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AB0383

LATENT TUBERCULOSIS INFECTION SHOULD BE MONITORED IN BOTH TUMOR NECROSIS FACTOR INHIBITORS AND NON-TUMOR NECROSIS FACTOR INHIBITORS IN BIOLOGIC-NAÏVE PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The risk of latent tuberculosis infection (LTBI) increased during the treatment of biologic agents for patients with rheumatoid arthritis. Taiwan rheumatology association recommend performing at least annual interferon-gamma release assays (IGRAs) testing during biologic treatment course because of the moderate prevalence of tuberculosis in Taiwan.[1] Although increased tuberculosis reactivation rate in patients with TNF inhibitor is reported, the risk of LTBI in patients with RA treated by non-TNF inhibitors is limited.

Objectives: The aim is to use serial interferon-gamma release assays (IGRAs) as a diagnostic tool for LTBI in biologic-naïve patients with rheumatoid arthritis treated with TNF and non-TNF inhibitors in Taiwan.

Methods: We retrospectively collected 313 biologic-naïve patients with rheumatoid arthritis receiving biologic agents between 2013 to 2017 in Chang Gung Memorial hospital in Taiwan. All RA patients underwent semi-annual IGRA test during biologic agent treatment. Cox proportional hazard model was used for analysis to compared RA patients with TNF and non-TNF inhibitors.

Figure 1

Results: The age of patients and disease duration are 55.9 13.1 year-old and 5.2 2.0 years (Table 1). The LTBI rate in patients with rheumatoid arthritis after biologic treatment is 6.7%. Out of the 21 patients with LTBI, 12(6%) patients were treated with TNF inhibitors, 9(8%) patients were treated with non-TNF inhibitors (Figure 1). 42.9%(9/21) received chemoprophylactic therapy by isoniazid but no patient suffered from active TB till the end of study period. Patients with TNF inhibitors was associated with a hazard ratio (HR) of 4.43 (95% CI, 0.80-24.39) after adjusted age, sex, diabetes history, prednisolone use and disease duration. This

Cox regression analysis of RA patients found that the risk of LTBI was not different in TNF or non-TNF inhibitors.

Conclusion: Our study revealed biologic-naïve patients with rheumatoid arthritis have the same risk of LTBI. All RA patients who need either TNF or non-TNF inhibitors should be monitored LTBI in moderate prevalence TB area.

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Table 1. Baseline characteristics in patients with RA treated with TNF or non-TNF inhibitors

	Total (n=313)	TNF inhibitors (n=200)	Non-TNF inhibitors (n=113)	p- value
Gender, female	259 (82.7%)	169(84.5%)	90(79.6%)	0.109
Age (Mean± standard deviation)	55.9	55.0	57.6	0.102
Disease duration (Mean± standard deviation)	13.1 5.2	12.3 5.5	14.4 4.7	0.001*
Diabetes mellitus	2 (0.6%)	1.8 (0.9%)	2.2 (1.9%)	0.019*
Liver cirrhosis	2(0.6%)	2(1.0%)	0(0.0%)	0.280
Prednisolone mean dose (mg/day)	223 (71.2%) 8.0	145(72.5%) 8.2	78 (69.0%) 7.6	0.479 0.623
	7.7	9.1	3.8	

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AB0384

PROMISPAIN INTERFERENCE 6B AND FATIGUE 7A SHORT FORMS AND PROFILE-29 IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TNF INHIBITORS

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Background: PROMIS (Patient Reported Outcomes Measurement Information System) has been used in rheumatoid arthritis (RA) patients (Pts) to assess disease activity across multiple domains (i.e. physical function, fatigue, pain interference). AWARE (Comparative and Pragmatic Study of Golimumab IV Versus Infliximab in Rheumatoid Arthritis) is an ongoing Phase 4 study designed to provide a real-world assessment of intravenous Tumor Necrosis Factor inhibitor (TNFi) medications in RA pts. The study utilizes PROMIS and Clinical Disease Activity Index (CDAI) to assess effectiveness.

Objectives: This analysis examined select PROMIS measures to assess (1) relationship between baseline (BL) CDAI and PROMIS-scores, (2) responsiveness of PROMIS after initiation of TNFi and (3) relationship between PROMIS T-scores of the 4 item Profile29v2 Fatigue and Pain Interference domains and respective PROMIS Short Forms (SF).

Methods: AWARE is a prospective, noninterventional, 3-year study at 100 US sites. RA pts were enrolled when initiating TNFi treatment. Treatment decisions are at the discretion of the treating rheumatologist. We report on data from Pts' BL PROMIS Pain Interference 6b (PI), Fatigue7a (F), Profile29v2 and CDAI. PROMIS T-scores were compared across CDAI disease category (high, moderate etc) using ANOVA. We dichotomized pts based on whether their BL T-score was within 0.5SD of the population mean (i.e. 'normal') or not to evaluate for effect modification in the subsequent change in PROMIS T-scores. Data shown are mean ± std dev.

Results: Pts (N=1220) were 59.5± 13.2 yrs, disease duration 8.2 ± 9.9 yrs, 83.4% female, body weight 85.1± 24.2 kg, BMI 31.4 ± 8.51, BL CDAI 32.4 ± 15.6. A significant relationship between PROMIS T-scores (PI, F) and BL CDAI disease activity category was confirmed. There was minimal change in T-score of pts with BL PI and F T-scores <=55 and PF>=45 over 5 infusions (approx. 5-7 months). Depending on domain,

14.7-27.3% of pts had initial PROMIS T-scores within 0.5SD of normal. There was a significant ($p<0.0001$) relationship between PI and F T-scores and the respective 4 questions on the P29v2.

Conclusion: Avoiding floor effects in pts who initiated TNFi therapy with near-normal PROMIS scores, PROMIS instruments demonstrated a robust T-score change in response to initiation of TNFi therapy.

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PROMIS Physical Function T-Score Change:

Effect of Baseline Assessment

PROMIS Pain Interference SF6b T-Score Change:

Effect of Baseline Assessment

PROMIS Fatigue SF7a T-Score Change:

Effect of Baseline Assessment

Figure 1

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AB0385

INTEGRATED SAFETY ANALYSIS ACROSS PHASE 3 CLINICAL STUDIES INCLUDING THE CONTROLLED AND UNCONTROLLED PERIODS FOR INTRAVENOUS GOLIMUMAB IN RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS, AND ANKYLOSING SPONDYLITIS

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Background: The GO-FURTHER, GO-VIBRANT, and GO-ALIVE randomized controlled trials evaluated the efficacy and safety of intravenous

(IV) golimumab (GLM) in patients (pts) with active rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS), respectively.

Objectives: This integrated analysis assessed safety events across indications in pts who received IV GLM.

Methods: Integrated safety data from 3 Phase 3, double-blind, placebo (PBO)-controlled trials were analyzed up to week (WK) 112 in RA pts and up to WK 60 in PsA and AS pts. Pts received either IV PBO or IV GLM (2 mg/kg) at 0, 4, 12, and 20 WKS. PBO pts crossed over to IV GLM at WK 24, except RA pts randomized to PBO who met early escape criteria crossed over at WK 16 and AS pts randomized to PBO who crossed over at WK 16. Cumulative adverse events (AEs) were reported by indication and pooled by treatment. Anti-drug antibodies (ADAs) were evaluated.

Table 1.

Variables	RA ^a IV GLM	PsA ^b IV GLM	AS ^b IV GLM	All IV GLM
Treated patients, n	584	460	204	1248
Average duration of follow up, wks	95.9	47.2	51.8	70.7
Patients who discontinued due to an AE	41 (7.0)	17 (3.7)	4 (2.0)	62 (5.0)
Patients with ≥1 AE	462 (79.1)	234 (50.9)	113 (55.4)	809 (64.8)
Patients with ≥1 SAE	106 (18.2)	24 (5.2)	7 (3.4)	137 (11.0)
Patients with ≥1 infection	287 (49.1)	105 (22.8)	67 (32.8)	459 (36.8)
Patients with ≥1 serious infection	36 (6.2)	10 (2.2)	3 (1.5)	49 (3.9)
Patients with ≥1 infusion reaction	27 (4.6)	4 (0.9)	3 (1.5)	34 (2.7)
ADA-positive patients ^c , %	23.4	22.0	20.2	22.3

Patients n (%) reporting safety events during the placebo-controlled and uncontrolled study periods are reported, unless otherwise specified.
^aBased on safety events that occurred up to week 112; ^bBased on safety events that occurred up to week 60
^cAssessed using a drug-tolerant enzyme immunoassay based on IV GLM patients with appropriate samples through week 52 (RA, n=552; PsA, n=450; AS, n=203; and All, n=1205)
 ADA, anti-drug antibody; AE, adverse event; AS, ankylosing spondylitis; IV GLM, intravenous golimumab; PsA, psoriatic arthritis; RA, rheumatoid arthritis; SAE, serious adverse event

Table 2.

Variables	RA ^a		PsA ^b		AS ^b		All	
	IV GLM	Placebo	IV GLM	Placebo	IV GLM	Placebo	IV GLM	Placebo
Treated patients, n	584	197	460	239	204	103	1248	539
Average duration of follow up, wks	95.9	21.0	47.2	23.2	51.8	16.1	70.7	21.0
Opportunistic infections (95% confidence interval)	0.4 (0.1, 1.0)	0 (0, 3.8)	0 (0, 0.7)	0 (0, 2.8)	0 (0, 1.5)	0 (0, 9.4)	0.2 (0.1, 0.6)	0 (0, 1.4)
All malignancies (95% confidence interval)	0.5 (0.2, 1.1)	0 (0, 3.8)	0.5 (0.1, 1.7)	0.2 (0, 6.8)	0 (0, 1.5)	0 (0, 9.4)	0.2 (0, 0.9)	0 (0, 3.3)
Active TB (95% confidence interval)	0.2 (0, 0.7)	0 (0, 3.8)	0.5 (0.1, 1.7)	0 (0, 2.8)	0 (0, 2.7)	0 (0, 9.4)	0.3 (0, 1.4)	0 (0, 1.4)
Death (95% confidence interval)	0.5 (0.2, 1.1)	1.3 (0, 7.0)	0.2 (0, 1.3)	1.9 (0, 6.8)	0 (0, 1.5)	0 (0, 9.4)	0.4 (0.1, 0.8)	1.4 (0.3, 4.0)

Incidence per 100 patient-years are reported, unless otherwise specified.
^aBased on safety events that occurred up to week 112
^bBased on safety events that occurred up to week 60
 AS, ankylosing spondylitis; IV GLM, intravenous golimumab; PsA, psoriatic arthritis; RA, rheumatoid arthritis; TB, tuberculosis

Results: Overall, 1248 pts were treated with IV GLM across indications. A numerically greater proportion (%) of IV GLM pts with RA reported safety events than pts with PsA or AS (Table 1): SAEs (18.2 vs 5.2 vs 3.4), infections (49.1 vs 22.8 vs 32.8), serious infections (6.2 vs 2.2 vs 1.5), and infusion reactions (4.6 vs 0.9 vs 1.5). Incidence (per 100 pt-years) of opportunistic infections, malignancy, active tuberculosis, and death with IV GLM was low (≤ 0.5) across indications (Table 2). Infections were the most commonly reported type of SAE among pooled IV GLM pts; the most frequent was pneumonia (10 [0.8%]). Incidence (per 100 pt-years) of serious infections was similar among IV GLM pts with and without corticosteroid use (3.35 vs 3.37, respectively). Overall, 1 IV GLM pt (PsA) experienced a demyelination event. A numerically greater proportion of IV GLM pts discontinued due to an AE than PBO pts (5.0% vs 0.9%, respectively). In IV GLM pts with baseline alanine aminotransferase (ALT) $\leq$ upper limit of normal (ULN), 1.2% had post-baseline ALT elevations $\geq 5\times$ ULN. The proportion of IV GLM and PBO pts with post-baseline ALT elevations $\geq 5\times$ ULN was 2.1% vs 0% with methotrexate and 0.7% vs 1.4% without methotrexate use at baseline, respectively. Using a drug-tolerant enzyme immunoassay, the incidence of ADAs was 22% through WK 52 across indications, which primarily consisted of low titer ADAs.

Conclusion: IV GLM demonstrated a consistent safety profile across indications in the PBO-controlled (up to WK 24) and uncontrolled study periods. Similar to WK 24 (1), more safety events occurred in RA pts, who represented the largest study population with older pts, longer disease duration, and more concomitant medication use.