Objectives: We attempted to identify specific biomarkers to distinguish AOSD from sepsis.

Methods: We measured serum levels of 45 cytokines in 66 AOSD patients, 17 sepsis patients and 133 age-matched controls by multi-suspension cytokine array. Japan College of Rheumatology-certified rheumatologists diagnosed with AOSD based on the Yamaguchi criteria. Cytokines were ranked by their importance by a multivariate classification algorithm. We performed a logistic regression analysis to determine specific biomarkers for discriminating AOSD from sepsis patients. To identify specific molecular networks, we performed a cluster analysis of each cytokine.

Results: Serum fibroblast growth factor 2 (FGF-2), vascular endothelial growth factor (VEGF), granulocyte-colony stimulating factor (G-CSF), and IL-18 levels were significantly elevated in the AOSD group versus the sepsis group. Multivariate classification algorithms followed by a logistic regression analysis revealed that the measurement FGF-2 distinguished AOSD patients from sepsis patients with the highest accuracy (cut-off value=28.5 pg/mL, sensitivity 100%, specificity 88.2%, accuracy 96.7%).

Abstract OP0084 – Table 1

variables (AOSD vs sepsis)	sensitivity	specificity	accuracy	AUC	AIC
FGF-2	1.000	0.882	0.967	0.972	24.50
IL-18	0.930	0.824	0.900	0.895	50.90
G-CSF	0.837	0.706	0.800	0.721	75.30
FGF-2 + IL-18	0.977	0.941	0.967	0.986	21.70

Conclusions: We have demonstrated that FGF-2 can be the best biomarker for differential diagnosis between AOSD and sepsis based on the measurement of multiple cytokines. Although the differential diagnosis between rheumatic diseases and infectious conditions is a great challenge in clinical practice, these findings help to improve the diagnostic performance of AOSD in daily practice.

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OP0085

SAFETY OF LONG-TERM (UP TO 6 YEARS) CANAKINUMAB THERAPY (<2, 2–<4 AND 4–<8MG/KG) IN PATIENTS AGED <4 TO 65 YEARS FROM BETA-CONFIDENT REGISTRY

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Background: The β -confident registry (NCT01213641), a multicenter, long-term (6 years; yrs), prospective, observational study has demonstrated the safety and effectiveness of canakinumab (CAN) in real life CAPS patients (pts) according to their phenotypes.¹ Here we report long-term safety of CAN in pts with CAPS and other autoinflammatory syndromes, enrolled in the β -confident registry, according to their age and dose administered.

Objectives: To monitor the long-term safety of different CAN doses (<2, 2–<4 and 4–<8 mg/kg) across different age groups (<4 to 65 years) in pts with CAPS and other autoinflammatory syndromes.

Methods: Cumulative safety data were reported as exposure adjusted incidence rate per 100 pt-years (IR/pyr) from the enrollment of the first pt (November 2009) until end of study (December 2015). Pts were followed up for at least 1 year. The protocol did not mandate any visits or procedures. All observed and reported AEs and SAEs were recorded for the following age groups:<4-, 4–<12-, 12–<18-, 18–<65 and $\geq$ 65 years.

Results: Of the 285 pts enrolled, 21% (n=60) discontinued the study mainly due to loss of follow-up (35%, n=21) followed by AEs (10%, n=6), poor efficacy (8%, n=5) and pt preference (3%, n=2). In total, 1114 AEs and 155 SAEs were reported in 223 pts (110.7 IR/100 pyr) and 83 pts (15.4 IR/100 pyr), respectively. Exposure adjusted incidence rate of AEs (IR/100 pyr) among pts in the <4 and 4–<12 year age group, were lowest in the pts who received <2 mg/kg dose (130.3 and 59.7, respectively) compared to pts who received 2–<4 mg/kg (450.8 and 169.6, respectively) and 4–<8 mg/kg (121.5 and 90.0, respectively) CAN dose. In pts

aged 12–<18 years, IR/100 pyr were lowest in pts who received 2–<4 mg/kg dose (118.2) compared to pts who received <2 mg/kg (169.6) and 4–<8 mg/kg (139.4) CAN dose. Similarly, in the 18–<65 year age group, IR/100 pyr were lowest in pts who received <2 mg/kg dose (93.1) compared to pts who received 2–<4 mg/kg (100.7) and 4–<8 mg/kg (154.4) CAN dose. In the $\geq$ 65 year age group, IR/100 pyr decreased with increase in dose (<2 mg/kg: 26, 2–<4 mg/kg: 17). Overall, 5, 13, 19, 84 and 7 SAEs were reported in <4-, 4–<12-, 12–<18-, 18–<65 and $\geq$ 65 year age groups, respectively. One death (metastatic rectal adenocarcinoma in a 76-yr-old MWS patient) was reported.

Conclusions: The β -confident registry is the largest CAPS cohort documented in a registry. In general, incidence of adverse events in each dose group increased with age (<4–<65 years). However, no meaningful pattern of AEs was observed with increased dose for each age group. Long-term treatment with canakinumab demonstrated favourable safety profile which was similar to that reported earlier² and is well tolerated in CAPS patients aged <4 to 65 years.

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OP0086

LONG-TERM EFFICACY AND SAFETY OF ADALIMUMAB BY IMMUNOSUPPRESSANT USE IN PATIENTS WITH NON-INFECTIOUS UVEITIS IN THE VISUAL III TRIAL

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Objectives: To evaluate the long-term safety and efficacy of adalimumab in patients with non-infectious intermediate, posterior, or panuveitis, by immunosuppressant (IMM) use.

Methods: Adult patients who completed or had a treatment failure in the VISUAL I/II trials were eligible to enter the Phase III open-label extension study, VISUAL III. Patients received adalimumab 40 mg every other week in VISUAL III, and interim follow-up data were collected through Weeks 0 to 78. Efficacy measures assessed included proportion of patients with: no active inflammatory lesions in both eyes; anterior chamber (AC) cell grade $\leq$ 0.5 + in both eyes; vitreous haze (VH) grade $\leq$ 0.5 + in both eyes; quiescence (defined as no active inflammatory lesions AND AC cell grade $\leq$ 0.5 + AND VH grade $\leq$ 0.5+); and steroid-free quiescence. Mean steroid dose and mean best corrected visual acuity (BCVA) were also assessed. Missing data were imputed using non-responder imputation for categorical endpoints, last observation carried forward for continuous variables, and as-observed for steroid dose. Efficacy was analysed by IMM (methotrexate, cyclosporine, mycophenolate mofetil, or azathioprine) use. Adverse events (AEs) were reported from first adalimumab dose in VISUAL III through interim cut-off date of Oct 31, 2016, with analysis by IMM use.

Results: Of 371 patients included in the intent-to-treat analysis, 117 (31.5%) were using IMM at VISUAL III baseline (BL) and 30 (8.1%) started IMM during VISUAL III. The proportion of patients with quiescence improved over time irrespective of IMM use; compared with Week 0, 95% confidence intervals were non-overlapping at most time points (figure 1). Numeric improvements were achieved in steroid-free quiescence, steroid dose reduction, and BCVA, with no difference by IMM use. No new safety signals were detected through 130 weeks of treatment and AE rates were generally consistent with previous VISUAL trials; some AEs, notably serious infections and malignancies, were slightly higher with concomitant IMM use.

Abstract OP0086 – Figure 1. proportion of patients in quiescence by IMM use in VISUAL III

Conclusions: Exploratory analyses from the VISUAL III trial demonstrated that efficacy in adalimumab-treated patients was sustained or improved through 78 weeks of treatment, irrespective of IMM use. AE rates were consistent with previous VISUAL trials, although numerically higher rates for a subset of AEs were observed in patients taking IMM.

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OP0087

INCREASED RISK OF ISCHAEMIC HEART DISEASE AND MORTALITY AMONG FMF PATIENTS – PERSPECTIVE FROM A BIG DATABASE

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Background: Familial Mediterranean fever (FMF) is a systemic autoinflammatory monogenic disease. It has been previously reported that FMF patients are prone to develop ischaemic heart disease (IHD),^{1,2} mostly due to increased inflammatory activity and endothelial dysfunction.^{3,4} However, large-scale information regarding the extent and prognosis of IHD among FMF patients is lacking.

Objectives: To check whether an association exists between FMF and IHD, and to assess the long-term prognostic significance of IHD among FMF patients using a big data registry with a 15 year follow-up period.

Methods: Utilising the medical records of Clalit Health Services, the largest HMO in Israel, we extracted a cohort of FMF patients along with their age-and-sex matched controls. Dates of registration in the medical records of FMF, IHD and death, as well as anthropometric information and medical comorbidities were extracted from the database. To compare the distribution of variables across the cohort strata, univariate analysis was performed using Chi-square and student t-test. Multivariate analysis using a logistic regression model was used to find variables associated with IHD. Survival analysis using Cox proportional hazards method and a log-rank test was performed to find variables associated with increased risk of all-cause mortality.

Results: The cohort included 7,670 FMF patients and 7670 age-and-sex matched controls. The mean age of both groups was 39.1, and both consisted 50.1% females. IHD was observed among 491 FMF patients (6.4%) vs 375 controls (4.89%), $p < 0.001$. In multivariate logistic regression, FMF was found to be

independently associated with a diagnosis of IHD (OR 1.44, 95% CI: 1.21 to 1.72). After over 15 years of follow-up, 345 (4.5%) of FMF patients had died, compared to 271 (3.53%) of the controls ($p < 0.001$). In multivariate survival analysis, both FMF and IHD were found to be significantly associated with increased risk to all-cause mortality (HR 1.29, 95% CI: 1.10 to 1.53 and HR 1.57, 95% CI: 1.29 to 1.9, respectively).

Conclusions: IHD is associated with worse prognosis among FMF patients compared to controls. Proper screening methods are recommended to assess whether early identification and treatment may improve life expectancy.

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OP0088

IMMUNE-RELATED ADVERSE EVENTS OF CANCER IMMUNOTHERAPY – WHEN INFLAMMATORY SIDE EFFECTS ARE ASSOCIATED WITH SURVIVAL: A SINGLE-CENTRE PROSPECTIVE COHORT STUDY

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Background: Immune checkpoint inhibitors (ICI) represent a new standard of care for the treatment of selected advanced cancers and are still being investigated in many other tumour types. By enhancing the T-cell activation, a unique spectrum of inflammatory side effects has emerged, also known as immune-related adverse events (irAEs), including various well-described rheumatic manifestations. Data regarding the association between irAEs and patient outcomes are conflicting.

Objectives: To evaluate the incidence and characteristics of irAEs in patients receiving ICI, as well as the correlation with tumour response and patient survival.

Methods: This was a single-centre prospective observational study including all cancer patients receiving ICIs. The occurrence of irAEs, tumour response and patient outcomes were assessed on a regular basis. Overall survival has been considered from the start of ICI.

Results: From May 2015 to September 2017, 636 patients (70% male, mean age 64 years) have been included in this cohort while receiving anti PD-1 (n=435), anti PD-L1 (n=66) or anti CTLA-4 (n=3) as single agent or as sequential (n=100) or combined (n=32) therapies. Cancer types were mainly melanoma (n=293), non-small cell lung cancer (n=150) and renal carcinoma (n=83). Overall, 274/633 patients (43%) experienced irAEs, either 1 irAE (n=162), 2 irAEs (n=78) or ≥ 3 irAEs (n=34), with a median exposure time of 52 days³⁰⁻⁹¹ for the first irAE. Dermatological irAEs were by far the most frequent (n=160), followed by digestive