

Supplementary Table S3. Results of the linear mixed models performed on laboratory measurements in (post)pubertal boys from diagnosis up to 2 years post-treatment.

	Including all available samples of		Additional analyses including samples obtained from boys who were (post)pubertal at time of diagnosis							
	Boys who were (post)pubertal at time of diagnosis	Boys who were pre-pubertal at time of diagnosis	Treatment level				Treatment scheme			
			TL1	TL2	TL3	TL2 vs TL3 (P-value)	TL2/3 COPDAC-28 arm	TL2/3 DECOPDAC-21 arm	COPDAC-28 vs DECOPDAC-21 (P-value)	
FSH										
Intercept:	-1.7 (-8.6; 5.2)	-2.1 (-3.3; 1.0)	-2.6 (-9.9; 4.7)	-2.8 (-9.9; 4.3)	-1.0 (-8.0; 6.1)	0.43	-0.5 (-8.8; 7.7)	-0.1 (-8.9; 8.6)	0.81	
T0: at diagnosis										
T1: after 2xOEPA	5.2 (4.1; 6.4), P < 0.001	0.1 (-0.7; 0.8), P = 0.86	5.1 (2.1; 8.1), P = 0.001	4.1 (2.4; 5.9), P < 0.001	6.2 (4.5; 7.9), P < 0.001	0.06	6.0 (4.6; 7.5), P < 0.001	3.8 (1.8; 5.7), P < 0.001	0.80	
T1b/T2: after 1x COPDAC/2x (DE)COPDAC	4.9 (3.7; 6.0), P < 0.001	1.0 (0.2; 1.7), P = 0.01	5.4 (2.2; 8.5), P < 0.001	4.1 (2.3; 6.0), P < 0.001	5.3 (3.6; 7.0), P < 0.001	0.15	5.4 (3.9; 6.9), P < 0.001	3.8 (1.9; 5.7), P < 0.001	0.91	
T3: after 4x (DE)COPDAC	5.5 (4.1; 7.0), P < 0.001	0.7 (-0.2; 1.5), P = 0.12	-	-	5.8 (4.2; 7.4), P < 0.001	-	5.9 (4.1; 7.7), P < 0.001	4.8 (2.4; 7.1), P < 0.001	0.57	
T4: 2yPD	0.9 (-0.4; 2.3), P = 0.18	1.5 (0.7; 2.2), P < 0.001	0.8 (-2.5; 4.0), P = 0.63	0.4 (-1.7; 2.4), P = 0.74	1.4 (-0.5; 3.2), P = 0.14	0.13	1.0 (-0.8; 2.7), P = 0.28	1.4 (-0.8; 3.6), P = 0.22	0.42	
Inhibin B										
Intercept:	185.0	68.1	194.0	214.6	162.2	0.05	184.2	205.4	0.31	
T0: at diagnosis	(86.7; 283.2)	(22.7; 116.7)	(90.2; 297.9)	(115.0; 314.3)	(62.6; 261.9)		(64.7; 303.8)	(79.2; 331.6)		
T1: after 2xOEPA	-39.8 (-56.4; -23.2), P < 0.001	6.3 (-11.9; 24.4), P = 0.52	-65.1 (-109.4; -20.9), P = 0.004	-36.8 (-63.0; -10.7), P = 0.006	-35.0 (-59.4; -10.6), P = 0.005	0.06	-33.9 (-56.8; -11.1), P = 0.004	-38.5 (-68.5; -8.5), P = 0.012	0.42	
T1b/T2: after 1x COPDAC/2x (DE)COPDAC	-57.2 (-73.9; -40.5), P < 0.001	17.6 (-0.8; 36.0), P = 0.08	-60.9 (-105.1; -16.6), P = 0.007	-63.3 (-90.1; -36.4), P < 0.001	-50.9 (-75.2; -26.6), P < 0.001	0.16	-42.2 (-65.7; 18.7), P < 0.001	-79.1 (108.5; -49.8), P < 0.001	0.53	
T3: after 4x (DE)COPDAC	-65.7 (-87.0; -44.4), P < 0.001	14.2 (-7.8; 35.1), P = 0.22	-	-	-62.1 (-85.8; -38.5), P < 0.001	-	-50.8 (-78.6; -23.0), P < 0.001	-87.7 (-124.1; -51.2), P < 0.001	0.80	
T4: 2yPD	-19.0 (-39.0; 0.9), P = 0.06	43.4 (16.4; 58.7), P < 0.001	-14.5 (-61.6; 32.7), P = 0.55	-6.5 (-36.3; 23.3), P = 0.67	-28.8 (-55.3; -2.3), P = 0.03	0.004	-5.4 (-32.0; 21.1), P = 0.69	41.7 (-75.5; -7.9), P = 0.016	0.87	
Inhibin B:FSH ratio										
Intercept:	399.0	442.6	388.8	418.0	372.0	0.10	352.0	364.4	0.65	
T0: at diagnosis	(261.5; 536.5)	(253.6; 631.7)	(242.9; 534.8)	(276.1; 560.0)	(230.7; 513.2)		(196.9; 507.1)	(200.5; 528.2)		
T1: after 2xOEPA	-26.5 (-57.1; 4.1), P = 0.09	-35.0 (-140.4; 70.5), P = 0.51	39.9 (-40.8; 120.6), P = 0.33	-65.2 (-112.7; -17.7), P = 0.007	-12.1 (-57.2; 33.1), P = 0.60	0.75	-31.6 (-68.5; 5.3), P = 0.09	-44.2 (-92.5; 4.2), P = 0.07	0.96	
T1b/T2: after 1x COPDAC/2x (DE)COPDAC	-62.7 (-93.6; -31.7), P < 0.001	-136.4 (-243.1; -29.6), P = 0.01	-47.4 (-131.2; 36.4), P = 0.27	-80.8 (-129.6; -32.0), P = 0.001	-51.8 (-96.8; -6.7), P = 0.02	0.66	-65.5 (-103.5; -27.5), P < 0.001	-64.1 (-111.6; -16.7), P = 0.008	0.73	
T3: after 4x (DE)COPDAC	-50.9 (-89.9; -12.0), P = 0.01	-123.9 (-247.3; -0.5), P = 0.049	-	-	-41.2 (-85.0; 2.5), P = 0.07	-	-60.3 (-104.9; -15.7), P = 0.008	-36.4 (-95.0; 22.1), P = 0.22	0.33	
T4: 2yPD	-3.0 (-37.6; 31.7), P = 0.87	-134.2 (-248.6; -19.9), P = 0.02	-21.8 (-107.0; 63.5), P = 0.62	16.8 (-35.9; 69.5), P = 0.53	-12.9 (-60.5; 34.7), P = 0.59	0.02	-1.7 (-42.8; 39.5), P = 0.94	-10.7 (-63.8; 42.4), P = 0.69	0.72	

FSH, follicle-stimulating hormone; COPDAC-28, cyclophosphamide, vincristine, prednisone, and dacarbazine; DECOPDAC-21, doxorubicin, etoposide, cyclophosphamide, vincristine, prednisone, and dacarbazine; TL, treatment level; yPD, years post-diagnosis.

Linear mixed models on FSH, inhibin B levels, and the inhibin B:FSH ratio. Analyses were adjusted for age at time of sampling. Reported estimated effect of all treatment-level and treatment scheme subgroups were calculated using the FSH, inhibin B, or inhibin B:FSH ratio at diagnosis (T0) as intercept in the model. P-values represent the estimated differences between subgroups, using the respective T follow-up as intercept in the model.

More specifically: the numbers presented in columns 'TL1', 'TL2', 'TL3', 'TL2/3 COPDAC-28', and 'TL2/3 DECOPDAC-21' display the observed trend in the respective subgroup of patients over time. A statistically significant result ($P < 0.05$) indicates that, within that specific subgroup, the measured hormone levels are significantly different compared to the baseline level (intercept value, T0 at diagnosis).

The numbers presented in columns 'TL2 vs TL3 (P-value)' and 'COPDAC-28 vs DECOPDAC-21 (P-value)' display the assessed difference between the subgroups at each time point. A P-value < 0.05 indicates a statistically significant difference between the two compared subgroups.