

Supplemental Figure 1: Box plots of serum cortisol on study day 10 (white) and study day 40 (grey) prior to ACTH stimulation and 30 and 60 minutes after ACTH stimulation with 250 mg IM of ACTH in the men randomly assigned to receive 800 mg of ketoconazole daily between study day 3 and study day 10 (n=8). *p<0.05 compared to baseline and day 10. The dotted line represents the generally accepted threshold for the diagnosis of adrenal insufficiency after ACTH stimulation is given intramuscularly. Min=minutes after ACTH stimulation.

Supplemental Figure 2A-B: Serum gonadotropins at baseline, 48 hours after acyline administration (day 3) and one week after oral medication administration (day 10) by treatment group. Dashed lines represent the lower end of the normal reference range. Pla=placebo; K400=ketoconazole 400mg; K800=ketoconazole 800mg; Dut=dutasteride 2.5mg; Ana=anastrozole 1mg.

*p<0.05 for all treatment groups compared to baseline

** p<0.05 compared to day 3

† p<0.05 for all treatment groups compared to day 3

‡ p<0.05 for ketoconazole groups compared to the Acyline + Pla and Acyline + Ana groups at day 10

Supplemental Figure 3A-B: Box and whiskers plots of serum androstenedione (A) and serum dehydroepiandrosterone (DHEA) (B) in gonadotropin suppressed subjects on Day 3 and Day 10, by treatment group. Pla=placebo; K400=ketoconazole 400mg; K800=ketoconazole 800mg; Dut=dutasteride 2.5mg; Ana=anastrozole 1mg.

*p<0.05 compared to baseline

** p<0.05 compared to all non-ketoconazole treatment groups at day 10

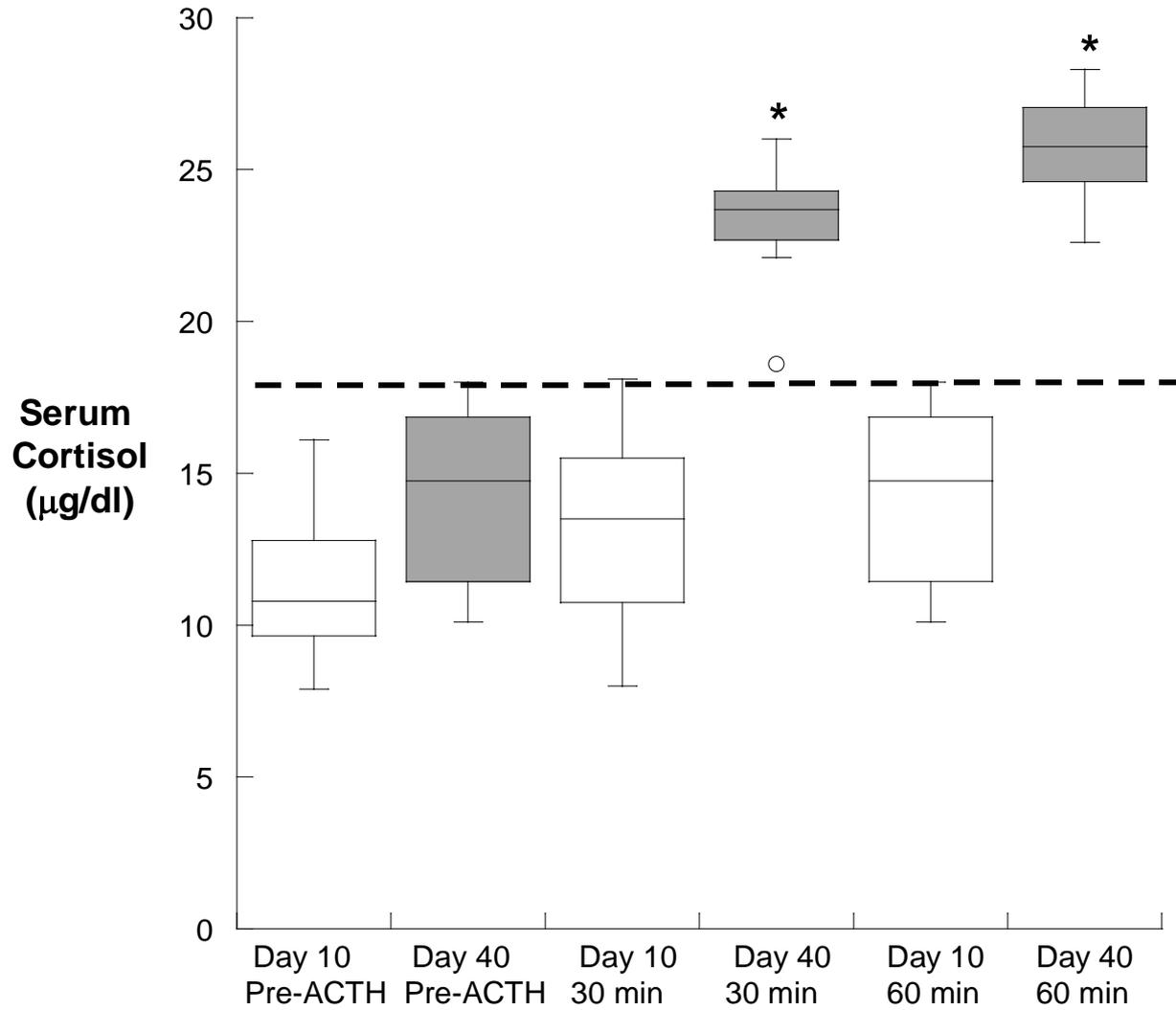
Supplemental Table 1: Number of subjects with adverse events (percentage in parentheses) occurring among 40 participants by treatment group. Pla=placebo; K400=ketoconazole 400mg; K800=ketoconazole 800mg; Dut=dutasteride 2.5mg; Ana=anastrozole 1mg.

	Acyline + Pla (N=8)	Acyline + K400 (N=8)	Acyline + K800 (N=8)	Acyline + Dut (N=8)	Acyline + Ana (N=8)	All Subjects (N=40)
Bruise on abdomen	0	0	1 (2.5)	0	0	1 (2.5)
Change in mood/irritability	0	0	0	1 (2.5)	0	1 (2.5)
Decreased libido	0	0	0	0	1 (2.5)	1 (2.5)
Finger laceration	0	0	0	0	1 (2.5)	1 (2.5)
Headache	0	0	3 (7.5)	0	2 (5)	5 (12.5)
Pain						
At spermatic cord	1 (2.5)	0	0	0	0	1 (2.5)
At scrotum	0	0	0	1 (2.5)	0	1 (2.5)
Plantar fasciitis	1 (2.5)	0	0	0	0	1 (2.5)
Prostatitis	0	1 (2.5)	0	0	0	1 (2.5)
Seasonal allergies	2 (5)	1 (2.5)	1 (2.5)	0	0	4 (10)
Skin itching/rash	0	0	1 (2.5)	0	0	1 (2.5)
Testicular hematoma and hematocele	0	1 (2.5)	0	0	0	1 (2.5)
Upper respiratory infection	1 (2.5)	1 (2.5)	0	0	1 (2.5)	3 (7.5)

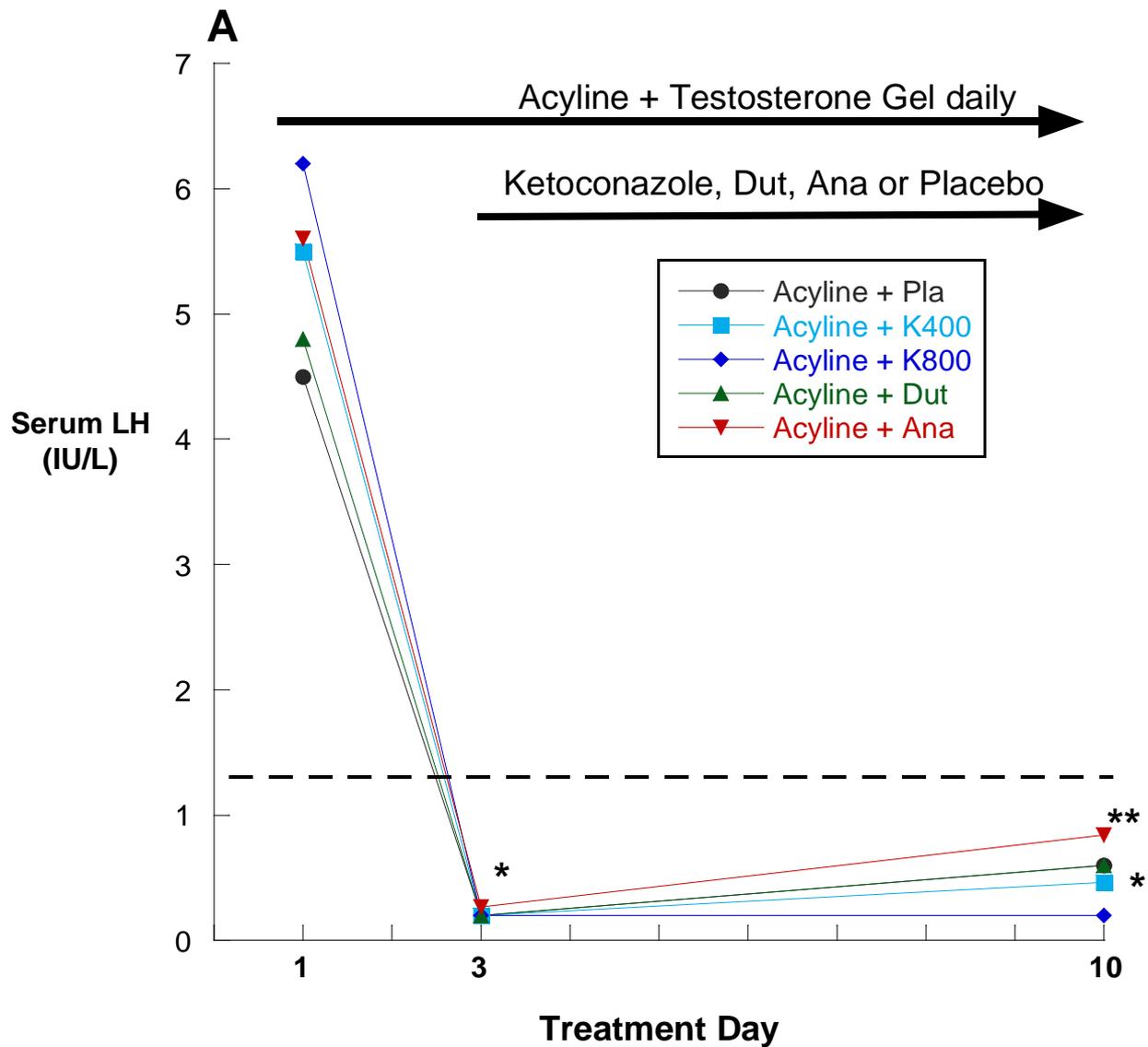
Supplemental Table 2: Testicular aspirate volumes for all 40 subjects by treatment group.

Treatment group	Subject	Day 3 testicular aspirate volumes (µl)	Day 10 testicular aspirate volumes (µl)	Treatment group	Subject	Day 3 testicular aspirate volumes (µl)	Day 10 testicular aspirate volumes (µl)
Acyline + Placebo	1	14.5	4.5	Acyline + Dutasteride 2.5mg daily	1	7.5	10.5
	2	14.6	9.0		2	1.8	24.4
	3	27.3	18.6		3	13.8	1.7
	4	46.1	48.3		4	16.1	15.5
	5	6.3	38.7		5	1.5	18.6
	6	1.7	15.9		6	4.1	17.8
	7	13.4	70.0		7	15.6	11.6
	8	8.5	20.7		8	4.0	4.7
Acyline + Ketoconazole 400mg daily	1	3.9	11.7	Acyline + Anastrozole 1mg daily	1	5.1	9.2
	2	3.1	7.4		2	4.5	6.2
	3	13.9	22.2		3	6.2	18.8
	4	3.2	27.8		4	2.6	1.7
	5	12.4	2.9		5	2.3	11.5
	6	2.3	34.5		6	2.6	5.8
	7	13.4	13.4		7	2.2	101.0
	8	19.9	2.8		8	18.8	25.9
Acyline + Ketoconazole 800mg daily	1	1.0	0.2				
	2	253.5	9.2				
	3	3.5	9.8				
	4	8.5	26.8				
	5	88.9	5.4				
	6	18.9	26.5				
	7	53.0	53.0				
	8	34.1	58.1				

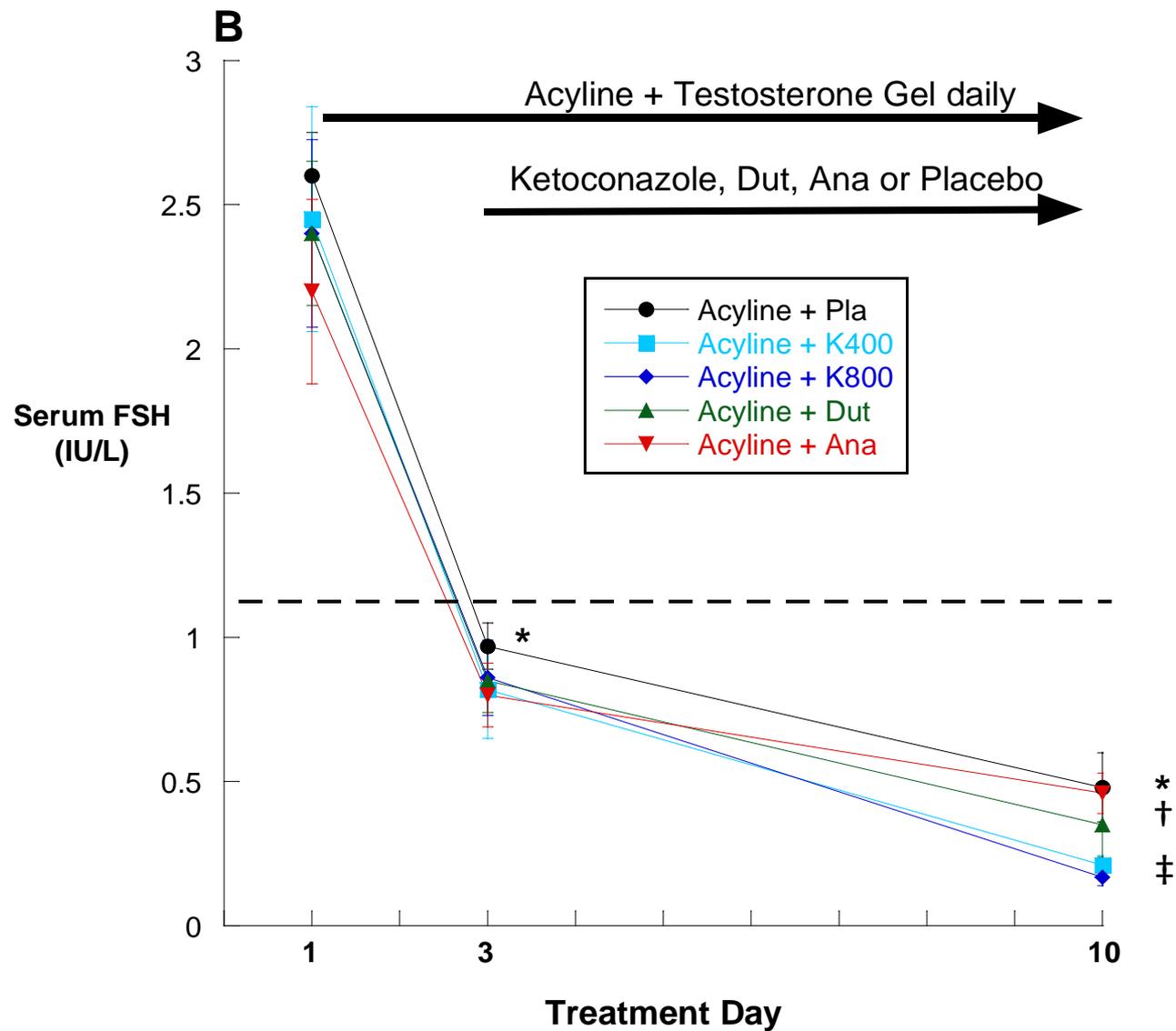
Supplemental
Figure 1



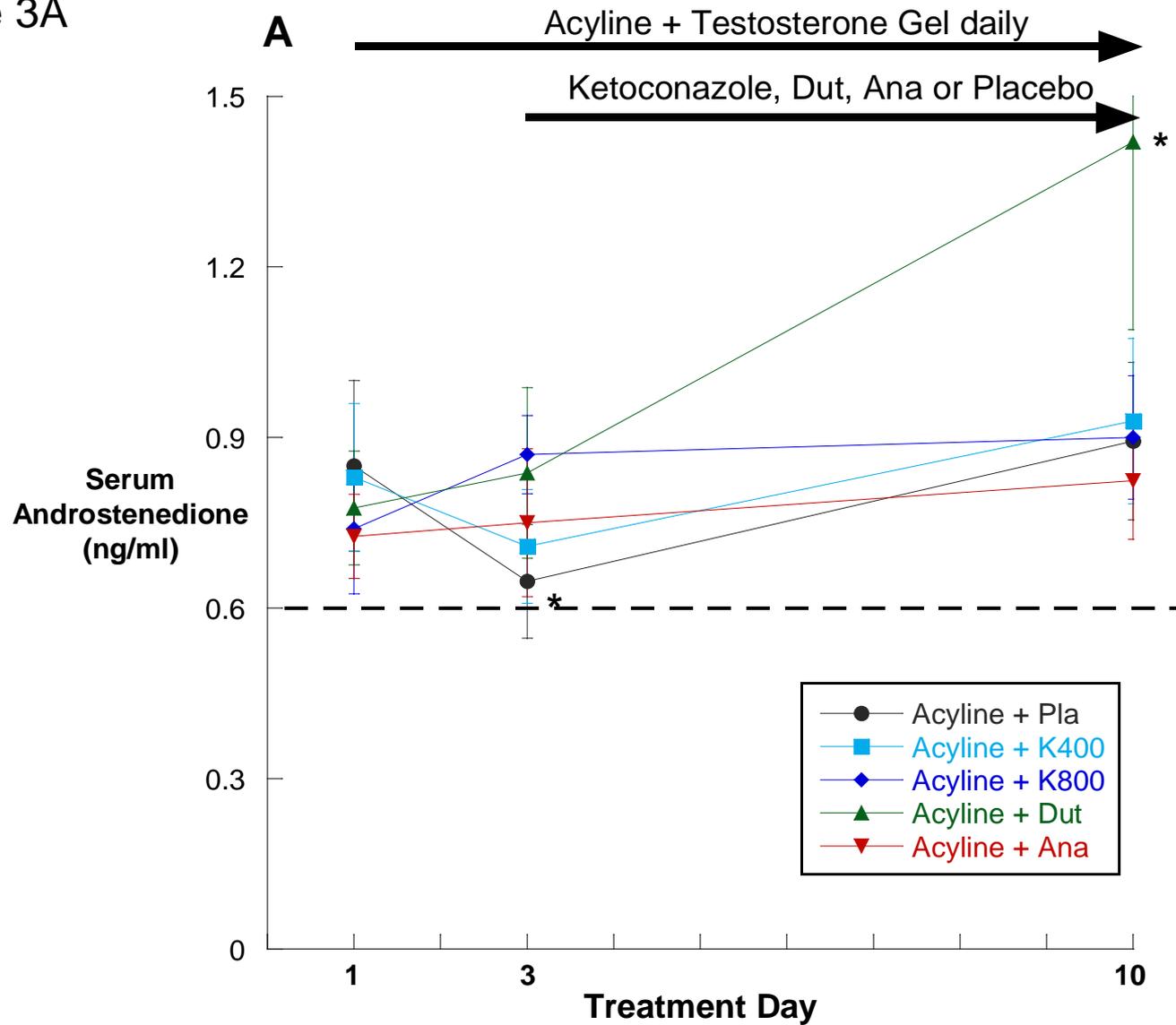
Supplemental
Figure 2A



Supplemental
Figure 2B



Supplemental
Figure 3A



Supplemental
Figure 3B

