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| RAPID RESPONSE | |
| **Key**   * Summary from Source * *Gilead’s analysis for internal use only* * Reactive response to unsolicited inquiries, unless otherwise noted   **Rheum Resources**  **External Materials – Now Available**   * [ACR 2020 CORE Post-Con deck](https://gileadconnect.sharepoint.com/:p:/r/Sites/GPART-FILGOOD/_layouts/15/Doc.aspx?sourcedoc=%7B3A8106B3-0871-42D6-B47A-F4BE8E466241%7D&file=ACR%202020%20CORE%20Post-Con%20Deck_REAC_30NOV2020.pptx&action=edit&mobileredirect=true) – Includes FIL in RA ISS up to 5.5 years and adjudicated MACE and VTE in FIL RA program safety data sets   For questions or suggestions/comments on future MIIRA communications, please contact: [miira@gilead.com](mailto:miira@gilead.com)  For past MIIRA issues, please visit [FILGOOD](https://gileadconnect.sharepoint.com/Sites/GPART-FILGOOD/MEDICAL1/Forms/AllItems.aspx?RootFolder=%2FSites%2FGPART%2DFILGOOD%2FMEDICAL1%2FGENERAL%2F2%2E%20MIIRA&View=%7B7FA8C7B6%2D6E3A%2D4C8B%2DB494%2D1361745A885B%7D) | **Xeljanz (tofacitinib [TOFA]) failed to show non-inferiority to TNFi in ORAL Surveillance post-marketing safety study (Pfizer)**   * ORAL Surveillance evaluated thesafety of TOFA 5mg and 10mg BID vs TNFi in 4,362 patients with RA ≥50 yrs with ≥1 additional cardiovascular risk factor * The study failed to meet prespecified non-inferiority criteria on both co-primary endpoints of MACE and malignancies (excl. non-melanoma skin cancer) * Based on the prespecified secondary comparisons, there was no evidence of a difference in primary endpoints between TOFA 5mg and 10 mg BID groups * Myocardial infarction and lung cancer were the most frequently reported MACE and malignancy reported with TOFA, respectively * Full study results, including pulmonary embolism and mortality, are not available yet.  |  |  |  |  |  | | --- | --- | --- | --- | --- | |  | **TOFA 5mg BID** | **TOFA 10mg BID** | **TOFA combined** | **TNFi** | | Total subjects | 1455 | 1456 | 2911 | 1451 | | **Adjudicated MACE** | | | | | | # with first event within risk period (%) | 47 (3.23) | 51 (3.50) | 98 (3.37) | 37 (2.55) | | Person-yrs | 5166.32 | 4871.96 | 10038.28 | 5045.27 | | IR (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 TOFA vs TNFi | 1.24 (0.81, 1.91) | 1.43 (0.94, 2.18) | 1.33 (0.91, 1.94)\* |  | | **Adjudicated malignancies excl. NMSC** | | | | | | # with first event within risk period (%) | 62 (4.26) | 60 (4.12) | 122 (4.19) | 42 (2.89) | | Person-yrs | 5491.48 | 5311.71 | 10803.19 | 5482.30 | | IR (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 TOFA vs TNFi | 1.47 (1.00, 2.18) | 1.48 (1.00, 2.19) | 1.48 (1.04, 2.09)\* |  |   \* non-inferiority not met   * *A safety signal detected from the interim analysis of this study had led both FDA and EMA to issue a Boxed Warning on the increased risk of blood clots and death with TOFA 10mg BID.* * *Full data from the study will be used to determine a final recommendation for the higher dose.* * *At this time it is unclear how the new findings will impact JAK inhibitors more broadly*   [Source:](https://www.pfizer.com/news/press-release/press-release-detail/pfizer-shares-co-primary-endpoint-results-post-marketing) Pfizer press release, January 27, 2021. |