Conclusion: Response criteria are more discriminative than status criteria. ASDAS-CII and ASDAS-MI showed the best discrimination between treatment/placebo arms. Using the ASDAS-CII as primary outcome in future RCTs can reduce the number of patients needed to be included while keeping the same statistical power.

Table. Discriminative performances of response and status criteria in RCTs of biological and targeted synthetic DMARDs in axial spondyloarthritis

Minimum set of outcomes	Set 1: ASAS20,- 40,-PR, BASDAI50	Set 2: ASAS20,-40,- 5/6,-PR BASDAI50	Set 3: ASAS20,-40,- 5/6,-PR BASDAI50 ASDAS-CII, -MI, -ID	Set 4: All
N° of RCTs Total=16*	16	11	8	3
Descending X ² order	X ²	X ²	X ²	X ²
1	ASAS40 339	ASAS5/6 334	ASDAS-CII 309	ASDAS-CII 124
2	ASAS20 316	ASAS40 266	ASDAS-MI 253	ASDAS-MI 65
3	BASDAI50 297	ASAS20 254	ASAS40 169	ASAS5/6 48
4	ASAS-PR 146	BASDAI50 248	BASDAI50 163	BASDAI50 39
5	-	ASAS-PR 119	ASDAS-ID 117	ASAS40 34
6	-	-	ASAS20 98	ASDAS-LDA 27
7	-	-	ASAS-PR 80	ASAS-PR 22
8	-	-	-	ASAS20 21
9	-	-	-	ASDAS-ID 7

Legend. *total of 16 RCTs analysed, with different sets of RCTs within the 16 analysed based on the availability of response criteria; X²=Chi-square; RCTs=randomized controlled trials; BASDAI= Bath Ankylosing Spondylitis Disease Activity Index; ASAS= Assessment in SpondyloArthritis International Society; PR= partial remission; CII= clinically important improvement; MI= major improvement; LDA= low disease activity; ID= inactive disease

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New perspectives on therapeutic immune tolerance.

OP0316 EMERGING BEST-IN-CLASS IL-2 VARIANT HIGHLIGHTS TREG-DIRECTED THERAPY FOR AUTOIMMUNE DISEASE

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Background: Impairment or deficiency of regulatory T cells (Treg) is associated with chronic inflammation and autoimmune diseases. Interleukin 2 (IL-2) is a cytokine indispensable for Treg expansion and immunosuppressive function. However, expansion of cytotoxic effector T (Teff) and NK cells and the associated vascular leakage side effect limit the use of IL-2 in autoimmune diseases [1].

Objectives: Cugene developed a long-acting IL-2 variant with high Treg specificity and low toxicity to restore immune homeostasis and self-tolerance, and potentially cure autoimmune and inflammatory diseases.

Methods: IL-2 variants were generated based on the quaternary structure of IL-2 and IL-2Rαβ (alpha, beta, gamma) complex. Biological activity was determined by examining differential signaling activity in induction of STAT5 phosphorylation in defined lymphocyte populations of human PBMC using flow cytometry. Binding activity was evaluated by ELISA. Pharmacokinetics, pharmacodynamics, safety and tolerability were assessed in mice and cynomolgus monkeys. Treg suppressive function was determined *in vivo/ex vivo*, and anti-inflammatory and anti-antibody production efficacy were determined in delayed-type hypersensitivity (DTH) and T-cell-dependent antibody response (TDAR) models.

Results: Structure-based rational design and activity-guided fine-tuning generated an optimized IL-2 variant, CUG252. It demonstrated a strong and near wild-type IL-2 ability to stimulate STAT5 phosphorylation in IL-2Rαβ dominant Treg cells but abolished activities in IL-2Rβγ dominant effector CD4, CD8 and NK cells. This was a result of biased binding activity to IL-2Rα while dramatically

attenuated binding to IL-2Rβγ complex. In mice and monkeys, administration of CUG252 resulted in dose-dependent increases in Treg proliferation and expansion by more than 10- and 30-fold, respectively, with largely abolished activities in CD4+ T conventional, cytotoxic CD8+ Teff and NK cells. The ratio of Treg/Teff cells achieved was as high as 0.4 in mice and 1.2 in monkeys. Both CD4+ and CD8+ Tregs were expanded with preferential increases in memory over naïve subsets. A substantial increase in Treg-suppressive capacity over T effector cells was corroborated by enhanced expression of functional and inhibitory markers, including CD25, Foxp3, PD-1, CTLA-4, Tim3 and ICOS. In DTH and TDAR models, CUG252 strongly inhibited antigen-driven inflammation, B cell maturation, and antibody production. The sustained PK/PD profile supports monthly dosing or better in humans. CUG252 was well-tolerated and no changes in body weight, body temperature, clinical pathology or signs of vascular leakage were observed. Moreover, CUG252 demonstrated superior manufacturability.

Conclusion: CUG252 demonstrates an emerging best-in-class profile among IL-2 variants. It displayed exquisite Treg-selectivity while retaining potency comparable to wild-type IL-2. It showed strong anti-inflammatory and anti-antibody production efficacy with significantly improved therapeutic index and manufacturability. Its favorable drug-like property and robust preclinical efficacy warrant further evaluation in patients with a variety of inflammation and autoimmune diseases.

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Pathological calcification in rheumatic diseases

OP0317 ACCURACY OF THE OMERACT DEFINITIONS FOR IDENTIFICATION OF CALCIUM PYROPHOSPHATE CRYSTALS WITH ULTRASOUND: FINAL RESULTS OF THE OMERACT US IN CPPD SUB-TASK FORCE STUDY

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Background: The OMERACT Ultrasound (US) in calcium pyrophosphate deposition disease (CPPD) sub-task force has been working on the use of US in CPPD since 2014 first creating definitions for CPPD identification and then assessing the reliability[1].

Objectives: Objective of this study is to assess the diagnostic accuracy (truth) of US in CPPD.

Methods: Consecutive patients waiting to undergo knee replacement surgery due to osteoarthritis were enrolled in 12 centres from 6 countries. Each patient underwent US examination of the knee, focusing on the menisci and the hyaline cartilage, the day prior to surgery, scoring each site for presence/absence of CPP as defined previously[1]. After surgery, the menisci and the condyles were retrieved and examined microscopically. Six samples were collected, both from the surface and from the internal part of menisci and cartilage trying to cover a large part of it. All slides were observed under transmitted light microscopy and by compensated polarised microscopy. A dichotomous score was given for the presence/absence of CPP. US and microscopic analysis were performed by different operators, blind to each other's findings.

Sensitivity and specificity of US were calculated using microscopic findings as the gold standard.

Results: 101 patients have been enrolled in the study. 33 patients have been excluded due to loss of anatomical pieces at surgery. The mean age of the remaining 68 pts was 71yo (± 8), 44 women, 34 were affected by CPPD according to microscopy. Overall and per site diagnostic US accuracy results are presented in table 1

	Diagnostic accuracy	Sensitivity	Specificity	Positive Predictive value	Negative Predictive value
Global	0.75	0.91	0.59	0.69	0.87
Medial meniscus	0.82	0.87	0.77	0.77	0.87
Lateral meniscus	0.75	0.83	0.68	0.68	0.83
Medial cartilage	0.86	0.79	0.92	0.88	0.85
Lateral cartilage	0.82	0.71	0.88	0.77	0.84
Medial side (combined cartilage and meniscus)	0.82	0.88	0.76	0.79	0.87
Lateral side (combined cartilage and meniscus)	0.78	0.88	0.69	0.73	0.86

Conclusion: Our results demonstrate that US is an accurate exam for identification of CPPD. The best combination of sensitivity and specificity is achieved by examining the medial aspect of the knee.

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OP0318

THE ROLE OF DUAL ENERGY COMPUTED TOMOGRAPHY (DECT) IN THE DIFFERENTIATION OF GOUT AND CALCIUM PYROPHOSPHATE DEPOSITION DISEASE

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Background: Differentiation of gout and calcium pyrophosphate deposition disease (CPPD) is sometimes difficult as patients often present with a similar clinical picture. Arthrocentesis and subsequent polarization microscopy (PM) remains the gold standard but novel diagnostic approaches such as non-invasive dual

energy computed tomography (DECT) have recently been validated for gout. Currently, limited data is available on DECT in patients with CPPD.

Objectives: To analyse the diagnostic impact of DECT in gout and CPPD when compared to the gold standard of PM. We further compared the results of PM to ultrasound (US), conventional radiographs (CR), and suspected clinical diagnosis (SCD). Additionally, 15 laboratory parameters were analysed.

Methods: Twenty-six patients diagnosed with gout (n = 18) or CPPD (n = 8) who received a DECT and underwent arthrocentesis were included. Two independent readers assessed colour coded, as well as 80 and 120 kV DECT images for signs of monosodium urate (MSU) crystals or CPP deposition. US and CR from the patient's initial visit along with the SCD were also compared to PM. US examinations were performed by certified musculoskeletal ultrasound specialists. The association of up to 15 laboratory parameters such as uric acid, thyroid stimulating hormone, and C-reactive protein (CRP) with the PM results was analysed. **Results:** Sensitivity of DECT for gout was 67% (95% CI 0.41-0.87) with a specificity of 88% (95% CI 0.47-1.0). Concerning CPPD, the sensitivity and specificity of DECT was 63% (95% CI 0.25-0.91) and 83% (95% CI 0.59-0.96) respectively. US had the highest sensitivity of 89% (95% CI 0.65-0.99) with a specificity of 75% (95% CI 0.35-0.97) for gout, while the sensitivity and specificity for CPPD were 88% (95% CI 0.47-1.0) and 89% (95% CI 0.65-0.99) respectively. The SCD had the second highest sensitivity for gout at 78% (95% CI 0.52-0.94) with a comparable sensitivity of 63% (95% CI 0.25-0.92) for CPPD. Uric acid levels were elevated in 33% of gout patients and 25% of CPPD patients. While elevated CRP levels were observed in 59% of gout patients and in 88% of CPPD patients, none of the 15 analysed laboratory parameters were found to be significantly linked.

Conclusion: DECT provides a non-invasive diagnostic tool for gout but might have a lower sensitivity than suggested by previous studies (67% vs 90%). DECT sensitivity for CPPD was 63% (95% CI 0.25-0.91) in a sample group of eight patients. Both US and the SCD had higher sensitivities than DECT for gout and CPPD. Further studies with larger patient cohorts are needed in order to determine the diagnostic utility of DECT in CPPD.

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OP0319-PARE SEE ME HEAR ME: AN ANCA-ASSOCIATED VASCULITIS PATIENT CO-CREATION INITIATIVE

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Background: ANCA-associated Vasculitis (AAV) is a rare, severe small vessel vasculitis that affects multiple organs with a high acute mortality risk. As every patient presents differently, diagnosis is often delayed. Although treatments exist, responses vary, and remission is often not achieved or sustained. From the time of initial diagnosis onwards, patients suffer from an impaired quality of life. Coping with pain, fatigue, ongoing symptoms and combating challenges becomes a complex task and patients may be challenged in how best to communicate these emotions with health care professionals. We aimed to develop an initiative with Art and Voice, that would seek to empower people living with AAV and their carers in feeling understood, seen and heard in a meaningful way. This would invite a collective understanding of 'how people make sense of key life experiences and what it means to them' by creating a common language to address poorly addressed issues.

Objectives: This project aims to provide a voice to patients to express personal experiences and complexity of everyday living and empower people to feel in control of their own health through an online platform. It should also allow practitioners to gain new awareness about issues faced by their patients, to better understand the relationships between caring and curing, hearing and listening.

Methods: We collaborated with 10 patient association groups representatives, 17 AAV patients and 9 of their carers across 7 European countries. A series of workshops were set up to discuss issues faced and aid the subsequent production of a range of materials designed to provide clear, comprehensive content that would help individuals cope with the physical and emotional impact of AAV from diagnosis to living with it. This work was supported by a digital artist who is a rheumatologist living with vasculitis.

Results: The co-creation of patient information materials featuring real life patients was successful and led to the development of a creative initiative called SEE ME.HEAR ME with an online platform www.myancavasculitis.com. This includes: (1) an awareness programme featuring artwork created by the digital artist and advised by the patients which captures the essence of AAV from the patients view (see Figure). (2) a series of first-hand patient and carer stories capturing their authentic voice on 'what it is like to live with the disease'. (3) extensive