

Supplemental table.

Overview of studies evaluating the effect of puberty suppression and GAH on bone mineral density in TGD youth.

Study	Number of participants	Medications used	Duration of treatment	Age (yrs)	Tanner stage at PS	Outcome (Z-scores)					
						Parameters	Start PS	Start GAH	After GAH	Δ1	Δ2
Klink et al., 2014	19 FtM	Triptorelin 3.75 mg/4wk s.c.	1.5 years (0.25–5.2)	15.0 ± 2.0	Tanner 4	aBMD-LS	0.17 ± 1.18	-0.72±0.99§ _{PS}	-0.33 ± 1.12	-0.89	+0.39
						BMAD-LS	0.28 ± 0.90	-0.50±0.81§ _{PS}	0.03±0.95§ _{GAH}	-0.78	+0.53
		T i.m. every 2-4 wk at incremental dose	5.4 years (2.8–7.8)	16.4 (2.3)		aBMD-FN	0.36 ± 0.88	-0.35±0.79§ _{PS}	-0.35±0.74§ _{GAH}	-0.71	0
						BMAD-FN	0.01 ± 0.70	-0.28 ± 0.74	--	-0.29	-
	15 MtF	Triptorelin 3.75 mg/4wk s.c.	1.3 years (0.5–3.8)	14.9 ± 1.9	Tanner 5	aBMD-LS	-0.77 ± 0.89	-1.01 ± 0.98	-1.36 ± 0.83	-0.24	-0.35
						BMAD-LS	-0.44 ± 1.10	-0.90 ± 0.80	-0.78 ± 1.03	-0.46	+0.12
		17-β-estradiol orally	5.8 years (3.0–8.0)	16.6 ± 1.4		aBMD-FN	-0.66 ± 0.77	-0.95 ± 0.63	-0.69 ± 0.74	-0.29	+0.26
						BMAD-FN	-0.93 ± 1.22	-1.57 ± 1.74	--	-0.64	-
Schagen et al., 2020~	FtM 70 PS	Triptorelin 2x 3.75 mg/2 wk s.c., then every 4 wk	1.8 ± (1.11) years	14.5 ± 2.0	20% Tanner 2-3	aBMD-LS	-0.28 (0.27)	-1.30(0.43)§ _{PS}	0.11(0.58)§ _{GAH}	-1.02	+1.41
						BMAD-LS	-0.15 (0.29)	-1.01(0.49)§ _{PS}	0.12 (0.51)§ _{GAH}	-0.86	+1.13
						aBMD-FN	0.09 (0.26)	-0.82(0.33)§ _{PS}	0.59 (0.43)§ _{GAH}	-0.91	+1.41
						BMAD-FN	-0.23 (0.25)	-0.71(0.37)§ _{PS}	0.01 (0.43)§ _{GAH}	-0.48	+0.72
	42 GAH	T i.m. every 2-4 wk at incremental dose (up to 125 mg/2 wk)	3 years	16.9 ± 1.1	80% Tanner 4-5	aBMD-LS	0.38 (0.14)	-0.68(0.16)§ _{PS}	-0.26(0.22)§ _{GAH}	-1.06	+0.42
						BMAD-LS	0.33 (0.14)	-0.61(0.18)§ _{PS}	-0.04(0.18)§ _{GAH}	-0.94	+0.57
						aBMD-FN	0.93 (0.01)	-0.50(0.12)§ _{PS}	0.12(0.16)§ _{GAH}	-1.43	+0.62
						BMAD-FN	0.04 (0.12)	-0.41(0.14)§ _{PS}	-0.10(0.16)	-0.45	+0.31
	MtF	Triptorelin 2x 3.75 mg/2	2.0 ± (0.94) years	14.1 ± 1.7	30% Tanner 2-3	aBMD-LS	-0.67 (0.26)	-1.37(0.30)§ _{PS}	-0.82(0.39)§ _{GAH}	-0.70	+0.55
						BMAD-LS	-0.33 (0.33)	-1.39(0.36)§ _{PS}	-0.49(0.40)§ _{GAH}	-1.06	+0.9

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	51 PS	wk s.c., then every 4 wk				aBMD-FN	-0.49 (0.24)	-0.99(0.23) \S_{PS}	-0.09(0.28) \S_{GAH}	-0.50	+0.90	
						BMAD-FN	-0.94 (0.27)	-0.88 (0.23)	-0.35(0.37) \S_{GAH}	+0.06	+0.53	
	36 GAH	17- β -estradiol orally (up to 2 mg/day)	3 years	16.2 \pm 1.2	70% Tanner 4-5	aBMD-LS	-0.33 (0.17)	-0.99(0.19) \S_{PS}	-1.05 (0.25)	-0.66	-0.06	
						BMAD-LS	-0.65 (0.20)	-1.29(0.23) \S_{PS}	-0.50(0.25) \S_{GAH}	-0.64	+0.79	
						aBMD-FN	-0.43 (0.16)	-0.86(0.14) \S_{PS}	-0.70 (0.18)	-0.43	-0.16	
						BMAD-FN	-1.01 (0.17)	-1.36(0.20) \S_{PS}	-1.21(0.24) \S_{GAH}	-0.35	+0.15	
	Stoffers et al., 2019	62 FtM	Triptorelin 3.75 mg/4wk s.c.	0.67 years (0.25-3.25)	16.5 (11.8-18.0)	Tanner 3-5	aBMD-LS	0.02 \pm 1.00	-0.81 \pm 1.02 \S_{PS}	-0.66 \pm 0.81	-0.83	+0.15
			T i.m. every 2wk at incremental dose (up to 250 mg/4 wk)	1 year (0.42-2.75)	17.2 (14.9-18.4)		aBMD-TH	-0.19 \pm 1.04	-1.07 \pm 0.85 \S_{PS}	-0.93 \pm 0.63	-0.88	+0.14
Vlot et al., 2017	42 FtM	Triptorelin 3.75 mg/4 wk s.c.	1.2 years	15.1 (11.7-18.6)	Tanner 2-5 Young group: BA<14	BMAD-LS	-0.05 (-0.78-2.94)	-0.84 \S_{PS} (-2.2-0.87)	-0.15 \S_{GAH} (-1.38-0.94)	-0.79	+0.69	
						BMAD-TH	-0.01 (-1.30-0.91)	-0.37 (-2.28-0.47)	-0.37 \S_{GAH} (-2.03-0.85)	-0.36	0	

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		T starting with 25 mg/m ² /2 wk i.m, increasing every 6 months up to 250 mg/4 wk.	2 years	16.3 (15.9–19.5)	Tanner 2-5	BMAD-LS	0.27 (-1.6–1.8)	-0.29 δ_{PS} (-2.28–0.90)	-0.06 δ_{GAH} (-1.76–1.61)	-0.56	+0.23
					Old group: BA>14	BMAD-TH	0.27 (-1.39–1.32)	-0.27 δ_{PS} (-1.91–1.29)	0.02 δ_{GAH} (-2.1–1.35)	-0.54	+0.29
	28 MtF	Triptorelin 3.75 mg/4 wk s.c.	2.5 years	13.5 (11.5–18.3)	Tanner 2-5	BMAD-LS	-0.2 (-1.82–1.18)	-1.52 δ_{PS} (-2.36–0.42)	-1.10 δ_{GAH} (-2.44–0.69)	-1.32	+0.42
					Young group: BA<15	BMAD-TH	-0.71 (-3.35–0.37)	-1.32 (-3.39–0.21)	-1.3 (-3.51–0.92)	-0.61	+0.02
		17- β -estradiol starting with 5 μ g/kg/day increasing every 6 months up to 2 mg/day, orally	2 years	16.0 (14.0–18.9)	Tanner 2-5	BMAD-LS	-1.18 (-1.78–1.09)	-1.15 (-2.21–0.08)	-0.66 δ_{GAH} (-1.66–0.54)	+0.03	+0.49
					Old group: BA>15	BMAD-TH	-0.44 (1.37–0.93)	-0.36 (-1.5–0.46)	-0.56 (-2.17–1.29)	+0.08	-0.20

Values are expressed as mean \pm SD; median (IQR) or median (range). Z-scores are calculated using a normative population matched for age and sex assigned at birth.

$\Delta 1$: absolute difference between mean or median Z-score at the start of PS and mean or median Z-score at the start of GAH.

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$\Delta 2$: absolute difference between mean or median Z-score at the start of GAH and mean or median Z-score at the re-evaluation after GAH.

\S_{PS} : significant decrease during puberty suppression.

\S_{GAH} : significant increase after GAH.

~ In this table the outcome is shown at the start of PS, at start of GAH and 3 years after, with the first outcome referring to the whole cohort of patients. In the original work, the authors also show the outcome after 2 and 3 years of puberty suppression in specific subgroups of patients.

Abbreviations: aBMD: areal bone mineral density; BA: bone age; BMAD: apparent bone mineral density; FN: femoral neck; GAH: gender affirming hormones; i.m.: intramuscular; LS: lumbar spine; PS: puberty suppression; s.c.: subcutaneously; T: testosterone; TH: total hip.