ministered at 4 mg/kg every 4 weeks (wk). Efficacy parameters (adapted ACR [aACR] paediatric responses, juvenile idiopathic arthritis [JIA] ACR responses, pts with inactive disease), CRP levels over 12 wk and safety were assessed by age grp. One study [NCT00426218] was excluded for efficacy outcomes.
Results: 216 children (2–<12 years [y]), 56 adolescents (12–<16 y) and 29 adults (≥16 y) were analysed for efficacy outcomes. The efficacy parameters across the 3 age grps were largely comparable (Table 1). The safety profile of CAN was similar across age grps (Table 2). One death was reported (adolescents grp). Clinical, laboratory and immunogenicity data showed no notable differences between the age grps.

Table 1. Responses by age grp and time point

Age group	%	aACR paediatric; n/N (%)		JIA ACR; n/N (%)	
		Day 15	Day 85	Day 15	Day 85
Children	≥30	158/216 (73.1)	90/133 (67.7)	169/216 (78.2	93/133 (69.9)
	≥70	109/216 (50.5)	77/133 (57.9)	111/216 (51.4)	77/133 (57.9)
	≥100	46/216 (21.3)	42/133 (31.6)	47/216 (21.8)	42/133 (31.6)
Adolescents	≥30	47/56 (83.9)	20/27 (74.1)	47/56 (83.9)	20/27 (74.1)
	≥70	33/56 (58.9)	18/27 (66.7)	33/56 (58.9)	18/27 (66.7)
	≥100	15/56 (26.8)	8/27 (29.6)	15/56 (26.8)	8/27 (29.6)
Adults	≥30	25/29 (86.2)	15/18 (83.3)	25/29 (86.2)	15/18 (83.3)
	≥70	19/29 (65.5)	13/18 (72.2)	19/29 (65.5)	12/18 (66.7)
	≥100	4/29 (13.8)	4/29 (13.8)	4/18 (22.2)	4/18 (22.2)

Age group	Inactive disease; n/N (%)		CRP, median; mg/L (n/N)	
	Day 15	Day 85	Day 15	Day 85
Children	40/216 (18.5)	32/133 (24.1)	12.00 (211/216)	9.75 (168/216)
Adolescents	18/56 (32.1)	10/27 (37.0)	10.00 (55/56)	8.40 (45/56)
Adults	6/29 (20.7)	8/18 (44.4)	4.50 (26/29)	7.80 (23/29)

Table 2. Adverse events (AEs)

	Children, n (%) N = 233	**Adolescents**, n (%) N = 60	**Adults**, n (%) N = 31
AEs (at least 1)	202 (86.7)	53 (88.3)	27 (87.1)
AEs leading to study drug discontinuation	26 (11.2)	10 (16.7)	6 (19.4)
AEs most common/special interest			
Infections and infestations	176 (75.5)	42 (70.0)	23 (74.2)
Gastrointestinal disorders	122 (52.4)	32 (53.3)	18 (58.1)
Musculoskeletal and connective tissue disorders	119 (51.1)	33 (55.0)	16 (51.6)
Opportunistic infections	3 (1.3)	4 (6.7)	1 (3.3)
Neutropenia	11 (4.7)	2 (3.3)	0
SAE (at least 1)	81 (34.8)	25 (41.7)	9 (29.0)

Conclusions: Pooled analyses indicate similar efficacy of CAN across all the age grps of children, adolescents and adult SJIA pts. There were no meaningful differences in safety profiles across the different age grp. These analyses suggest similar efficacy of CAN in AOSD pts as observed in the SJIA pts.
References:
[1] Jamilloux. Immunol Res 2015;61:53–62.
[2] Nirmala. Pediatric Rheumatol 2015;13:50.
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THU0503 IDENTIFICATION OF OPTIMAL SUBCUTANEOUS (SC) DOSES OF TOCILIZUMAB IN CHILDREN WITH POLYARTICULAR-COURSE JUVENILE IDIOPATHIC ARTHRITIS (PCJIA)

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Background: Efficacy and safety of intravenous (IV) tocilizumab (TCZ) have been shown in patients (pts) with pcJIA.[1]
Objectives: Determine appropriate dosing regimens of SC TCZ in pcJIA.
Methods: Pts were aged 1–17 y with pcJIA, inadequate response/intolerance to MTX and TCZ-naive or receiving TCZ IV with adequate disease control. TCZ SC was administered open label by body weight (BW)–based dosing modeled on IV dosing in pcJIA and SC dosing in adult rheumatoid arthritis: pcJIA pts <30kg received TCZ 162mg every 3 wks (Q3W) and pts ≥30kg received TCZ 162mg Q2W for 52 wks. Safety, efficacy (exploratory) and model-computed pharmacokinetic (PK) and pharmacodynamic (PD) parameters were assessed.
Results: 52 pts were enrolled; 27 <30kg and 25 ≥30kg BW; 85% and 56% were TCZ naive. Since no notable difference in steady state PK occurred in naive vs non-naive pts, pooled data are shown. Median C_{min} was similar between BW groups and higher than with TCZ IV (TCZ IV median C_{min}: 3.2 μg/mL for 10mg/kg <30kg BW and 7.3 μg/mL for 8mg/kg ≥30kg BW) ensuring adequate exposure from SC doses. Median C_{max} was lower from SC than IV dosing. Changes in PD parameters for TCZ-naive pts were consistent with those for TCZ IV. JADAS-71 generally improved (Table), with trends consistent with those for TCZ IV. Infections were the most frequent adverse event (AE), reported in 36 pts; 2 serious infections occurred in 1 pt. Injection site reactions occurred in 15% pts in the <30kg group and 44% pts in the ≥30kg group. The most common symptoms were erythema, swelling, hematoma, pain and pruritus. No serious hypersensitivity, AE leading to withdrawal, opportunistic infection, serious hepatic AE or death occurred. Overall there were 4 serious AEs in 3 pts (7.9/100 pt-y, consistent with that for TCZ IV).

	TCZ 162mg SC Q3W, BW <30kg (n=27)	TCZ 162mg SC Q2W, BW ≥30kg (n=25)
Model-computed steady state PK parameters, median [range]		
C_{min}, μg/mL	13.4 [0.2, 52.3]	12.7 [0.2, 23.8]
C_{max}, μg/mL	62.4 [39.4, 121.1]	29.7 [7.6, 50.3]
$AUC_{12weeks}$, μg/mL×day	2998 [1465, 7708]	1933 [324, 3098]
Change from baseline to week 52[a] in PD markers and efficacy, median [range]; TCZ-naive pts		
IL-6, pg/mL	27.3 [3.5, 173.9], n=11	12.2 [–6.2, 30.9], n=9
sIL-6R, ng/mL	612.1 [399.4, 808.4], n=14	429.3 [245.5, 585.6], n=11
CRP, mg/L	–1.3 [–17.0, 0.5], n=21	–0.8 [–22.9, 0.0], n=12
ESR, mm/h	–11.0 [–40.0, 0.0], n=21	–6.0 [–35.0, 0.0], n=12
JADAS-71	–16.8 [–40.3, –4.4], n=21	–12.9 [–48.1, –2.3], n=12

[a]Week 51 for Q3W group. AUC, area under the concentration curve; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; IL-6, interleukin-6; sIL-6R, soluble IL-6 receptor.

Conclusions: The BW-based TCZ SC dosing regimens for pcJIA provided adequate exposure to support efficacy comparable to that for TCZ IV, with an acceptable benefit-risk profile.
References:
[1] Brunner HI et al. Ann Rheum Dis 2014;74:1110–7.
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