an oral Janus kinase inhibitor for the treatment of RA. Live zoster vaccine (LZV) has shown 70% efficacy in immunocompetent adults aged 50–59 years and 51% efficacy in those aged ≥60 years.[2] We previously reported that pts with RA on background methotrexate who started 3 months of treatment with tofacitinib after LZV had similar varicella zoster virus (VZV)-specific immunity to placebo (PBO) pts, and their VZV immunity at Week 6 post-vaccination was comparable with healthy individuals aged ≥50 years.[3]

Objectives: To evaluate the long-term effectiveness of LZV in pts with RA via the incidence of HZ after treatment with tofacitinib for up to 27 months.

Methods: Data were analysed from a prior cohort of pts (n=100) given LZV and then randomised 2–3 weeks later to tofacitinib 5 mg twice daily (BID) or PBO for 12 weeks (A3921237 [NCT02147587]). At 14 weeks post-vaccination, pts joining the long-term extension (LTE) study ORAL Sequel (NCT00413699; study ongoing; database not locked) initiated open-label treatment with tofacitinib 5 or 10 mg BID. The incidence of HZ post-vaccination after tofacitinib exposure up to 27 months (based on an extended follow-up beyond January 2016 data snapshot) was evaluated. Among HZ cases, we analysed measures of VZV-specific immunity with average immunity after LZV.

Results: 112 pts were randomised to PBO (n=57) or tofacitinib 5 mg BID (n=55). 100 pts continued to receive tofacitinib in ORAL Sequel. Five cases (not adjudicated) of HZ occurred (#1: 202 days [219 days post-LZV], #2: 267 days [281 days post-LZV], #3: 702 days [748 days post-LZV], #4: 699 days [741 days post-LZV], #5: 446 days [544 days post-LZV] after initiation of tofacitinib. Cases #1, #2, #3 and #4 were monodermatomal; #5 involved 5 dermatomes. All cases resolved with treatment. Cases #1, #4 and #5 had undetectable ELISPOT measures at baseline and Week 6 post-vaccination, indicating a lack of VZV-specific immunity. Cases #2 and #3 responded adequately to vaccination by both immunoglobulin G (IgG) and ELISPOT measures, but had lower than average VZV IgG levels, both at baseline and at Week 6. (Table).

Table. VZV ELISPOT and IgG levels

	Case #1 (HZ 219 days after zoster vaccine)	Case #2 (HZ 281 days after zoster vaccine)	Case #3 (HZ 748 days after zoster vaccine)	Case #4 (HZ 741 days after zoster vaccine)	Case #5 (HZ 544 days after zoster vaccine)	Study A3921237 Tofacitinib 5 mg BID (N=54)
VZV IFNγ ELISPOT at baseline (SFCs/10⁶ PBMCs)	25 (LOD)	41	25 (LOD)	25 (LOD)	25 (LOD)	48
VZV IFNγ ELISPOT at Week 6 (SFCs/10⁶ PBMCs)	25 (LOD)	76	51	25 (LOD)	25 (LOD)	70
Change from baseline in VZV ELISPOT at Week 6 (SFC fold-rise; SFCs/10⁶ PBMCs)	1.00	1.85	2.04	1.00	1.00	1.50
VZV IgG titer at baseline (gpELISA units/mL)	224	37	97	237	208	201
VZV IgG titer at Week 6 (gpELISA units/mL)	444	71	187	232	223	403
Change from baseline in VZV IgG titer at Week 6 (fold-rise; gpELISA units/mL)	1.98	1.92	1.93	0.98	1.07	2.11

Individual values shown for Cases #1–#5, mean values shown for Study A3921237.

One patient who lacked pre-existing varicella immunity developed disseminated primary varicella from the vaccine strain 16 days post-vaccination (reported previously[2]). This case was excluded from calculations for HZ.

BID, twice daily; HZ, herpes zoster; IFNγ, interferon gamma; IgG, immunoglobulin G; LOD, limit of detection; PBMC, peripheral blood mononuclear cell; SFCs, spot-forming cells; VZV, varicella zoster virus.

Conclusions: LZV prior to treatment with tofacitinib is effective at boosting IgG levels and cell-mediated immunity towards VZV. No pts who developed both strong cell-mediated and humoral immunity against VZV developed HZ. Of the 5 pts who developed HZ, 3 did not have any cell-mediated response and 2 had a low humoral response.

References:
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LB0003 **TOFACITINIB WITH AND WITHOUT METHOTREXATE VERSUS ADALIMUMAB WITH METHOTREXATE FOR THE TREATMENT OF RHEUMATOID ARTHRITIS: RESULTS FROM ORAL STRATEGY, A PHASE 3B/4 RANDOMISED TRIAL**
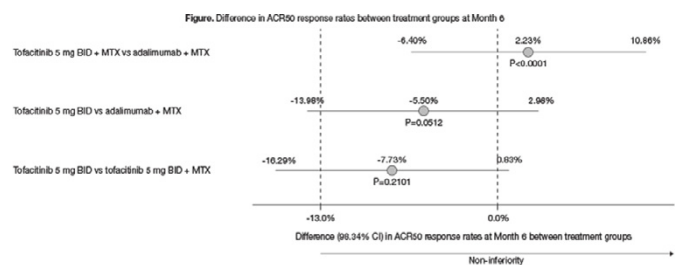
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Background: Tofacitinib is an oral JAK inhibitor for the treatment of RA. There is no direct comparison of tofacitinib monotherapy vs tofacitinib +MTX in MTX inadequate responders (IR) and limited data comparing tofacitinib (±MTX) vs adalimumab (ADA) +MTX in patients (pts) with RA.

Objectives: To compare efficacy and safety of tofacitinib monotherapy, tofacitinib+MTX, and ADA+MTX in a head-to-head, non-inferiority trial in MTX-IR pts.

Methods: In this randomised, triple-dummy, active-controlled, 1-year, Phase 3b/4 trial (ORAL Strategy; NCT02187055), pts had active RA (≥4 tender/painful joints on motion and ≥4 swollen joints [28-joint count] at baseline [BL]) inadequately controlled with MTX. Pts were randomised 1:1:1 to receive tofacitinib 5 mg twice daily (5 mg mono BID), tofacitinib 5 mg BID +MTX (5 mg BID+MTX) or subcutaneous ADA 40 mg every other week +MTX (ADA+MTX); MTX dose: 15–25 mg/wk. The primary endpoint was ACR50 at Month (Mo) 6. Non-inferiority between treatments was declared if the lower bound of the 98.34% two-sided confidence intervals of the difference of ACR50 response at Mo 6 was larger than -13% (based on meta analysis of ADA trials[1]), and superiority if it was larger than 0%. Other endpoints included: ACR20/50/70 and least-squares mean changes from BL in SDAI, DAS28-4(ESR) and HAQ-DI at Mos 6 and 12. Safety was assessed throughout the trial.

Results: 1146 pts were randomised and treated (5 mg mono BID: n=384; 5 mg BID+MTX: n=376; ADA+MTX: n=386). Demographics and BL disease characteristics were similar across groups. Most pts were female (82.7–83.1%), white (75.9–77.1%), with a mean age of 49.7–50.7 years, median disease duration of 5.4–6.1 years and mean HAQ-DI score of 1.6. Across groups, 80.2–81.6% of pts completed the study. ACR50 response rate at Mo 6 was 38.3% for 5 mg mono BID, 46.0% for 5 mg BID+MTX and 43.8% for ADA+MTX. Non-inferiority was demonstrated for 5 mg BID+MTX vs ADA+MTX (P<0.0001) but not for 5 mg mono BID vs ADA+MTX (P=0.0512) or 5 mg mono BID vs 5 mg BID+MTX (P=0.2101) which, although numerically different, were not statistically different (Figure). Tofacitinib monotherapy achieved the efficacy expected of an effective immunomodulator in this pt population. Secondary efficacy analyses were generally consistent with the primary analysis (Table). Adverse event (AE), serious AE and discontinuation due to AE rates were generally clinically similar across groups, though numerically fewer pts had increased alanine aminotransferase with 5 mg mono BID vs 5 mg BID+MTX or ADA+MTX.

Figure. Difference in ACR50 response rates between treatment groups at Month 6

Tofacitinib 5 mg BID + MTX vs adalimumab + MTX: -6.40% / 2.23% / 10.86%, P<0.0001
Tofacitinib 5 mg BID vs adalimumab + MTX: -13.98% / -5.50% / 2.98%, P=0.0512
Tofacitinib 5 mg BID vs tofacitinib 5 mg BID + MTX: -16.29% / -7.73% / 0.83%, P=0.2101

Difference (98.34% CI) in ACR50 response rates at Month 6 between treatment groups

Non-inferiority / Superiority

Non-inferiority was demonstrated if the lower bound of the confidence interval was larger than -13.0%; superiority was demonstrated if the lower bound of the confidence interval was larger than 0.0%. P-values presented are from non-inferiority hypothesis testing. P-values are multiplicity-adjusted and should be compared with 0.025.

Table. Efficacy analyses and summary of safety by treatment group

	Tofacitinib 5 mg BID monotherapy (N=384)		Tofacitinib 5 mg BID + MTX (N=376)		ADA 40 mg EOW + MTX (N=386)	
EFFICACY	Mo 6	Mo 12	Mo 6	Mo 12	Mo 6	Mo 12
ACR50, n (%) – primary endpoint at Mo 6	147 (38.3)	151 (39.3)	173 (46.0)	179 (47.6)	169 (43.8)	177 (45.9)
ACR20, n (%)	249 (64.8)	237 (61.7)	275 (73.1)	264 (70.2)	274 (71.0)	261 (67.6)
ACR70, n (%)	70 (18.2)	81 (21.1)	94 (25.0)	109 (29.0)	80 (20.7)	100 (25.9)
SDAI, LSM (SE) change from BL	-23.7 (0.6)	-25.1 (0.7)	-26.6 (0.6)	-28.7 (0.7)	-25.6 (0.6)	-28.1 (0.7)
DAS28-4(ESR), LSM (SE) change from BL	-2.1 (0.1)	-2.3 (0.1)	-2.4 (0.1)	-2.7 (0.1)	-2.4 (0.1)	-2.6 (0.1)
HAQ-DI, LSM (SE) change from BL	-0.5 (0.03)	-0.6 (0.03)	-0.6 (0.03)	-0.6 (0.03)	-0.5 (0.03)	-0.6 (0.03)
SAFETY						
AEs, n (%)	226 (58.9)		231 (61.4)		253 (65.5)	
SAEs, n (%)	35 (9.1)		27 (7.2)		24 (6.2)	
Discontinuations due to AEs, n (%)	23 (6.0)		26 (6.9)		37 (9.6)	
Herpes zoster, n (%)	4 (1.0)		8 (2.1)		5 (1.3)	
Nasopharyngitis, n (%)	22 (5.7)		16 (4.3)		18 (4.7)	
Upper respiratory tract infection, n (%)	25 (6.5)		37 (9.8)		29 (7.5)	
Alanine aminotransferase increased, n (%)	8 (2.1)		23 (6.1)		26 (6.7)	
Deaths, n (%)	2 (0.5)		0 (0.0)		0 (0.0)	

Efficacy data are for the full analysis set. ACR20/50/70 used component-wise LOCF before dropout and NRI after dropout; continuous endpoint data are from a Mixed-effect Model of Repeated Measurements.
Safety analysis set was identical to the full analysis set.
ACR, American College of Rheumatology; ADA, adalimumab; AE, adverse event; BID, twice daily; BL, baseline; DAS, Disease Activity Score; ESR, erythrocyte sedimentation rate; EOW, every other week; HAQ-DI, Health Assessment Questionnaire-Disability Index; LOCF, last observation carried forward; LSM, least-squares mean; Mo, month; MTX, methotrexate; NRI, non-responder imputation; SAE, serious AE; SDAI, Simplified Disease Activity Index; SE, standard error.

Conclusions: Tofacitinib 5 mg BID+MTX was as effective as ADA+MTX in

MTX-IR pts with RA. However, clinical outcomes of all 3 regimens, including tofacitinib 5 mg BID monotherapy, were comparable. There were no new or unexpected safety issues.

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FRIDAY, 16 JUNE 2017

New treatments in SLE, Sjögren's and APS

OP0231 | **THE EFFECT OF "TRIPLE THERAPY" WITH ANTICOAGULATION PLUS CORTICOSTEROIDS PLUS PLASMA EXCHANGE AND/OR INTRAVENOUS IMMUNOGLOBULINS ON THE MORTALITY OF CATASTROPHIC ANTIPHOSPHOLIPID SYNDROME (CAPS) PATIENTS**

I. Rodríguez-Pintó [1], G. Espinosa [1], D. Erkan [2], Y. Shoenfeld [3], R. Cervera [1] on behalf of CAPS Registry Project Group (European Forum on Antiphospholipid Antibodies). *[1] Department of Autoinmune Disease, Hospital Clínic, Barcelona, Spain; [2] Barbara Volcker Center for Women and Rheumatic Disease, Hospital for Special Surgery, New York, United States; [3] Zabludowicz Center for Autoimmune Diseases, Sheba Medical Center, Tel Aviv, Israel*

Background: Triple therapy (anticoagulation plus corticosteroids plus plasma exchange and/or intravenous immunoglobulins) is empirically prescribed for the management of catastrophic antiphospholipid syndrome (CAPS). However, previous analyses have been inconsistent regarding the beneficial effect of triple therapy on patients' survival.

Objectives: The objective of this study was to assess the effect that triple therapy has on the mortality risk of CAPS patients.

Methods: In a cohort including 525 episodes of CAPS (CAPS Registry), we evaluated the relationship between triple therapy and mortality. Patients were grouped in three based on their treatments: a) triple therapy (anticoagulation plus corticosteroids plus plasma exchange and/or intravenous immunoglobulins); b) drugs included in the triple therapy but in different combinations; c) none of the treatments included in the triple therapy. The primary endpoint was all-cause mortality. Multivariate logistic regression models were used to compare mortality risk between groups taking into account a set of possible confounding variables.

Results: The "CAPS registry" cohort included 525 episodes of CAPS accounting for 502 patients. After excluding 38 episodes (7.2%), a total of 487 episodes of CAPS accounting for 471 patients (mean age 38 years; 67.9% female; primary APS patients 68.8%) were analyzed. Overall, 177 (36.3%) patients died. Triple therapy was prescribed in 197 episodes (40.5%), other combinations in 278 (57.1%), and none of those treatments in 12 episodes (2.5%). According to these three groups, mortality rate increased up to 27.9%, 40.6%, and 75%, respectively. Triple therapy was positively associated with a higher chance of survival when compared to non-treatment (adjusted odds ratio [OR]: 7.7 95%; confidence interval [95CI] 2.0–29.7) or to treatment with other combinations of drugs included in the triple therapy (adjusted OR 6.8; 95CI 1.7–26.9). Triple therapy accounted for a 64% decrease of the risk of death in patients with CAPS that received this combination of drugs.

Conclusions: Triple therapy is independently associated to a higher survival rate among CAPS.

OP0232 | **SUSTAINED SAFETY AND EFFICACY OVER 10 YEARS WITH BELIMUMAB (BEL) PLUS STANDARD SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) THERAPY (SOC) IN PATIENTS WITH SLE**

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Background: Preliminary safety and efficacy data from the Phase II BEL open-label extension study (LBSL02; NCT00071487) have been reported.

Objectives: Here we present the final 10-year data.

Methods: This was a multicentre, open-label, continuation trial (BEL112626; NCT00583362) of BEL + SoC in patients with a satisfactory response in the parent study. Patients received intravenous BEL 10 mg/kg every 4 weeks. Baseline was prior to the first ever dose of BEL.

Results: Of 298 patients in the continuation trial, 131 (44%) remained at Year 10. Total BEL exposure was 2154 patient-years. Adverse events (AEs) remained stable or decreased (Table). Two deaths (pseudomonal lung infection; cytomegaloviral pneumonia) were possibly related to BEL. SLE Responder Index (SRI) response increased (Figure). A British Isles Lupus Assessment Group (BILAG) flare (1 new A/2 new B scores) occurred in 72.6% of patients and 41.9% had a severe flare (SLE Flare Index). Prednisone dose decreased from baseline to Year 10 (Table). Of patients receiving >7.5 mg/day baseline prednisone, 32.6%

Abstract OP0232 – Table 1

	0–1y (N=296)	1–2y (N=294)	2–3y (N=276)	3–4y (N=250)	4–5y (N=223)	5–6y (N=209)	6–7y (N=192)	7–8y (N=178)	8–9y (N=169)	9–10y (N=152)	10–11y (N=131)
Incidence of ≥1 AE, n (%)											
Overall	291 (98.3)	283 (96.3)	260 (94.2)	239 (95.6)	203 (91.0)	190 (90.9)	182 (94.8)	162 (91.0)	157 (92.9)	137 (90.1)	105 (80.2)
Resulting in discontinuation	2 (0.7)	3 (1.0)	3 (1.1)	7 (2.8)	5 (2.2)	6 (2.9)	6 (3.1)	1 (0.6)	3 (1.8)	5 (3.3)	2 (1.5)
Serious AE	41 (13.9)	43 (14.6)	50 (18.1)	30 (12.0)	40 (17.9)	33 (15.8)	35 (18.2)	34 (19.1)	28 (16.6)	25 (16.4)	14 (10.7)
Serious infections/infestations	11 (3.7)	13 (4.4)	9 (3.3)	9 (3.6)	6 (2.7)	6 (2.9)	12 (6.3)	10 (5.6)	8 (4.7)	5 (3.3)	5 (3.8)
Death	1 (0.3)	0	1 (0.4)	1 (0.4)	0	1 (0.5)	2 (1.0)	0	0	1 (0.7)	0

		Y1	Y2	Y3	Y4	Y5	Y6	Y7	Y8	Y9	Y10
Prednisone											
median % change from baseline;		-0.4;	-25.0;	-36.9;	-50.0;	-48.3;	-60.0;	-62.5;	-70.0;	-66.7;	-65.8;
25th, 75th percentile (n)		-50.0, 0 (186)	-74.2, 0 (172)	-80.0, 0 (153)	100.0, 0 (140)	-100.0, 0 (128)	0 (115)	-100.0, -10.7 (105)	-100.0, -1.6 (94)	-100.0, -0 (91)	-100.0, 0 (84)