the mean CDAI was 7.5 (84.5% patients with low disease activity, and 2.8% in clinical remission). While switching to tofacitinib 11mg QD for 3 months, no significant difference was observed in terms of the ratio of DAS28-ESR LDA or CDAI LDA, but numerically more patients achieved DAS28-ESR LDA or CDAI LDA (32 and 64, respectively). During the 3-month follow-up period, no new adverse events were present.

Conclusion: Our study showed that RA patients switching from tofacitinib 5mg BID to tofacitinib 11mg QD sustained the effectiveness with no adverse clinical impact.

Table 1. Clinical demographics and laboratory variables

	Baseline	Before Switching to 11mg QD	After switching to 11mg QD
Age, mean (SD)	57.4 (12.7)		
Female proportion (%)	85		
RF positivity (%)	78.9		
ACPA positivity (%)	80.3		
Bio-exposed (%)	70.1		
DAS28-ESR, mean (SD)	5.0 (1.1)	3.3 (0.3)	3.2 (0.4)
CDAI, mean (SD)	23.0 (8.7)	7.5 (2.8)	6.9 (2.7)
DAS LDA (n,%)		21 (29.6)	32 (45.0)
CDAI LDA (n,%)		60 (84.5)	64 (90.1)

REFERENCES:

- [1] Lamba M, Wang R, Fletcher T, et al. J Clin Pharmacol. 2016 Nov;56(11):1362-1371
- [2] Kuo CF, Luo SF, See LC, et al. Rheumatol Int. 2013 Feb;33(2):355-60.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.2924

FRI0160 PREPARATION AND PROPERTY OF IGURATIMOD NANOSCALE SUSTAINED-RELEASE SYSTEM

Zhenzhen Ma¹, Cheng Tao², Lin Sun¹, Jianjun Zhang², Jinxia Zhao¹. ¹Peking University Third Hospital, Department of Rheumatology and Immunology, Beijing, China; ²Beijing University of Chemical Technology, College of Chemical Engineering, Beijing, China

Background: Iguratimod, a methanesulfonanilide, has obvious anti-inflammatory function and has been developed exclusively in Asia-Pacific countries. As a novel disease-modifying anti-rheumatic drug, iguratimod is effective in the treatment of RA, but some side effects, such as liver damage and gastrointestinal discomforts are the main concerns in clinical application^[1]. Currently, iguratimod is practically insoluble in aqueous solvents and only available in oral dosage forms. The low solubility of drugs leads to incomplete absorption and bioavailability, which affects the clinical efficacy and increases the gastrointestinal side effects of drugs^[2].

Objectives: In order to improve the bioavailability and alleviate the side effect of gastrointestinal reaction, we changed the dosage form of iguratimod to Nanoliguratimod-loaded Hydrogel Composite.

Methods: Iguratimod nanoparticles (Nanoliguratimod) were prepared by using the high-gravity anti-solvent precipitation (HGAP) technique, and its properties were tested. The Nanoliguratimod-loaded Hydrogel Composite was prepared and the delivery of the payload was demonstrated. In vitro, the biological effects of Nanoliguratimod@Hydrogel on fibroblast-like synoviocytes (RA-FLS) were evaluated. In vivo, the pharmacokinetics of oral raw iguratimod or subcutaneous injection of Nanoliguratimod@Hydrogel was carried out in the healthy rats. Further, we evaluated the efficacy of Nanoliguratimod@Hydrogel in treating collagen-induced arthritis (CIA) rats.

Results: By the HGAP technique, we acquired the amorphous form Nanoliguratimod with an average size of 295nm, which had higher dissolution rates and higher stability. The release of iguratimod from hydrogel composite in PBS was gradual and sustained for up to 48h compared with Nanoliguratimod. Nanoliguratimod@Hydrogel inhibited the proliferation, migration, and invasion of RA-FLS in a dose dependent manner. The pharmacokinetic parameters showed better bioavailability and longer half-life time with Nanoliguratimod@Hydrogel by subcutaneous administration than oral raw iguratimod. Animal experiments confirmed that subcutaneous injection of Nanoliguratimod@Hydrogel (10mg/kg every three days) and oral raw iguratimod (10mg/kg daily) showed similar efficacy in decreasing arthritis index score, pathological score, and expression of cytokines (IL-6, TNF- α and IL-1 β).

Conclusion: Overall, our data suggested that Nanoliguratimod@Hydrogel provided new administration routes and extended the administration interval, it may serve as a promising drug delivery approach for the treatment of RA.

REFERENCES:

- [1] Hara M, Abe T, Sugawara S, et al. Long-term safety study of iguratimod in patients with rheumatoid arthritis[J]. Mod Rheumatol., 2007, 17(1):10-16.
- [2] Zhou T, Ding L, Li X, et al. Determination of iguratimod in rat plasma by high performance liquid chromatography: method and application[J]. Biomed Chromatogr, 2010, 22(3):260-264.

Figure: Preparation and Property of Iguratimod Nanoscale Sustained-Release System. (A): Synthesis scheme of Hyaluronic acid-acrylate (HA-AC). (B): Brief production process of Nanoliguratimod@Hydrogel. (C): TEM images of Nanoliguratimod. (D): Dissolution profiles of raw iguratimod, Nanoliguratimod and Nanoliguratimod-loaded Hydrogel. (E): Plasma concentrations and pharmacokinetic parameters of raw iguratimod and Nanoliguratimod-loaded Hydrogel. (F): Changes of arthritis index (AI) score in rats during drug intervention. (G): Results of HE staining and saffron O-fixing green staining on the ankle joints of rats. *p<0.05, **p<0.01, ***p<0.001, n=7 per group. Scar bar =200 μ m.

Acknowledgement: No

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.3436

FRI0161 PHARMACOKINETICS AND SAFETY OF A SINGLE ORAL DOSE OF PEFICITINIB (ASP015K) IN SUBJECTS WITH NORMAL AND IMPAIRED HEPATIC FUNCTION

Daisuke Miyatake¹, Tomohisa Shibata¹, Junko Toyoshima¹, Yuichiro Kaneko¹, Kazuo Oda², Tetsuya Nishimura¹, Masataka Katashima¹, Masashi Sakaki³, Kazuaki Inoue⁴, Takayoshi Ito⁵, Naoki Uchida⁶, Kenichi Furihata⁷, Akino Urae⁸. ¹Astellas Pharma, Inc., Tokyo, Japan; ²Astellas Research Institute of America LLC, Northbrook, United States of America; ³Showa University School of Medicine, Tokyo, Japan; ⁴Showa University Fujigaoka Hospital, Yokohama, Japan; ⁵Showa University Koto Toyosu Hospital, Tokyo, Japan; ⁶Clinical Research Institute of Clinical Pharmacology and Therapeutics, Showa University, Tokyo, Japan; ⁷P-One Clinic, Keiokai Medical Corporation, Tokyo, Japan; ⁸Mediscience Planning Inc., Tokyo, Japan

Background: Peficitinib (ASP015K), a novel oral Janus kinase inhibitor, demonstrated efficacy as once-daily therapy for moderate-severe rheumatoid arthritis in a phase 2b study (NCT01649999)¹ and 2 phase 3 studies (NCT02308163²; NCT02305849).³ Mean urinary excretion of peficitinib accounted for 9–15% of the oral dose.⁴ It produces 3 conjugated metabolites (H1, H2, H4), which show very weak in-vitro pharmacological action.

Objectives: To assess pharmacokinetics (PK) and safety of a single oral dose of peficitinib 150 mg in subjects with normal and impaired hepatic function.

Methods: This phase 1, open-label, single-dose, parallel-group study was conducted at six centres in Japan. Eligible subjects were aged 20–75 years, with body mass index ≥ 17.0 – <30.0 kg/m². Hepatic impairment was defined at screening using Child-Pugh classification: Class A, mild (5–6 points); Class B, moderate (7–9 points). Subjects with severe hepatic impairment (Child-Pugh classification Class C, 10–15 points) were excluded. Subjects received a single oral dose of peficitinib 150 mg under fasting conditions, based on daily dose in the 2 phase 3 studies. Blood samples for plasma PK analysis of peficitinib and its metabolites were collected before and up to 72 h post dose. Safety was assessed throughout the study.

Results: 24 subjects were enrolled (70.8% male): 16 with impaired and 8 with normal hepatic function (Table 1); all received study medication