EULAR response criteria for DAS28-CRP at Week 24 (Table 1) vs. 5/10 at Week 12 (one Week 12 responder was lost to follow-up). Similarly, 6/9 patients in the original, active VNS treatment groups met or exceeded the MCID in CDAI at Week 24 vs. 5/10 at Week 12. In the long-term extension, 1/4 sham crossover patients had both EULAR and CDAI response after 12 weeks of VNS (1/2 QD, 0/2 QID). Co-therapy with a b/tsDMARD was initiated in 2 subjects (Table 1). One crossover subject was treated with oral methylprednisolone at week 19 due to worsening RA disease activity. VECTRA composite scores and component analysis revealed an 18-point decrease in median multi-analyte disease activity index in the QD group over 24 weeks of VNS with a decrease in serum levels of several analytes in key component categories (IL-6, serum amyloid A, and VCAM-1). Erosion progression by hand MRI was stabilized or decreased in all but 1 of the stimulated patients at Week 24.

Table 1. Change in DAS28-CRP at Week 24

Subject	Treatment	DAS28-CRP (MCID -1.2) *added b/tsDMARD co-therapy
005-01	QD	-2.4
005-03	QD	-2.21
006-01	QD	-0.07
002-01	QD	-4.95 *
005-06	QD	-0.72 *
006-03	QID	-0.69
008-01	QID	0.49
008-03	QID	-3.14
008-04	QID	1.43
005-05	Sham to QD	0.39
006-04	Sham to QD	-0.78
006-02	Sham to QID	-0.22
008-02	Sham to QID	-0.09

Conclusion: Improvements in clinical disease activity and pro-inflammatory cytokine suppression were maintained through 24 weeks of VNS treatment. Safety outcomes continue to support the risk/benefit profile of VNS as a treatment option for patients with multiple-drug refractory RA.

REFERENCES:
[1] Koopman PNAS 2016
[2] Genovese et al. Lancet Rheum 2020.

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POS0237

MAJOR ADVERSE CARDIOVASCULAR EVENTS, MALIGNANCIES AND VENOUS THROMBOEMBOLISM BY BASELINE CARDIOVASCULAR RISK: A POST HOC ANALYSIS OF ORAL SURVEILLANCE

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Background: ORAL Surveillance was a post-authorisation safety study of tofacitinib vs TNF inhibitors (TNFi) in rheumatoid arthritis (RA) patients (pts) aged ≥50 yrs with ≥1 additional cardiovascular (CV) risk factor and an inadequate response to methotrexate (MTX). CV disease has overlapping risk factors with malignancies and venous thromboembolism (VTE), including older age, smoking, hypertension and diabetes.[1,2]

Objectives: To evaluate the impact of pts' baseline (BL) CV risk on the incidence and risk of major adverse CV events (MACE), malignancies and VTE in ORAL Surveillance.

Methods: Pts on stable MTX were randomised 1:1:1 to receive tofacitinib 5 or 10 mg twice daily (BID) or a TNFi (adalimumab 40 mg every 2 weeks or etanercept 50 mg once weekly). Incidence rates (IRs; pts with first events/100 pt-yrs) and hazard ratios (HRs; tofacitinib vs TNFi) were evaluated for adjudicated MACE (defined as CV death [excluding CV death due to pulmonary embolism (PE)], non-fatal MI and non-fatal stroke), malignancies (excluding NMSC) and VTE (including fatal/non-fatal deep vein thrombosis and PE). Across safety outcomes, IRs/HRs were stratified by BL CV risk score: pts were first categorised by history of coronary artery disease (HxCAD); pts without a HxCAD were further stratified by BL CV risk score categories (high [≥20%], intermediate [≥7.5–<20%], borderline [≥5–<7.5%] and low [<5%] risk), with a 1.5 multiplier applied per EULAR recommendations.[3]

Results: 4362 pts were included: tofacitinib 5 mg BID, n=1455; tofacitinib 10 mg BID, n=1456; TNFi, n=1451. In these treatment groups, during a median follow-up of 4.0 yrs, MACE was reported in 47 (3.2%), 51 (3.5%) and 37 (2.6%) pts, malignancies in 62 (4.3%), 60 (4.1%) and 42 (2.9%) pts, and VTE in 17 (1.2%), 34 (2.3%) and 10 (0.7%) pts, respectively. Approximately two-thirds of pts had intermediate to high CV risk, or HxCAD, and risk was well-balanced across treatment groups (Table 1). Across treatments, MACE and malignancies IRs were highest in pts with a HxCAD or a high BL CV risk score (Figure 1). IRs/HRs for MACE, malignancies and VTE were generally higher with tofacitinib vs TNFi. Differences between tofacitinib vs TNFi in MACE and malignancy IRs/HRs were typically more pronounced in pts with a HxCAD or at least intermediate BL CV risk score, and less so in pts with lower BL CV risk score (Figure 1). In tofacitinib 10 mg BID-treated pts, VTE IRs/HRs (vs TNFi) were clearly highest in pts with a HxCAD or high BL CV risk score; no association between VTE and BL CV risk scores was observed with tofacitinib 5 mg BID or TNFi (Figure 1).

Table 1. Percentages of pts with a HxCAD and pts without a HxCAD categorised by BL CV risk scores, per ASCVD-PCE risk calculator[4] with a 1.5 multiplier applied[3]

	Tofacitinib 5 mg BID (N=1455)	Tofacitinib 10 mg BID (N=1456)	TNFi (N=1451)
HxCAD, n (%)	161 (11.1)	172 (11.8)	164 (11.3)
No HxCAD: BL CV risk score, per ASCVD-PCE risk calculator, n (%)			
High (≥20%)	274 (18.8)	303 (20.8)	296 (20.4)
Intermediate (≥7.5–<20%)	490 (33.7)	516 (35.4)	505 (34.8)
Borderline (≥5–<7.5%)	200 (13.7)	174 (12.0)	155 (10.7)
Low (<5%)	313 (21.5)	272 (18.7)	315 (21.7)
Missing data	17 (1.2)	19 (1.3)	16 (1.1)

HxCAD is defined as any history of MI, coronary heart disease, stable angina pectoris or coronary artery procedures n, number of pts with specified characteristics; N, number of evaluable pts

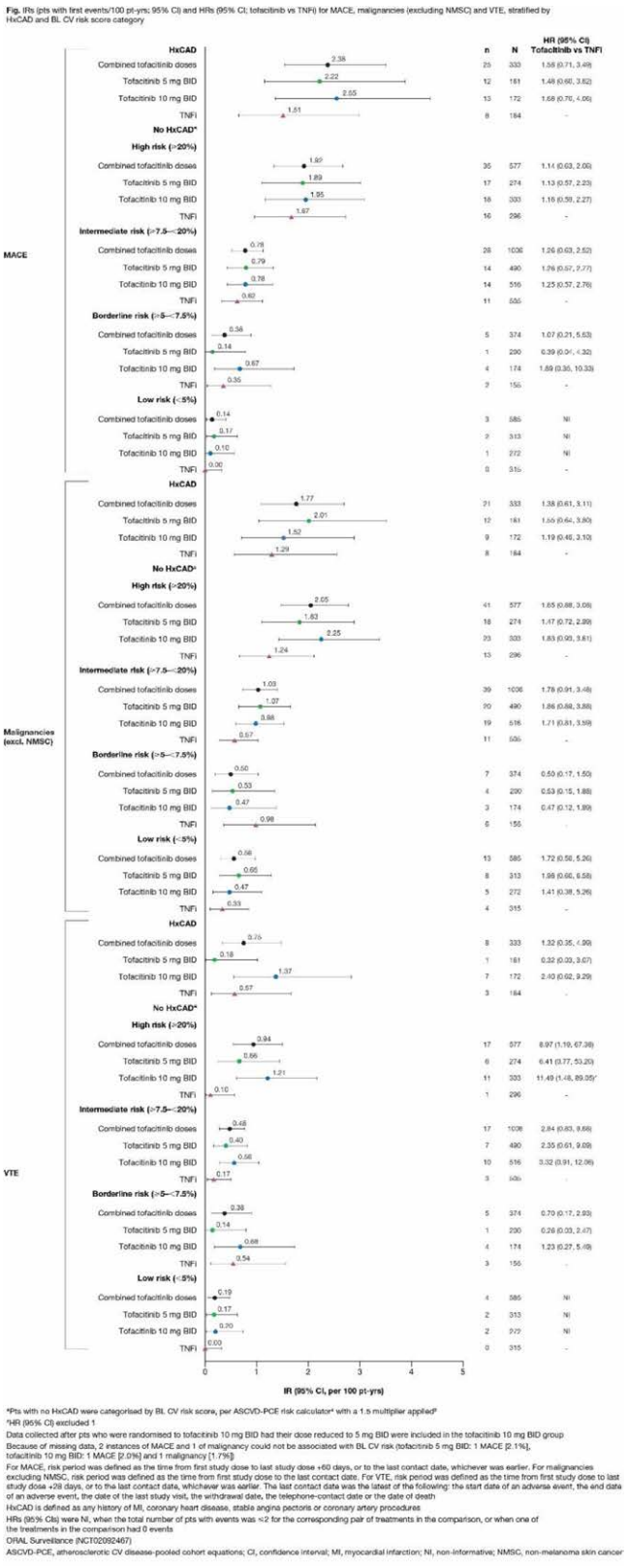

Fig. IRs (pts with first events/100 pt-yrs; 95% CI) and HRs (95% CI; tofacitinib vs TNFi) for MACE, malignancies (excluding NMSC) and VTE, stratified by HxCAD and BL CV risk score category

Pts with no HxCAD were categorised by BL CV risk score, per ASCVD-PCE risk calculator with a 1.5 multiplier applied*
†HR (95% CI) excluded 1
Data collected after pts who were randomised to tofacitinib 10 mg BID had their dose reduced to 5 mg BID were included in the tofacitinib 10 mg BID group
Because of missing data, 2 instances of MACE and 1 of malignancy could not be associated with BL CV risk (tofacitinib 5 mg BID: 1 MACE [2.1%], tofacitinib 10 mg BID: 1 MACE [2.0%] and 1 malignancy [1.7%])
For MACE, risk period was defined as the time from first study dose to last study dose +60 days, or to the last contact date, whichever was earlier. For malignancies excluding NMSC, risk period was defined as the time from first study dose to the last contact date. For VTE, risk period was defined as the time from first study dose to last study dose +28 days, or to the last contact date, whichever was earlier. The last contact date was the latest of the following: the start date of an adverse event, the end date of an adverse event, the date of the last study visit, the withdrawal date, the telephone-contact date or the date of death
HxCAD is defined as any history of MI, coronary heart disease, stable angina pectoris or coronary artery procedures
HRs (95% CIs) were NI, when the total number of pts with events was <2 for the corresponding pair of treatments in the comparison, or when one of the treatments in the comparison had 0 events
ORAL Surveillance (NCT02092467)
ASCVD-PCE, atherosclerotic CV disease-pooled cohort equations; CI, confidence interval; MI, myocardial infarction; NI, non-informative; NMSC, non-melanoma skin cancer

Conclusion: In this post hoc analysis of data from ORAL Surveillance, IRs for MACE and malignancies (excluding NMSC) were highest across treatments, and increased with both tofacitinib doses vs TNFi, in pts with a HxCAD or high BL CV risk score; a similar finding was observed for VTE IRs in pts treated with tofacitinib 10 mg BID. These findings support recommendations to regularly assess and address CV risk in RA pts.

REFERENCES:
[1] Koene et al. Circulation 2016; 133: 1104-1114.
[2] Ageno et al. Circulation 2008; 117: 93-102.
[3] Agca et al. Ann Rheum Dis 2017; 76: 17-28.
[4] American College of Cardiology, American Heart Association. ASCVD risk estimator. https://tools.acc.org/ldl/ascvd_risk_estimator/index.html#!/calulate/estimator/.

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POS0238 SIDE EFFECT PROFILE OF HYDROXYCHLOROQUINE USE IN PATIENTS WITH RA, SLE, AND OTHER RMDS OVER 20 YEARS

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Background: During the pandemic, hydroxychloroquine (HCQ) became a household name, yet despite more than 70 years as a csDMARD treatment, relatively little is known about its overall side effect (SE) profile.
Objectives: To understand the types, severity, and rates of patient-reported side effects of HCQ in adults with RA, SLE, and other RMDs alone and in comparison with methotrexate (MTX).
Methods: Adult participants in the Forward Databank observational registry reported all medication use and medication side effects through biannual questionnaires from 1999 through 2021. Incident use of HCQ and MTX were measured at enrollment and longitudinally with additional reporting of severity of side effects, certainty of medication as cause of side effect, and affected body systems. We analyzed incident rates of side effects overall and by HCQ or MTX categorical use, respectively: monotherapy, with concomitant use of another csDMARD, or with concomitant use of a bDMARD or tsDMARD. Finally, the likelihood of having any side effects was analyzed in Cox regression models by comparing HCQ initiators to MTX initiation, and within each, combination MTX or HCQ with csDMARD or bDMARD to monotherapy; these