REFERENCES:


Disclosure of Interests: None declared


**Characteristics of Gut Microbiome and Their Associations with Peripheral Lymphocyte Subpopulations and Cytokines in Rheumatoid Arthritis Patients Complicated with Osteoporosis**

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Background: Osteoporosis (OP) is one of the major comorbidities of rheumatoid arthritis (RA) which is associated with immune disorders[1]. The gut microbiota has been highlighted to be an important environmental factor to influence immune system in maintaining bone health and regulating bone remodeling[2]. However, the alterations of intestinal flora and its relationship with immune system in RA patients with OP are unclear.

Objectives: To investigate the characteristics of gut microbiome as well as the associations between flora and peripheral lymphocyte subpopulations and cytokines in rheumatoid arthritis patients complicated with osteoporosis.

Methods: Total 28 RA patients were divided into 14 RA-non-OP and 14 gender- and age-matched RA-OP groups according to their bone mineral density (BMD) and the history of fragility fracture. Gut microbiota of participants were investigated by 16s RNA and peripheral lymphocyte subsets and cytokines were assessed via flow cytometry. Indicators like erythrocyte sedimentation rate (ESR), C-reaction protein (CRP), anti-cyclic citrullinated peptide antibody (ACPA) and anti-mutated citrullinated vimentin (MVC) antibody were recorded simultaneously. Alpha diversity (ACE, Chao 1, Simpson, Shannon) and beta diversity indices were analyzed using QIMEM. Biomarker species were recognized based on STEMP. Spearman analysis was adopted for correlation of two variables. All P-values reported herein were two-tailed and P-value<0.05 was taken as statistically significant.

Results: The alpha-diversity have no significant difference between RA-non-OP and RA-OP groups (P>0.05, Figure 1A). The community structure of microflora differed between two groups (P<0.05, Figure 1B). As for the composition of intestinal flora at genus level, Faecalibacterium, Proteus, Catenibacterium, Enterobacter and Erspiplasloclotstriodium in RA-OP group were also Lachnospiraceae_NK4A136_group, Parasutterella, Megaplasma, Tyzzerella, UCG-005, Clostridium_stricto_stricto_1, UCG-002, Lachnospiraceae_NK4A136_group, Christensenellaceae_R-7_group, Prevotella, Parabacteroides in RA-non-OP group were significantly increased (Figure 1C). There were positive correlations between Lachnospiraceae_NK4A136_group and the level of T, Th1 and Th17 cells, but negative relevance with ESR, CRP and IL-10 (P<0.05, Table 1). The relative abundance of Faecalibacterium was negatively correlated with IL-2, IL-4, TNF-α and MCV with P<0.05, Clostridium_sensu_stricto_1 and Lachnospiraceae_ND3007_group were negatively correlated with ACPA and MCV respectively as well as IL-2 (P<0.05, Figure 1D-E).

Conclusion: Abnormality of immune system may contribute directly or indirectly to OP in RA, which may be related to the disturbance of gut microbiota.

REFERENCES:


without CPPD (6 vs 5.1 days; p < 0.001) while mean total charges were not statistically different between the 2 groups (p = 0.344). CPPD patients were more likely to be discharged to rehabilitation or other nursing facilities (p < 0.001).

Table 1. Demographics, clinical characteristics, outcomes and resource utilization of patients with and without CPPD who underwent hip arthroplasty between 2006-2014.

<table>
<thead>
<tr>
<th>No CPPD, n (%)</th>
<th>CPPD, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(N=4106510)</td>
<td>(N=6198)</td>
</tr>
<tr>
<td>P-value*</td>
<td></td>
</tr>
<tr>
<td>Age in years at admission, median (mean ± SD)</td>
<td>75 (72.7 ± 31.5)</td>
</tr>
<tr>
<td>Female</td>
<td>2507971 (61.1%)</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>516688 (12.5%)</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>684171 (16.6%)</td>
</tr>
<tr>
<td>Gout</td>
<td>139648 (3.4%)</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>199175 (4.8%)</td>
</tr>
<tr>
<td>Hyperparathyroidism</td>
<td>7959 (0.2%)</td>
</tr>
<tr>
<td>Hypomagnesaemia</td>
<td>100390 (2.4%)</td>
</tr>
<tr>
<td>Charlson Comorbidity Index score ≥ 2</td>
<td>365990 (89.1%)</td>
</tr>
</tbody>
</table>

* Chi-square P except t-test for all others include transfer to nursing or rehabilitation facility.

Conclusion: CPPD patients who underwent THA were more likely to be older, with a higher comorbidity burden, longer length of stay, and discharged to a non-home setting, than non-CPPD patients.

REFERENCES:

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 Disclosure of Interests: Gema Ariceta Speakers bureau: I have received honoraria for lectures, presentations, or educational events from Alexion Pharmaceuticals, Recordati Rare Disease, Advicence, Chiesi, Kyowa Kirin, Consultant of: I have participated on Advisory Boards for Alexion Pharmaceuticals, Advicence, Chiesi, Dicerna, and Alnylam; Employee of: Empoyee of Kyowa Kirin International, Angela Williams Employee of: Employee of Kyowa Kirin International, Dirk Schnabel Speakers bureau: I received an honorarium from various companies for scientific lectures (i.e. Ascendis, BioMarin, Ferring Pharma, Hexal / Sandoz, Ipsen Pharma, Kyowa Kirin, Merck Serono, Novo Nordisk); Consultant of: Biomarin; Kyowa Kirin


POS1155

THE INTERNATIONAL X-LINKED HYPOPHOSPHATAMIA (XLH) REGISTRY: OVERVIEW OF THE DATA SET

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Background: X-Linked Hyophosphataemia (XLH) is a rare, progressive, lifelong, hereditary renal tubule phosphate-wasting disorder characterised by a pathological increase in fibroblast growth factor 23 concentration/activity. 1

Despite XLH being increasingly recognised as a chronic progressive disease, there are few data documenting its natural history or the impact of treatment on patient outcomes. 1 The International XLH Registry was established to address this lack of information on XLH to help inform future clinical management. The Registry will collect data to characterise the treatment, burden of disease, disease progression and long-term outcomes of XLH.

Objectives: To provide an overview and status update of the International XLH Registry as of 31 December 2021.

Methods: The International XLH Registry (NCT03193476) was initiated in August 2017, aims to recruit 1,200 children and adults with XLH, and will run for 10 years. This Registry is an international, multicentre, non-interventional data collection programme and will provide the largest single dataset representing children and adults with XLH. To be eligible for inclusion in the registry, patients must meet all the following criteria:1) Male or female subjects of all ages; 2) Diagnosis of XLH with clinical, radiological, biochemical and/or genetic findings consistent with XLH. The Registry captures any treatment details and clinical outcome variables in patients with XLH and patients are followed for as long as informed consent is present, and where applicable and regulatory permissions are maintained. Only data collected during standard routine examinations are recorded within the Registry, and no specific examination/data entries are mandated. Parameters collected at baseline included demographics, medical and treatment history, and clinical presentation data. The conduct of the International XLH Registry is overseen by 17 Steering Committee physician members representing the region.

Results: As of 31 December 2021, 1,043 subjects diagnosed with XLH were enrolled from 88 hospital sites in 19 countries. The geographic distribution of subjects is as follows: Belgium n=29, Bulgaria n=7, Czech Republic n=8, Denmark n=23, France n=267, Germany n=79, Hungary n=11, Ireland n=5, Israel n=21, Italy n=88, The Netherlands n=26, Norway n=23, Portugal n=9, Slovakia n=5, Slovenia n=3, Spain n=55, Sweden n=43, Switzerland n=17, and the UK n=324. A further 30 sites are yet to enrol (including sites in Austria and Latvia). Overall, 400 adults (18-29y, n=116; 30-39y, n=81; 40-49y, n=95; 50-59y, n=38; ≥60y, n=50) and 620 paediatric subjects (<5y, n=138; 5-12y, n=321; 13-17y, n=161) have been enrolled (date of birth not reported, n=23). The majority of enrolled subjects are female (648 (62.1%), with 372 male (35.7%) and 23 for whom sex was not reported (2.2%). The quantity of data from the patients included in this Registry will enable ongoing snapshot and prospective analyses to be conducted over the coming years to answer the research questions and inform clinical practice.

Conclusion: This International XLH Registry forms the largest dataset of subjects with XLH collected to date. Patients have been recruited from a wide geographical region and baseline demographics are consistent with a hereditary X-linked dominant disease. Information collected during the 10-year Registry duration will generate real-world evidence to help inform clinical practice throughout the region, with the aim of improving the care and quality of life of adults and children living with this debilitating disease.

REFERENCES:

Disclosure of Interests: Authors acknowledge the contribution of all International XLH Registry Steering Committee members, and all the investigators participating in the International XLH Registry.

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POS1156

PHASE 1 TRIALS OF NOVEL ORAL ENZYME THERAPY (ALLN-346) FOR HYPERURICEMIA & GOUT: SAFETY, PHARMACODYNAMICS, AND LACK OF SYSTEMIC ABSORPTION OF SINGLE AND MULTIPLE ASCENDING DOSES IN HEALTHY VOLUNTEERS

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Background: Currently available therapies for gout in patients with advanced chronic kidney disease (CKD) are either dose-limited or contraindicated due to safety and tolerability concerns. In gout patients with advanced CKD, the intestinal tract becomes the major route of urate elimination, in contrast to healthy people with normal kidney function whose kidneys are the primary route of uric acid excretion. 1 Considering some of the limitations of present urate lowering thera-pies (ULTs) in gout & CKD and the extra-renal pathway of urate secretion, a new oral therapy with ALLN-346 (engineered urate oxidase) is under development as a non-absorbed, urate specific enzyme, designed to enhance degradation and secretion of urate in the intestinal tract. 2

Objectives: To assess safety and tolerability and evidence for the lack of systemic absorption at various dose levels of ALLN-346 in normal healthy volunteers (NHV) up to 7 days.

Methods: Two randomized, double-blind Phase 1 studies of ALLN-346 or placebo were conducted in adult NHV in a domicile setting; a single-ascending dose (SAD) study of 3 doses on a single day of dosing, and a multiple ascending dose (MAD) study of 2 doses during 7 days (NCT04236219 and NCT04829435, respectively). In the SAD study, subjects received 3 ascending doses of ALLN-346 in NHV up to 7 days.

Results: In both studies, all randomized subjects completed treatment with 100% compliance. ALLN-346 was well-tolerated, with no serious adverse