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ABSTRACT SUPPLEMENT

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Tasocitinib (CP-690,550) Appears To Be Effective and Tolerated When Administered Either as Long-Term Monotherapy or on Background Methotrexate in Patients with Rheumatoid Arthritis. Carol A. Connell[1], Richard Riese[2], Susan Wood[2], John Bradley[2] and Samuel H. Zwillich[2]. [1]Pfizer Inc, New London, CT, [2]Pfizer Inc

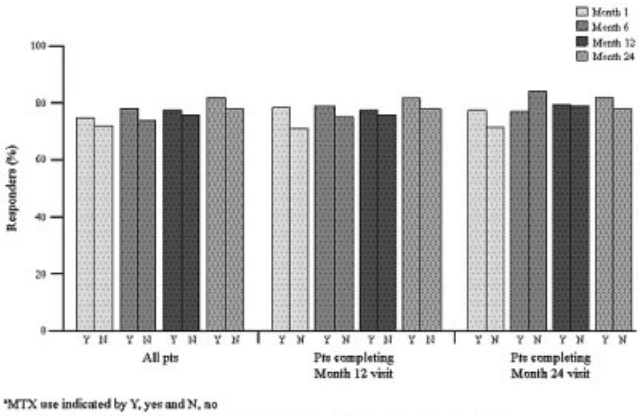
Background: Tasocitinib (CP-690,550) is an oral, selective Janus kinase inhibitor that has previously demonstrated efficacy in treating rheumatoid arthritis (RA) and a manageable safety profile in randomized studies. Patients were enrolled in this long-term follow-up study upon completion of participation in a prior randomized study of tasocitinib (PRST). Here safety and efficacy is compared between patients who received tasocitinib monotherapy and those on background methotrexate (MTX).

Methods: In this Phase 2/3 open label study of 1070 patients who had participated in a PRST, treatment was initiated with either 5 or 10 mg tasocitinib twice daily. Key outcome measures included safety and ACR20 response rates. Results are presented for all patients (ALL, n=1070), patients who completed Month 12 (M12, n=648), and patients who completed Month 24 (M24, n=207) visits. The baseline is that of the PRST for patients who enrolled within 14 days of PRST participation; if enrollment was >14 days after PRST participation, baseline was the start of this study. Some PRSTs required background MTX; others were conducted as monotherapy.

Results: Background MTX use was reported in 422/1070 (39.4%, ALL MTX), 332/648 (51.2%, M12 MTX), and 162/207 (78.3%, M24 MTX). Treatment-related adverse events (TRAEs) were generally manageable and infrequently led to discontinuation (70/1070). The most frequently reported TRAEs were infections and infestations for both MTX and non-MTX treatment groups. The most common TRAEs reported by MTX patients were urinary tract infection (4.7%), bronchitis (4.0%), and sinusitis (3.6%); in non-MTX patients, the most common TRAEs were upper respiratory tract infection (2.5%), bronchitis (2.3%), and herpes zoster (2.2%). These TRAEs and TRAEs of abnormal liver laboratory tests are presented by treatment group in the table below.

	Tasocitinib monotherapy (n=639)			Tasocitinib + MTX (n=422)		
Treatment-related AEs, n	**Mild**	**Mod**	**Severe**	**Mild**	**Mod**	**Severe**
Infections and Infestations, n (%)	**49 (7.7%)**	**38 (6.0%)**	**4 (0.6%)**	**47 (11.1%)**	**45 (10.7%)**	**14 (3.3%)**
Bronchitis	9	6	0	6	11	0
Herpes zoster	7	6	1	6	5	2
Nasopharyngitis	6	5	0	9	1	0
Sinusitis	2	1	0	7	8	0
Upper respiratory tract infection	13	3	0	8	5	0
Urinary tract infection	4	3	1	10	8	2
Liver Laboratory Test AEs, n (%)	**3 (0.5%)**	**5 (0.8%)**	**0**	**15 (3.6%)**	**11 (2.6%)**	**0**
Alanine aminotransferase increased	0	1	0	6	3	0
Aspartate aminotransferase increased	0	1	0	5	2	0
Gamma-glutamyl transferase increased	0	0	0	1	2	0
Hepatic enzyme increased	3	2	0	1	3	0
Liver function test abnormal	0	1	0	2	1	0

ACR20 response rates demonstrated similar efficacy of tasocitinib between ALL MTX and non-MTX patients, as well as M12 and M24 patients (Figure 1). ACR20 response rates at Month 24 were 81.8% and 77.8% for M24 MTX and non-MTX patients, respectively.



[a]MTX use indicated by Y, yes and N, no

ACR, American College of Rheumatology; BID, twice daily; MTX, methotrexate; pts, patients

Figure 1. % responders for ACR20[a] by MTX use for pts initially treated with tasocitinib 5 or 10 mg BID.

Conclusion: The safety profile of tasocitinib, regardless of background MTX use, was generally tolerable and manageable. Tasocitinib demonstrated sustained efficacy over 24 months in the treatment of RA. ACR response rates were similar in patients receiving tasocitinib monotherapy compared with patients on background MTX therapy.

Disclosure: C. A. Connell: Pfizer Inc, 3; **R. Riese:** Pfizer Inc, 3; **S. Wood:** Pfizer Inc, 3; **J. Bradley:** Pfizer Inc, 3; **S. H. Zwillich:** Pfizer Inc, 3.

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A Randomized Dose-Ranging, Placebo-Controlled Study of INCB028050, a Selective JAK1 and JAK2 Inhibitor in Subjects with Active Rheumatoid Arthritis. Maria W. Greenwald[1], Rosanne Fidelus-Gort[4], Rich Levy[4], Jinjin Liang[4], Kris Vaddi[4], William V. Williams[3], Robert Newton[4], Swamy Yeleswaram[4], Robert Flores[4], Edward McKeever[4], James Rodgers[4], Stacey Shepard[4], Pierre-Yves Berclaz[2], Chin Hyok Lee[2] and Monica E. Luchi[3]. [1]Desert Medical, Palm Desert, CA, [2]Eli Lilly & Company, [3]Incyte Corporation, Wilmington, DE, [4]Incyte Corporation

Purpose: To characterize safety and efficacy of INCB028050 (050) in RA in subjects who have had an inadequate response to any DMARD therapy including biologics.

Methods: Subjects with active RA(≥6 tender>/4 swollen joints of 28), ESR≥28mm or CRP ≥ 7mg/L) despite DMARD therapy were randomized to placebo (PBO)or 050 at once daily oral doses of 4mg, 7 mg or 10 mg with background DMARDs (excluding biologics). After 12 weeks subjects randomized to placebo were re-randomized to 7mg or 10mg for an additional 12 weeks (wks). The primary analysis was at the end of the 12-week PBO-controlled period. Subjects remained blinded to treatment assignment during the 24-wk treatment period. Subjects could be on stable doses of methotrexate (MTX), hydroxychloroquine, leflunomide, corticosteroids (<10 mg/day) and/or sulfasalazine. Results below are at Wk 12. The study was not designed to test for statistically significant differences between individual dose groups and placebo; p-values and significance levels are not displayed.

Results: The study enrolled 127 subjects, eighty percent women. Two subjects were randomized but not treated. One subject had no post-baseline assessments. Mean ages across treatment groups 54–58yrs. Mean disease duration ranged from 7–9 yrs. The proportion of subjects on background MTX ranged from 72–77%. The proportion of subjects who failed biologics in the past was 13%, 38%, 6% and 20% for the PBO, 4mg, 7mg and 10mg groups respectively. Of the subjects who had failed biologics, 30% failed multiple biologics.

Response rates are expressed as mean % (also percent change from baseline for DAS28).

Wk 12 results	PBO n=31	4 mg 050 n=31	7 mg 050 N=32	10 mg 050 N=30
ACR20 (%)	32	52	59	53
ACR50 (%)	13	35	31	30
ACR70 (%)	3	16	9	10
DAS28 CRP Mean (%change)	5 (−19)	4 (−34)	4 (−32)	4 (−33)
DAS28 <=2.6 (%)	16	23	25	17

Responses were observed as early as the first assessment (Wk2), demonstrating a rapid onset of action. Similar ACR responses were achieved with 050 regardless of background therapy or previous biologic experience. ACR20 responses for biologic experienced subjects was 33% for PBO and 53%, 73% and 43% for 4mg, 7mg and 10mg, respectively. ACR50 responses for biologic experienced subjects was 11% for PBO and 33%, 45% and 29% for 4mg, 7mg and 10mg, respectively.

The nature of treatment-emergent adverse events (TEAEs) was similar across groups. The frequency of TEAEs in PBO, 4mg, 7 mg and 10 mg 050 groups was 61.3%, 48.4%, 59.4% and 74.2%, respectively. One subject reported an unrelated serious AE (GI bleed). The most frequently reported TEAEs were headache (active 10.6% vs. 6.5% PBO), URI (active 5.3% vs. 9.7% for PBO) and diarrhea (active 5.3% vs. 6.5% PBO). At Wk 12, two cases of herpes zoster were reported (2.1% active vs. 0% PBO). Increases were observed in HDL and LDL, and HDL:LDL ratios tended to increase with therapy (active 10.06% vs. 0.41% PBO).

Conclusion: In this study, INCB028050 given once a day over 12 weeks was well tolerated and demonstrated clinically meaningful responses in subjects with inadequate response to DMARDs including biologics over 12 wks of treatment. All three doses tested were effective.

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