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THU0212

FIRST LINE TREATMENT WITH CONVENTIONAL SYNTHETIC DISEASE MODIFYING ANTIRHEUMATIC DRUGS IN RHEUMATOID ARTHRITIS: A MULTINATIONAL POPULATION-BASED COHORT FROM 14 REAL WORLD HEALTHCARE DATABASES AND 9 COUNTRIES - REALITY VERSUS GUIDELINES

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Background: Treatment guidelines recommend early initiation of csDMARDs following diagnosis of rheumatoid arthritis (RA), with methotrexate (MTX) as first-line therapy. Scarce evidence exists on adherence to this guidance

Objectives: To characterize first-line csDMARD treatment during the first year following an RA diagnosis.

Methods: 14 real world databases (3 Primary care, 6 primary/secondary care records, 5 claims) from 9 countries were included, all mapped to the OMOP common data model.

Patients were included on the earliest event of: 1st diagnosis of RA or 1st DMARD prescription with an RA diagnosis within 30 days. Patients were >18 years-old, required 1+ year pre-index data, and at least 1-year follow-up. Study period covered 2000-2018. Previous users of DMARDs or non-RA inflammatory arthritis history were excluded. Only MTX, Hydroxychloroquine (HCQ), Sulfasalazine (SSZ) and Leflunomide (LEF) were available in all databases.

Results: We identified 323,547 eligible participants. Large variation was observed internationally (Figure 1). MTX as first-line monotherapy ranged from 33.3% to 74.5%, and in combination with HCQ from 2.1% to 6.7%. Three

additional csDMARDs were used as first-line: HCQ in 10.1% to 30.2%, SSZ in 0.9% to 28.7%, and LEF in 1.8% to 15.2%.

Figure 1. First line csDMARD treatment during 1yr from first observed RA diagnosis

Conclusion: We report wide heterogeneity of first-line csDMARDs regimens internationally. Despite recommendations for MTX to be first line therapy, data suggest that a large proportion of patients receive alternative csDMARD.

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THU0213

UPADACITINIB AS MONOTHERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS AND PRIOR INADEQUATE RESPONSE TO METHOTREXATE: RESULTS AT 84 WEEKS FROM THE SELECT-MONOTHERAPY STUDY

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Background: In the SELECT-MONOTHERAPY trial, upadacitinib (UPA), an oral JAK inhibitor, demonstrated significantly greater efficacy compared to continuing methotrexate (MTX) when used as monotherapy over 14 weeks (wks) in patients (pts) with rheumatoid arthritis (RA) and prior inadequate response to MTX.¹

Objectives: To describe the long-term safety and efficacy of UPA monotherapy in an ongoing long-term extension (LTE) of the SELECT-MONOTHERAPY trial.

Methods: Pts on stable MTX were randomized to either continue MTX (cMTX, given as blinded study drug) or switch to once-daily (QD) UPA 15 (UPA15) or 30 (UPA30) mg monotherapy for 14 wks. From Wk14, pts could enter a blinded LTE and continue to receive UPA15 or UPA30; pts randomized to cMTX were switched to UPA15 or UPA30 per pre-specified assignment at baseline. Treatment-emergent adverse events (TEAEs) per 100 pt yrs (PYs) of exposure are summarized up to a cut-off date of 5 February 2019, when all pts had reached Wk84. Efficacy outcomes through Wk84 are reported as observed and using non-responder imputation.

Results: Of 648 pts randomized, 598 (92%) completed 14 wks and entered the LTE on blinded UPA. By the cut-off date, 20% in total had discontinued due to the following: AE (6%), consent withdrawal (4%), lost to follow-up (2%), lack of efficacy (1%), or other reasons (7%). Cumulative exposures were 421.5 and 425.9 PYs for UPA15 and UPA30, respectively. The most frequently reported TEAEs were urinary tract infection, creatine phosphokinase (CPK) increase, upper respiratory tract infection, nasopharyngitis, worsening of RA, bronchitis, herpes zoster (HZ), and alanine aminotransferase increase; the most common serious AE was pneumonia. Events of HZ, hepatic disorder, and CPK elevations were higher among pts receiving UPA30, while rates of serious infection and malignancy appeared comparable between doses (Figure). Most HZ events involved 1-2 dermatomes, with a single disseminated cutaneous event (UPA30) and none with CNS involvement. Five patients experienced MACE, and there were 5 VTE events (UPA15: 4; UPA30: 1). All MACE and VTE events occurred in pts with underlying risk factors. Pts continuing to receive UPA15 and UPA30 achieved stringent endpoints at Week 84 (Table). Pts who switched from cMTX to UPA15 or UPA30 demonstrated comparable efficacy responses to those initially randomized to UPA.

Conclusion: The adverse event profile associated with long-term exposure to UPA15 or 30 as monotherapy was consistent with an integrated analysis of UPA safety across the entire phase 3 program, with no new safety signals identified. Further, UPA15 or 30 monotherapy resulted in continued and sustained improvements in RA signs and symptoms through 84 wks.

References:

[1] Smolen, et al. *Lancet* 2019;393(10188):2303-11.

Figure. Treatment-emergent Adverse Events Through ≥84 Weeks (E/100 PYs, 95% CI).

Table. Proportion of Patients at Week 84

Parameter (%)	cMTX→UPA 15 mg n=108		cMTX→UPA 30 mg n=108		UPA 15 mg n=217		UPA 30 mg n=215	
	AO	NRI	AO	NRI	AO	NRI	AO	NRI
ACR20/50/70	86/71/49	67/56/39	90/68/50	66/51/38	88/71/54	65/53/41	96/78/66	74/62/52
DAS28(CRP) ≤3.2/≤2.6	80/56	64/44	79/63	62/49	76/60	57/46	85/77	67/61
CDAI ≤10/≤2.8	78/38	62/30	85/29	65/22	74/34	55/25	85/49	67/39
Boolean Remission	27	22	23	18	26	20	41	33

AO, as observed; NRI, non-responder imputation.

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THU0214

LONG-TERM EFFECTIVENESS OF METHOTREXATE WITH STEP DOWN GLUCOCORTICOID BRIDGING (COBRA SLIM) VERSUS OTHER CONVENTIONAL DMARD REGIMENS AS INITIAL RA THERAPY: 5-YEAR OUTCOMES OF THE CARERA TRIAL.

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Background: The treat-to-target Care in Early Rheumatoid Arthritis (CareRA) trial demonstrated that remission induction with csDMARD combinations and step-down glucocorticoids (GCs) was not superior over methotrexate (MTX) monotherapy with step-down GCs (Cobra Slim) in RA patients with a high-risk profile (1). Moreover, Cobra Slim showed benefit over a tight step-up with MTX in monotherapy (TSU) in RA patients with a low-risk profile.

Objectives: To compare the long term outcomes up to 5 years of different initial intensive treatment strategies in participants of the CareRA-plus study.

Methods: In the CareRA trial, patients with DMARD naïve early RA were stratified in a high- or low-risk group based upon the presence of serum markers, disease activity and erosive status. High-risk patients were randomised to Cobra Classic (MTX+sulphasalazine with highly dosed GC remission induction scheme), Cobra Avant-Garde (MTX+leflunomide with moderately dosed GC scheme) or Cobra Slim. Low-risk patients were randomised to Cobra Slim or TSU. Patients completing this trial were eligible for the CareRA-plus observational study. Here, patients were evaluated 6-monthly over 3 years. Therapy adaptation was left to the treating physician. Efficacy was assessed by DAS28-CRP and HAQ and compared between the originally allocated treatment arms. The 5-year evolution