

Supplementary Information

Supplementary Table 1 Changes in secondary efficacy indicators from baseline in placebo and ZSP1601 treatment groups

		Pooled placebo	ZSP1601		
		(N=9)	50 mg QD(N=9)	50 mg BID(N=9)	100 mg BID(N=9)
Lipids	LSmean (95%CI)	1.09(-0.60 to 2.78)	-0.18(-1.85 to 1.49)	-0.81(-2.25 to 0.62)	-0.29(-2.21 to 1.64)
	TG, mmol/L				
	LSmean difference(95%CI)	-	-1.27(-3.38 to 0.84)	-1.90(-4.15 to 0.35)	-1.38(-3.62 to 0.87)
	P value	-	0.3731	0.1216	0.3574
	TC, mmol/L				
	LSmean (95%CI)	-0.18(-0.63 to 0.27)	-0.34(-0.81 to 0.12)	-0.69(-1.09 to -0.28)	-0.69(-1.17 to -0.21)
	LSmean difference (95%CI)	-	-0.16(-0.75 to 0.42)	-0.51(-1.13 to 0.11)	-0.51(-1.10 to 0.08)
	P value	-	0.8711	0.1403	0.1101
	LDL-C, mmol/L				
	LSmean (95%CI)	-0.19(-0.63 to 0.25)	0.16(-0.31 to 0.63)	-0.43(-0.81 to -0.04)	-0.27(-0.74 to 0.19)
	LSmean difference (95%CI)	-	0.35(-0.23 to 0.93)	-0.24(-0.84 to 0.36)	-0.09(-0.66 to 0.49)
	P value	-	0.3684	0.7016	0.9776
	HDL-C, mmol/L				
	LSmean (95%CI)	0.05(-0.12 to 0.21)	-0.07(-0.23 to 0.10)	0.01(-0.13 to 0.15)	0.06(-0.12 to 0.23)
	LSmean difference (95%CI)	-	-0.12(-0.33 to 0.09)	-0.04(-0.26 to 0.17)	0.01(-0.20 to 0.22)
P value	-	0.4303	0.9552	0.9992	
Blood glucose, mmol/L	LSmean (95%CI)	0.22(-0.41 to 0.86)	0.20(-0.44 to 0.83)	0.07(-0.49 to 0.62)	0.01(-0.67 to 0.68)
	LSmean difference (95%CI)	-	-0.03(-0.85 to 0.80)	-0.15(-1.02 to 0.71)	-0.22(-1.06 to 0.62)
	P value	-	0.9998	0.9610	0.8941
Blood insulin, µU/mL	LSmean (95%CI)	49.48(-32.70 to 131.66)	46.81(-35.35 to 128.97)	34.96(-37.00 to 106.92)	35.85(-51.14 to 122.85)
	LSmean difference (95%CI)	-	-2.67(-107.54 to 102.21)	-14.51(-124.34 to 95.31)	-13.62(-121.44 to 94.19)
	P value	-	0.9999	0.9837	0.9857
Non-invasive biomarkers	CAP*, dB/m				
	LSmean(95%CI)	22.94(-3.80 to 49.69)	6.24(-20.29 to 32.77)	6.95(-16.65 to 30.56)	-14.38(-43.80 to 15.03)
	LSmean difference(95%CI)	-	-16.71(-50.68 to 17.27)	-15.99(-51.12 to 19.13)	-37.33(-73.26 to -1.39)
P value	-	0.5446	0.6055	0.0395	
e biomarkers	LSmean(95%CI)	1.36(0.16 to 2.56)	0.94(-0.23 to 2.11)	1.42(0.29 to 2.55)	1.17(-0.14 to 2.47)
	LSM*, Kpa				
	LSmean difference(95%CI)	-	-0.42(-1.82 to 0.98)	0.06(-1.40 to 1.51)	-0.19(-1.67 to 1.28)
P value	-	0.8433	0.9996	0.9839	
FAST	LSmean(95%CI)	0.01(-0.10-0.12)	-0.12(-0.23 to -0.01)	-0.08(-0.17 to 0.02)	-0.19(-0.31 to -0.07)

		LSmean difference(95%CI)	-	-0.13(-0.27 to 0.01)	-0.09(-0.23 to 0.05)	-0.20(-0.35 to -0.06)
		P value	-	0.0642	0.3073	0.0037
		mean (SD)	-0.06(0.14)	-0.18(0.11)	-0.10(0.14)	-0.23(0.12)
		Difference between groups , P value	-	0.2106	0.8633	0.0379
		LSmean(95%CI)	-0.01(-0.24 to 0.23)	0.08(-0.15 to 0.30)	-0.04(-0.24 to 0.16)	-0.05(-0.29 to 0.19)
	FIB4	LSmean difference(95%CI)	-	0.08(-0.20 to 0.37)	-0.03(-0.32 to 0.26)	-0.04(-0.33 to 0.25)
		P value	-	0.8574	0.9926	0.9782
		LSmean(95%CI)	-0.02(-0.15 to 0.11)	-0.04(-0.17 to 0.09)	-0.10(-0.22 to 0.01)	-0.17(-0.31 to -0.03)
	APRI score	LSmean difference(95%CI)	-	-0.02(-0.19 to 0.15)	-0.08(-0.25 to 0.09)	-0.15(-0.32 to 0.03)
		P value	-	0.9894	0.6092	0.1238
		LSmean(95%CI)	-0.01(-0.15 to 0.12)	0.08(-0.05 to 0.21)	-0.01(-0.12 to 0.11)	0.00(-0.15 to 0.14)
	TNF- α , pg/mL	LSmean difference(95%CI)	-	0.09(-0.08 to 0.26)	0.01(-0.16 to 0.18)	0.01(-0.17 to 0.19)
		P value	-	0.4468	0.9988	0.9979
		LSmean(95%CI)	0.39(-1.30 to 2.08)	0.87(-0.70 to 2.44)	1.79(0.41 to 3.18)	1.05(-0.67 to 2.77)
	IL-6, pg/mL	LSmean difference(95%CI)	-	0.48(-1.66 to 2.62)	1.40(-0.74 to 3.54)	0.66(-1.41 to 2.73)
		P value	-	0.9288	0.3018	0.8220
	Inflammatory cytokines	LSmean(95%CI)	6.07(-30.13 to 42.28)	7.71(-24.03 to 39.44)	12.08(-15.82 to 39.99)	13.60(-24.24 to 51.43)
	IP-10, pg/mL	LSmean difference(95%CI)	-	1.63(-45.92 to 49.18)	6.01(-39.32 to 51.33)	7.52(-34.07 to 49.12)
		P value	-	0.9997	0.9836	0.9601
		LSmean(95%CI)	-479.64(-825.87 to -133.41)	-391.61(-750.58 to -32.65)	-410.13(-710.42 to -109.85)	-450.11(-821.55 to -78.67)
	CK-18, pg/mL	LSmean difference(95%CI)	-	88.02(-358.79 to 534.84)	69.50(-395.57 to 534.58)	29.53(-423.61 to 482.66)
		P value	-	0.9493	0.9768	0.9980
	Obesity parameters*	Bodyweight, kg	-1.53(1.39)	-0.80(0.97)	-1.26(0.86)	-1.29(1.31)
		BMI, kg/m ²	-0.53(0.48)	-0.27(0.36)	-0.46(0.34)	-0.44(0.49)
		Waist circumference, cm	-1.72(1.88)	-1.27(1.08)	-2.37(2.17)	-1.23(1.70)
		Abdominal circumference, cm	-2.29(2.16)	-1.56(1.39)	-1.71(1.25)	-1.23(1.54)

Note: *Number of subjects to CAP and LSM in ZSP1601 100 mg BID group was eight. Kruskal Wallis test was also used for FAST score. LS means of other indicators were obtained from an ANCOVA model with group as a fixed effect , and baseline values as covariates. Obesity parameters showed the absolute change from baseline. Bold fonts denoted statistically significant values. Statistical test used was two-sided.