OP0062 ASSESSMENT OF BIOTHERAPIES' EFFICACY IN BLAU SYNDROME: DATA FROM AN INTERNATIONAL RETROSPECTIVE COHORT OF 23 CASES

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Background: Blau Syndrome (BS) is a rare autosomal dominant inflammatory disease characterized by early-onset granulomatous arthritis, dermatitis and recurrent uveitis (1). Mutations in the nucleotide-binding domain (NBD) of *CARD15/NOD2* gene (mainly R334W, R334Q and L469F) have been identified in Blau syndrome (2). Despite advances in BS knowledge, patients' functional prognosis remains uncertain, BS potentially leading to visual impairment or joint deformities. Optimal treatments have not been determinated yet.
Objectives: To assess the efficacy of several biologic agents in this affection
Methods: We conduct an observational, international, retrospective cohort of BS collecting clinical, biological and histological data.
Results: Among the twenty-three patients included in the cohort, 14 patients were treated by one or several lines of biologic agents, mostly by TNF blockers (80%), IL1 blockers (16%) or treatment targeting CTLA-4 (4%). Fifty-seven percent of patients achieved remission after almost two lines of treatment (1.75 lines; [0.8–2.7]). Association with csDMARDs did not significantly improved response to biologics. Considering the 3 mains symptoms independently, TNF blockers were associated with a better response in case of articular or skin features but less effective in case of ocular involvement, a clinical situation in which IL-1 targeting should be preferentially chosen.
Conclusions: Biologic treatments appeared to be effective in BS but additional data prospectively collected are still needed in order to define their place in the therapeutic strategy in order to minimize functional consequences.
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OP0063 CANAKINUMAB TREATMENT IN PATIENTS WITH COLCHICINE-RESISTANT FMF (CRFMF), HIDS/MKD AND TRAPS: EFFICACY IN THE 16 WEEKS RANDOMISED CONTROLLED PHASE AND MAINTENANCE OF DISEASE CONTROL AND SAFETY AT WEEK 40

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Background: Canakinumab (CAN) is a fully human monoclonal antibody targeting IL-1β, a key cytokine in the pathogenesis of periodic fever syndromes (PFS) including familial Mediterranean fever (FMF), hyper-IgD syndrome/mevalonate kinase deficiency (HIDS/MKD) and TNF receptor-associated periodic syndrome (TRAPS).
Objectives: The CLUSTER trial (NCT02059291) studied efficacy and safety of CAN in crFMF, HIDS/MKD and TRAPS. The primary objective was to demonstrate that CAN150 mg every 4 weeks (q4w) is superior to placebo (PBO) in resolving the flare by Day 15 with no new flares over 16 weeks (wks). Secondary objectives included the proportion of patients (pts) who maintained optimal control of disease activity (absence of new flares) between Wk 16 and Wk 40 after dose reduction.
Methods: The study comprised 4 epochs (E1-E4).[1] After lead-in E1, in E2 patients at time of an active fever flare were randomised to CAN 150mg q4w or PBO for 16 wks. Responders in E2 were re-randomised to PBO or 150 mg q8w for 24 wks. During E3, pts who escaped to open-label CAN in E2, were similarly down-titrated to open-label CAN q8w to gain additional information on the long-term maintenance dose. In pts with a flare, dose could be escalated up to 300 mg q4w. Safety assessments included adverse events (AEs) and serious AEs.
Results: The proportion of responders at Wk 16 was statistically higher with CAN vs PBO (Table). In E3, among the 41 re-randomised pts (PBO vs CAN 150 mg q8w) the proportion of pts who did not present new flares was numerically higher in the CAN vs PBO group (Table). Overall at Wk 40 (end of E3), including re-randomised pts and pts treated in open-label, 46% of the crFMF pts, 53% of the TRAPS pts and 23% of the HIDS/MKD pts maintained disease control with 150 mg q8w. Conversely, up-titration to 300 mg q4w was required in 28.8% of HIDS/MKD pts, and in 10.2% and 8.3% of pts with crFMF and TRAPS, respectively. In E3, the majority of pts who received CAN had PGA <2, normal CRP and SAA levels in all 3 cohorts. No new safety findings nor death were reported in CAN-treated pts through E3 (Table).

Table. Efficacy results and summary of safety

Efficacy

	Cohort	CAN 150 mg q4w N=90	PBO N=91	OR (95% CI)	p-value
Proportion of responders at Week 16 (E2), n/m (%)	crFMF	19/31 (61.3)	2/32 (6.3)	23.8 (4.4, 227.5)	<0.0001*
	HIDS/MKD	13/37 (35.1)	2/35 (5.7)	8.9 (1.7, 86.4)	<0.002*
	TRAPS	10/22 (45.5)	2/24 (8.3)	9.2 (1.5, 94.6)	0.005*
	Cohort	CAN 150 mg q8w N=19	PBO N=22	OR (95% CI)	p-value
Proportion of pts with no new flare at Week 40 (E3), n/m (%)	crFMF	7/9 (77.8)	3/10 (30.0)	8.2 (0.8, 113.4)	0.0513
	HIDS/MKD	3/6 (50.0)	1/7 (14.3)	6.0 (0.3, 366.2)	0.2168
	TRAPS	3/4 (75.0)	2/5 (40.0)	4.5 (0.15, 313.5)	0.3571

Safety: Summary of AEs and SAEs

	All	crFMF		HIDS/MKD		TRAPS	
	PBO N=24	Any CAN* E2 N=58	Any CAN* E2+E3 N=61	Any CAN* E2 N=68	Any CAN* E2+E3 N=71	Any CAN* E2 N=43	Any CAN* E2+E3 N=61
Exposure to CAN, PY	2.0	16.4	45.6	19.1	51.0	12.1	39.2
Number of AEs	34	134	332	251	613	112	265
AE rate/100 PY	1698.8	816.7	728.2	1313.6	1201.2	925.7	676.2
Number of SAEs	1	7	17	11	20	3	5
SAE rate/ 100 PY	50.0	42.7	37.3	57.6	39.2	24.8	12.8

*Indicates statistical significance (one-sided) at the 0.025 level. *Any patient who received a dose of CAN during E2 or 3. n=number of patients who responded; m=number of patients evaluated for response; AE, adverse event; CAN, canakinumab; CI, confidence interval; E, epoch; OR, odds ratio; PBO, placebo; PY, patient-years; q4w, every 4 weeks; q8w, every 8 weeks; SAE, serious adverse event

Conclusions: Canakinumab (150 mg q4w) was efficacious in resolving flare at Day 15 and preventing new flares over 16 wks. In the longer term (40 wks), absence of flares was maintained in more than half patients at the extended dosing interval (150 mg q8w) in the crFMF and TRAPS cohorts. A higher dose was needed in HIDS/MKD patients. No unexpected safety issues were reported over 40 wks of canakinumab treatment.
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