Table 1. TEAEs and Key Safety Outcomes Week 0-24 by Age Group, n (%)

Regimen	<65 yrs (n=335)			≥65 yrs (n=113)		
	FIL 200 (n=112)	FIL 100 (n=117)	PBO (n=106)	FIL 200 (n=35)	FIL 100 (n=36)	PBO (n=42)
TEAE	72 (64.3)	81 (69.2%)	70 (66.0%)	30 (85.7%)	16 (44.4%)	30 (71.4%)
Serious AE	4 (3.6)	7 (6.0%)	4 (3.8%)	2 (5.7%)	1 (2.8%)	1 (2.4%)
TEAE leading to study drug discontinuation	4 (3.6)	6 (5.1%)	1 (0.9%)	1 (2.9%)	0	2 (4.8%)
Infection	39 (34.8)	47 (40.2%)	27 (25.5%)	14 (40.0%)	5 (13.9%)	11 (26.2%)
Herpes Zoster (uncomplicated)	2 (1.8)	2 (1.7)	0	0	0	0
Serious infection	1 (0.9)	3 (2.6)	2 (1.9)	0	0	0
MACE	0	1 (0.9)	1 (0.9)	0	0	0
Retinal vein occlusion	1 (0.9)	0	0	0	0	0

Table 2. Week 24 Key Efficacy Measures by Age Group

Regimen	<65 yrs (n=335)			≥65 yrs (n=113)		
	FIL 200 (n=112)	FIL 100 (n=117)	PBO (n=106)	FIL 200 (n=35)	FIL 100 (n=36)	PBO (n=42)
ACR20 n (%) ¹	78 (70)‡	60 (51)†	33 (31)	24 (69)*	24 (67)*	18 (43)
DAS28(CRP) <2.6 n (%) ¹	33 (30)‡	26 (22)*	11 (10)	12 (34)	14 (39)*	7 (17)
HAQ-DI mean CFB (SD)	-0.75 (0.66)‡	-0.60 (0.66)*	-0.40 (0.58)	-0.74 (0.48)*	-0.59 (0.67)	-0.48 (0.65)
SF-36 PCS mean CFB (SD)	9.4 (8.6)‡	9.2 (8.7)†	6.2 (8.2)	9.4 (6.7)*	8.5 (7.8)	7.5 (7.4)
FACIT-Fatigue mean (SD)	11.2 (11.6)†	9.6 (11.1)	7.2 (10.1)	12.9 (12.2)*	10.3 (8.3)	6.4 (10.7)

*p<0.05, †p<0.01, ‡p<0.001 CFB, change from BL. ¹Nonresponder imputation.

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Daiichi Sankyo, Eisai, Eli Lilly Japan, Janssen, Mitsubishi Tanabe, Nippon Kayaku, Novartis, Pfizer Japan Inc, Taiho, Taisho Toyama, Takeda, Teijin, Speakers bureau: AbbVie GK., Bristol-Myers K.K., Chugai Pharmaceutical Co. Ltd., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Astellas Pharma Inc, Daiichi Sankyo Co. Ltd., Eisai Co. Ltd., Sanofi K.K., Teijin Pharma Ltd., Takeda Pharmaceutical Co. Ltd., Novartis Pharma K.K., Kurt de Vlam Consultant for: Pfizer Inc, Consultant for: Johnson & Johnson, David Walker: None declared

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FRI0155

A COMPARISON OF UPADACITINIB PLUS METHOTREXATE AND UPADACITINIB PLUS OTHER csDMARDs IN PATIENTS WITH RHEUMATOID ARTHRITIS: AN ANALYSIS OF TWO PHASE 3 STUDIES

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Background: Upadacitinib (UPA), a selective JAK1 inhibitor, has shown efficacy in patients with rheumatoid arthritis (RA) when combined with methotrexate (MTX) or other conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs).^{1,2} However, the efficacy of UPA plus MTX has not been directly compared with UPA plus other csDMARDs.

Objectives: To compare the efficacy of UPA in combination with MTX versus UPA in combination with other csDMARDs in patients with an inadequate response (IR) to csDMARDs (SELECT-NEXT¹) or biologic DMARDs (bDMARDs; SELECT-BEYOND²).

Methods: 661 patients in SELECT-NEXT and 498 patients in SELECT-BEYOND received UPA 15 mg or 30 mg once daily (QD) or placebo (PBO) for 12 weeks; all patients received concomitant csDMARD(s). The primary endpoints for both studies were rates of ACR20 response and DAS28(CRP) ≤3.2. Additional endpoints included DAS28(CRP) <2.6, CDAI low disease activity (≤10), and CDAI remission (≤2.8). Patients were grouped according to concomitant csDMARD use (MTX vs non-MTX csDMARDs); patients receiving both MTX and a non-MTX csDMARD were included in the MTX group. p-values were calculated based on a logistic regression model with treatment group and type of background csDMARD as fixed factors, adjusting for demographic and baseline factors. p-values from the interaction between treatment group and background csDMARD were also calculated, to assess the consistency of the effects of study treatments for different background csDMARD type. Non-responder imputation was used for missing data.

Results: In SELECT-NEXT and SELECT-BEYOND, 535 and 410 patients, respectively (80%), were receiving concomitant MTX (mean dose 17 mg/week), and 124 and 82 patients were receiving non-MTX csDMARDs. Demographics and disease characteristics were broadly similar between treatment groups; the majority of patients were female and of white ethnicity, and around half were using oral corticosteroids at baseline. Across all subgroups, the proportion of patients achieving efficacy outcomes was higher with both UPA doses compared with PBO (Table). There were no significant differences between efficacy outcomes with UPA in combination with MTX versus UPA in combination with non-MTX csDMARDs in either patient population. This included ACR20 response as well as low disease activity and remission defined by DAS28(CRP) and CDAI.

Table. Week 12 efficacy outcomes by concomitant treatment

Patients (n)	SELECT-NEXT (n=661)						SELECT-BEYOND (n=498)					
	MTX			Non-MTX csDMARDs			MTX			Non-MTX csDMARDs		
	PBO	UPA 15 mg QD	UPA 30 mg QD	PBO	UPA 15 mg QD	UPA 30 mg QD	PBO	UPA 15 mg QD	UPA 30 mg QD	PBO	UPA 15 mg QD	UPA 30 mg QD
ACR20	27.2	65.1	67.4	27.6	58.8	61.4	27.6	65.1	67.4	27.6	65.1	67.4
DAS28(CRP) <2.6	16.8	45.1	45.1	16.8	45.1	45.1	16.8	45.1	45.1	16.8	45.1	45.1
DAS28(CRP) <3.2	49	89.4	89.4	49	89.4	89.4	49	89.4	89.4	49	89.4	89.4
CDAI <10	38.3	65.4	65.4	38.3	65.4	65.4	38.3	65.4	65.4	38.3	65.4	65.4
CDAI <2.8	2.6	8.9	8.9	2.6	8.9	8.9	2.6	8.9	8.9	2.6	8.9	8.9

¹Based on logistic regression analysis for the comparison of UPA in combination with MTX versus UPA in combination with non-MTX csDMARDs, with treatment group and background csDMARD type as fixed factors and sex and baseline factors as covariates.

Conclusion: In this post hoc analysis, the efficacy of UPA in patients with RA appeared comparable whether administered in combination with MTX or non-MTX csDMARDs.

REFERENCES:

- [1] Burmester GR, et al. *Lancet* 2018;391:2503–12;
- [2] Genovese MC, et al. *Lancet* 2018;391:2513–24

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FRI0156

A PHASE 1, SINGLE AND MULTIPLE ASCENDING DOSE STUDY OF TAS5315—A NOVEL HIGHLY SELECTIVE INHIBITOR OF BRUTON'S TYROSINE KINASE—IN HEALTHY MALE VOLUNTEERS

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Background: Bruton's tyrosine kinase (BTK) is expressed in the cells of the immune system and osteoclasts, and plays an important role in inflammation and bone resorption¹. TAS5315 is a novel, highly selective inhibitor of BTK. In animal models, TAS5315 suppressed the inflammation at the joints and significantly suppressed extreme bone destruction, in a dose-dependent manner. It has the potential to become a treatment option in patients with rheumatoid arthritis (RA).

Objectives: To evaluate the safety, pharmacokinetics (PK), and pharmacodynamics (PD) of TAS5315 in healthy male volunteers.

Methods: The single ascending dose (SAD) study, which was the first-in-human study, and the multiple ascending dose (MAD) study were conducted as randomized, double-blind, placebo-controlled and parallel-group comparative studies in a single center. In the SAD study, 70 subjects were enrolled and received 0.01–8 mg of TAS5315 or placebo. In the MAD study, 31 subjects were enrolled and received 1–8 mg of TAS5315 or placebo once daily for 7 days. The allocation ratio (TAS5315: placebo) was 7:3 in the SAD study and 6:2 in the MAD study. The PD of TAS5315 was assessed by measuring the rate of BTK occupancy in peripheral blood mononuclear cells using a fluorescence probe. The expression level of CD203c in peripheral blood basophils treated with anti-IgE antibodies was also measured with a flow cytometer. The SAD and MAD studies were reviewed and approved by the IRB of Kitasato University Hospital.

Results: The observed PK profile of TAS5315 was linear in the dose range of 0.01–8 mg. TAS5315 was rapidly absorbed (median T_{max} : 0.5–1.5 hr) and eliminated (mean $T_{1/2}$: 1.00–1.37 hr). The maximum percentage of BTK occupancy by TAS5315 increased dose-dependently at 0.01–2 mg in SAD study. The occupancy rate of BTK peaked at 2 mg and was almost 100% at 2–8 mg, 6 hr after administration and remained almost 80% or higher for up to 24 hr. The expression level of CD203c after basophil activation decreased by 80% at 2–8 mg of TAS5315 6 hr after administration. No changes in the PD biomarkers were observed in the placebo group. The PD response was maintained after the reduction in the drug concentration. In the SAD and MAD studies, the incidence of adverse drug reactions (ADR) in the TAS5315 groups was 6.1% and 13.0%, respectively. Two subjects (8.7%) experienced subcutaneous hemorrhage in MAD study. No other ADR occurred twice in SAD and MAD studies. The severity of all ADR in SAD and MAD studies was mild and

they were resolved without any treatment. There were no serious adverse events. None of the ADR showed a tendency towards a dose-dependent increase. The administration of TAS5315 resulted in a decrease in platelet aggregation and prolonged bleeding time. These changes returned to baseline level in the follow up measurement and there were no clinical safety concerns.

Conclusion: TAS5315 was tolerable when administered as repeated doses of up to 8 mg once daily for 7 days. The inhibitory effect of BTK by TAS5315 was demonstrated and this provides the basis for an early Phase II study to evaluate the efficacy of TAS5315 in patients with RA.

REFERENCE:

- [1] *Drug Discov Today*. 2014;19:1200-4.

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FRI0157

OBSERVATIONAL STUDY OF HAIR FALL IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH LOW DOSE METHOTREXATE COMPARED TO HEALTHY CONTROLS

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Background: Chemotherapeutic drugs are known to cause of hair loss (typically anagen effluvium, starts at 2-4 weeks and most apparent at 1-2 months).(1) The effect of hair fall (or the perceived possibility of it) can be so distressing that up to 8% of patients may choose less effective chemotherapy regimens that do not cause hair loss.(2) Low dose methotrexate used in rheumatology has a different mode of action and side