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 cytokokine.

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 measurements 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%).

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.

REFERENCES:

Disclosure of Interest: None declared

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


Background: The β-concordant 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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REFERENCE:

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LONG-TERM EFFICACY AND SAFETY OF ADA LUMAB BY IMMUNOSUPPRESSIVE USE IN PATIENTS WITH NON-INFECTIONOUS UVEITIS IN THE VISUAL III TRIAL

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Background: AOSD andother autoinflammatory syndromes, enrolled in the β-concordant 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-concordant registry, according to their age and dose administered.

Objectives: To monitor the long-term safety of different CAN doses (<2, 2–<4 and 4–<8mg/kg) among 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 ≥65 years.

Results: Of the 265 pts enrolled, 21% (n=56) 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 (54.4 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 186.9, 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 >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 ≥65 year age groups, respectively. One death (metastatic rectal adenocarcinoma in a 76-year-old MWS patient) was reported.

Conclusions: Of the 265 pts enrolled, 21% (n=56) 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 (54.4 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 186.9, 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 >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 ≥65 year age groups, respectively. One death (metastatic rectal adenocarcinoma in a 76-year-old MWS patient) was reported.
Conclusions: Exploratory analyses from the VISUAL III trial demonstrated that efficacy in adalimumab-treated patients was sustained or improved through 78 weeks of VISUAL III trials, 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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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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Disclosure of Interest: None declared


OP0086 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), mostly due to increased inflammatory activity and endothelial dysfunction. 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 cancer 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 ICI. 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=435), 2 irAEs (n=78) or ≥3 irAEs (n=6), with a median exposure time of 52 days for the first irAE. Dermatological irAEs were by far the most frequent (n=160), followed by digestive...