MIIRA

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 – 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

For past MIIRA issues, please visit FILGOOD

Xeljanz (tofacitinib [TOFA]) failed to show non-inferiority to TNFi in ORAL Surveillance post-marketing safety study (Pfizer)

- ORAL Surveillance evaluated the safety 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: Pfizer press release, January 27, 2021.