Clinical response was defined as a decrease from baseline in the total Mayo score of ≥3 points and ≥30%, with an accompanying decrease in the subscore for rectal bleeding of ≥1 point or an absolute subscore for rectal bleeding of 0 or 1[1]

**XELJANZ is approved for use in patients with inadequate response or intolerance to TNF blockers.[1]**

[a]The total number of patients does not include those who received XELJANZ 15 mg BID (n=22). XELJANZ 15 mg twice daily is not an approved dose.[1,3]
[b]Patients who completed 1 of the OCTAVE induction studies (UC-I or UC-II) but did not achieve clinical response.[3]
[c]Final open-label extension data (August 2020).[4]

## IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

**Patients treated with XELJANZ* are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.**

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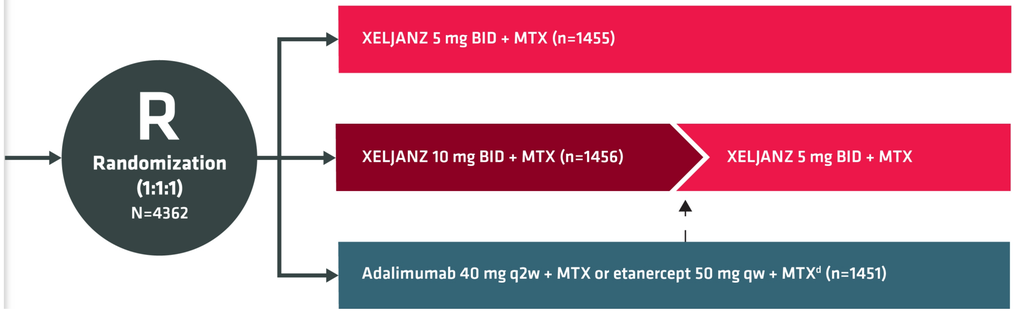
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# ORAL Surveillance Study Design[1,2]

| | |
|---|---|
| DESIGN | Phase 3b/4 randomized, parallel-arm, open-label, safety endpoint–driven study (N=4362[a]) |
| PRIMARY OBJECTIVE | Evaluate the safety of XELJANZ at 2 doses vs a TNF blocker in RA patients who were ≥50 years old with at least 1 CV risk factor |
| COPRIMARY ENDPOINTS | Adjudicated MACE[b] and adjudicated malignancies (excluding NMSC)[c] |
| OTHER ENDPOINTS | Mortality, serious infections, and thromboembolic events |
| STATISTICAL PLAN | Assess noninferiority of XELJANZ combined doses vs TNF blocker; determine whether the upper bound of the 95% CI for the hazard ratio for the primary comparison of XELJANZ (combined doses) vs TNF blocker met prespecified noninferiority criterion (ie, upper limit of 95% CI <1.8 for analyses of MACE and malignancy [excluding NMSC]) |
| PROTOCOL AMENDMENT FEBRUARY 2019 | Amendment was based on an ad hoc safety analysis in which the DSMB observed an increased occurrence of pulmonary embolism and overall mortality in the XELJANZ 10 mg BID arm vs the 2 other arms. The 10 mg BID dose was discontinued, and patients in this arm were allowed to switch to 5 mg BID dosing |
| STUDY COMPLETION REQUIREMENTS | The study was event driven, requiring at least 1500 patients to be followed for 3 years, with 103 cases of adjudicated MACE and 138 cases of adjudicated malignancies (excluding NMSC) |

**KEY ELIGIBILITY CRITERIA**

- Moderate to severe RA, including ≥6 tender or painful joints and ≥6 swollen joints (28-joint count)
- Taking MTX without adequate control of symptoms
- ≥50 years of age
- ≥1 CV risk factor
  - Current cigarette smoker
  - Diagnosis of hypertension
  - High-density lipoprotein <40 mg/dL
  - Diabetes mellitus




## IMPORTANT SAFETY INFORMATION

**SERIOUS INFECTIONS**

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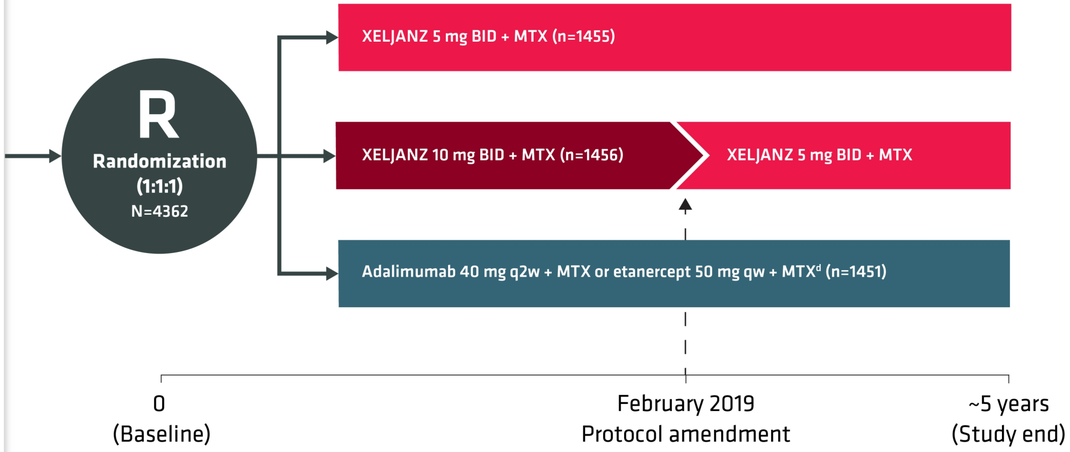
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  - High-density lipoprotein <40 mg/dL
  - Diabetes mellitus
  - History of coronary artery disease
  - History of premature coronary heart disease or sudden death documented in first-degree relative
  - Presence of extra-articular disease associated with RA[e]




**XELJANZ 10 mg twice daily dosage is not recommended for the treatment of RA, PsA, AS, or pcJIA.[1,f]**

[a]Randomized patients who received study drug.[6] [b]MACE includes CV death, nonfatal myocardial infarction, and nonfatal stroke of any classification.[1] [c]An independent committee conducted a blinded evaluation of the coprimary endpoints according to predefined criteria (adjudication).[1] [d]Patients randomized to TNF blocker in the United States, Puerto Rico, and Canada received adalimumab 40 mg q2w; in all other countries, those randomized to TNF blockers received etanercept 50 mg qw.[6] [e]Extra-articular diseases may include nodules, Sjögren's syndrome, anemia of chronic disease, and pulmonary manifestations.[6] [f]Study pcJIA-I included patients with active polyarthritis including RF negative, RF positive, extended oligoarthritis, systemic JIA without system manifestations, as well as jPsA and ERA patients.[1]

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# Patient Characteristics

| Selected Baseline Characteristics | OCTAVE Induction 1 and 2[2] | | OCTAVE Sustain[1,3] | | |
|---|---|---|---|---|---|
| | XELJANZ 10 mg Twice Daily (N=905) | Placebo (N=234) | XELJANZ 10 mg Twice Daily (N=197) | XELJANZ 5 mg Twice Daily (N=198) | Placebo (N=198) |
| Male, % | 59 | 56 | 56 | 52 | 59 |
| Mean age, years | 41 | 41 | 43 | 42 | 43 |
| Median duration of UC, years | 6 | 6 | 7 | 7 | 7 |
| Median total Mayo score | 9 | 9 | 3 | 3 | 3 |
| Prior TNF blocker exposure, % | 54 | 56 | 51 | 46 | 47 |
| Prior immunosuppressant exposure,[a] % | 76 | 68 | 74 | 75 | 68 |
| Prior oral corticosteroid exposure, % | 90 | 93 | 90 | 90 | 94 |
| Failed/intolerant to TNF blockers, % | 51 | 53 | 47 | 42 | 45 |
| Failed immunosuppressants, % | 73 | 68 | 72 | 72 | 65 |
| Failed corticosteroids, % | 72 | 77 | 76 | 73 | 76 |
| Oral corticosteroid use at start of study,[b] % | 46 | 48 | 44 | 51 | 51 |

- Oral corticosteroids were received as concomitant treatment for UC by 47% of patients (45% in OCTAVE Induction 1 and 48% in OCTAVE Induction 2) and 71% were receiving concomitant aminosalicylates as treatment for UC (71% in OCTAVE Induction 1 and 72% in OCTAVE Induction 2)[1]
- The baseline clinical characteristics were generally similar between the XELJANZ-treated patients and the patients receiving placebo in Induction 1 and 2[1]
- Prior TNF blocker failure was defined in this program as inadequate response, loss of response, or intolerance to TNF blocker therapy. Primary nonresponse was defined as a failure to achieve a response; secondary nonresponse was defined as a failure to maintain a response. Intolerance may have been due to an adverse event[1,2]

[a]Concomitant use of immunosuppressants was prohibited in OCTAVE Induction 1 and 2 and OCTAVE Sustain.[1,3]
[b]The maximum corticosteroid dose at baseline in OCTAVE Sustain was 25 mg/day of oral prednisone or equivalent, and 9 mg/day of budesonide. Tapering corticosteroids was mandatory starting the first week of the study at the following rates: The daily dose of prednisone or equivalent was decreased at a rate of 5 mg per week until the dose reached 20 mg/day, then by 2.5 to 5.0 mg per week until the dose reached 10 mg/day, and then by 2.5 mg per week until the dose was 0 mg. The daily dose of oral budesonide was decreased at a rate of 3 mg every 3 weeks until the dose reached 0 mg.[3]

IMPORTANT SAFETY INFORMATION

SERIOUS INFECTIONS

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# Definitions & Abbreviations

- Clinical response: A decrease from baseline in the total Mayo score ≥3 points and ≥30%, with an accompanying decrease in the subscore for rectal bleeding ≥1 point or an absolute subscore for rectal bleeding of 0 or 1.[1]
- Prior TNF blocker failure: Inadequate response, loss of response, or intolerance to TNF blocker therapy.[1]
- Remission: A total Mayo score ≤2, with no individual subscore >1 and a rectal bleeding subscore of 0.[1]
- Sustained corticosteroid-free remission: Remission (a total Mayo score ≤2, with no individual subscore >1 and a rectal bleeding subscore of 0) and not taking corticosteroids for at least 4 weeks prior to the visit at both week 24 and week 52 among patients in remission at baseline.[1]

5-ASA=5-aminosalicylate
ALC=absolute lymphocyte count
ANC=absolute neutrophil count
AS=ankylosing spondylitis
BID=twice daily
BL=baseline
BMI=body mass index
CI=confidence interval
CV=cardiovascular
DMARD=disease-modifying antirheumatic drug
DSMB=Data and Safety Monitoring Board
ERA=enthesitis-related arthritis
HAQ-DI=Health Assessment Questionnaire-Disability Index
HDL=high-density lipoprotein
HR=hazard ratio
IR=incidence rate
IV=intravenous
JAK=Janus kinase
JAKi=Janus kinase inhibitor
JIA=juvenile idiopathic arthritis
jPsA=juvenile psoriatic arthritis
MACE=major adverse cardiovascular events
MTX=methotrexate
NCEP=National Cholesterol Education Program
NSAID=nonsteroidal anti-inflammatory drug
NMSC=nonmelanoma skin cancer
pcJIA=polyarticular course juvenile idiopathic arthritis
PsA=psoriatic arthritis
PY=patient-years
q2w=every 2 weeks
qw=once weekly
RA=rheumatoid arthritis
RF=rheumatoid factor
SD=standard deviation
TNF=tumor necrosis factor
UC=ulcerative colitis
XR=extended release

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# INDICATIONS & IMPORTANT SAFETY

## INDICATIONS

### Ulcerative Colitis

- XELJANZ/XELJANZ XR (tofacitinib) is indicated for the treatment of adult patients with moderately to severely active ulcerative colitis (UC), who have had an inadequate response or intolerance to one or more TNF blockers.
- Limitations of Use: Use of XELJANZ/XELJANZ XR in combination with biological therapies for UC or with potent immunosuppressants such as azathioprine and cyclosporine is not recommended.

### Rheumatoid Arthritis

- XELJANZ/XELJANZ XR (tofacitinib) is indicated for the treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to one or more TNF blockers.
- Limitations of Use: Use of XELJANZ/XELJANZ XR in combination with biologic disease-modifying antirheumatic drugs (DMARDs) or with potent immunosuppressants such as azathioprine and cyclosporine is not recommended.

### Psoriatic Arthritis

- XELJANZ/XELJANZ XR (tofacitinib) is indicated for the treatment of adult patients with active psoriatic arthritis (PsA) who have had an inadequate response or intolerance to one or more TNF blockers.
- Limitations of Use: Use of XELJANZ/XELJANZ XR in combination with biologic DMARDs or with potent immunosuppressants such as azathioprine and cyclosporine is not recommended.

### Ankylosing Spondylitis

- XELJANZ/XELJANZ XR is indicated for the treatment of adult patients with active ankylosing spondylitis (AS) who have had an inadequate response or intolerance to one or more TNF blockers.
- Limitations of Use: Use of XELJANZ/XELJANZ XR in combination with biologic DMARDs or potent immunosuppressants such as azathioprine and cyclosporine is not recommended.

### Polyarticular Course Juvenile Idiopathic Arthritis

- XELJANZ/XELJANZ Oral Solution (tofacitinib) is indicated for the treatment of active polyarticular course juvenile idiopathic arthritis (pcJIA) in patients 2 years of age and older who have had an inadequate response or intolerance to one or more TNF blockers.
- Limitations of Use: Use of XELJANZ/XELJANZ Oral Solution in combination with biologic DMARDs or with potent

## IMPORTANT SAFETY INFORMATION

### SERIOUS INFECTIONS

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## IMPORTANT SAFETY INFORMATION

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# REFERENCES


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