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Supplementary Data

Supplementary Table S2. Serum reproductive markers and semen parameters per treatment level, at diagnosis and after 2 years in (post) pubertal boys.

	Treatment level and scheme					Comparisons	
(POST)PUBERTAL BOYS	TL1	TL2 COPDAC-28	TL2 DECOPDAC-21	TL3 COPDAC-28	TL3 DECOPDAC-21	TL2 vs TL3 (*P*-value)	TL2/3 COPDAC-28 vs TL2/3 DECOPDAC-21 (*P*-value)
Sperm parameters at diagnosis	*n* = 3	*n* = 11	*n* = 10	*n* = 16	*n* = 8		
Sperm volume (ml)	1.6 [1.6; 1.8]	1.0 [0.9; 1.9]	1.1 [0.4; 2.2]	1.1 [0.6; 2.2]	0.8 [0.6; 1.6]	0.91	0.42
Progressive sperm motility (A + B%)	71.0 [54.5; 75.0]	38.0 [33.0; 52.2]	31.5 [21.2; 45.5]	22.5 [6.5; 43.0]	6.6 [2.2; 19.5]	0.01	0.21
Sperm concentration (mil/ml)	30.0 [30.0; 60.0]	29.0 [11.8; 74.5]	12.5 [4.8; 36.1]	14.0 [0.2; 37.0]	2.3 [1.5; 14.5]	0.04	0.37
Abnormal sperm concentration (<15 ml/mil)	0 (0.0%)	4 (36.4%)	5 (50.0%)	8 (50.0%)	6 (75.0%)	0.46	0.43
Total motile sperm count (mil)	35.5 [34.8; 52.0]	13.9 [8.2; 32.9]	4.4 [0.3; 16.9]	7.0 [0.1; 26.5]	0.2 [<0.1; 5.5]	0.077	0.12
Laboratory measurements at diagnosis	*n* = 10	*n* = 16	*n* = 11	*n* = 20	*n* = 11		
FSH (IU/l)	2.0 [1.3; 3.9]	2.8 [1.6; 5.6]	3.1 [2.2; 4.7]	4.4 [2.6; 8.0]	4.3 [1.3; 5.9]	0.21	0.45
Elevated FSH (>7.6 IU/l)	0 (0.0%)	2 (12.5%)	1 (9.1%)	7 (35.0%)	0 (0.0%)	0.31	0.07
Inhibin B (ng/l)	170.0 [146.0; 236.5]	175.0 [125.0; 197.0]	186.0 [140.5; 263.5]	140.0 [120.0; 203.0]	175.0 [146.5; 204.5]	0.24	0.24
Decreased inhibin B (<100 ng/l)	1 (10.0%)	1 (6.2%)	1 (9.1%)	4 (20.0%)	1 (9.1%)	0.43	0.70
Inhibin B:FSH ratio	75.0 [50.3; 140.9]	69.3 [22.3; 182.2]	60.0 [39.4; 114.3]	35.6 [13.9; 59.6]	45.8 [25.3; 119.9]	0.17	0.44
Laboratory measurements after completion of chemotherapy*	*n* = 9	*n* = 14	*n* = 11	*n* = 21	*n* = 12		
FSH (IU/l)	4.8 [3.2; 12.2]	6.0 [3.7; 12.2]	9.2 [4.8; 10.0]	10.0 [5.0; 15.0]	9.8 [7.1; 11.8]	0.05	0.83
Elevated FSH (>7.6 IU/l)	3 (33.3%)	6 (42.9%)	7 (63.6%)	14 (66.7%)	8 (66.7%)	0.39	0.73
Inhibin B (ng/l)	141.0[76.0; 160.0]	161.5[95.0; 203.0]	75.0 [62.5; 162.0]	86.0 [48.0; 124.0]	81.0 [58.0; 97.2]	0.05	0.27
Decreased inhibin B (<100 ng/l)	3 (33.3%)	4 (28.6%)	6 (54.5%)	14 (66.7%)	9 (75.0%)	0.05	0.44
Inhibin B:FSH ratio	23.5 [10.9; 48.1]	21.2 [9.1; 58.4]	12.7 [6.7; 21.0]	8.0 [2.7; 20.4]	6.8 [4.3; 13.8]	0.04	0.53
Sperm parameters at 2 years post-diagnosis	*n* = 3	*n* = 5	*n* = 6	*n* = 9	*n* = 8		
Sperm volume (ml)	1.0 [1.0; 2.4]	1.8 [1.6; 2.1]	1.9 [0.7; 2.2]	1.7 [1.5; 3.2]	3.0 [1.7; 4.3]	0.34	0.52
Progressive sperm motility (A + B%)	70.0 [60.0; 82.0]	48.0 [47.0; 48.0]	47.0 [28.0; 58.5]	54.0 [15.0; 60.9]	16.5 [0.0; 51.2]	0.81	0.46
Sperm concentration (mil/ml)	44.8 [32.0; 65.4]	20.0 [13.0; 21.0]	29.0 [7.9; 49.8]	13.0 [5.6; 18.0]	1.4 [<0.1; 5.3]	0.07	0.31
Abnormal sperm concentration (<15 ml/mil)	0 (0.0%)	2 (40.0%)	2 (33.3%)	5 (55.6%)	7 (87.5%)	0.12	0.70
Total motile sperm count (mil)	42.1 [27.8; 100.6]	16.6 [16.1; 16.9]	5.6 [1.7; 40.9]	10.8 [1.0; 17.0]	0.9 [0.0; 15.7]	0.33	0.29
Laboratory measurements at 2 years post-diagnosis	*n* = 8	*n* = 14	*n* = 8	*n* = 19	*n* = 10		
FSH (IU/l)	4.8 [2.6; 5.7]	2.9 [1.6; 5.5]	2.8 [1.4; 4.5]	4.0 [3.1; 5.7]	5.8 [4.6; 11.6]	0.02	0.36
Elevated FSH (>7.6 IU/l)	0 (0.0%)	2 (14.3%)	2 (25.0%)	2 (10.5%)	3 (30.0%)	1.000	0.25
Inhibin B (ng/l)	154.0[126.0; 189.0]	181.5 [123.2; 253.0]	192.0 [148.8; 249.8]	157.0 [108.0; 188.5]	101.0 [69.0; 127.0]	0.02	0.35
Decreased inhibin B (<100 ng/l)	1 (12.5%)	3 (2.41%)	1 (12.5%)	3 (15.8%)	5 (50.0%)	0.65	0.30
Inhibin B:FSH ratio	38.3 [21.8; 69.3]	45.8 [30.7; 161.3]	67.9 [50.4; 159.6]	28.4 [23.2; 63.2]	18.8 [6.9; 27.2]	0.01	0.31

FSH, follicle-stimulating hormone; vs, versus. Results are presented as median (IQR) or number (%). *P*-values were calculated by Mann–Whitney *U*-tests (continuous) or chi-square/Fisher's exact (categorical).
Abnormal sperm concentration is defined as sperm count <15 mil/ml in line with WHO criteria (Cooper *et al.*, 2010).
* Timing of last checkup during treatment depended on assigned TL-stage, i.e. TL1 patients either had their last checkup during treatment at time of T1 (after 2× OEPA (in case of inadequate response)) or T1b (after 1× COPDAC-28 (in case of adequate response)), TL2 patients had their last checkup during treatment at time of T2 checkup (after 2× (DECOPDAC)) and TL3 patients had their last checkup during treatment at time of T3 checkup (after 4× (DE)COPDAC).