Table 2. Select randomized trials comparing moderate hypofractionation to conventionally fractionated radiation (KQ1 and 2)

Trial	N	Median Follow-Up	Design	Study Arms/ EQD2*	Technique	Cancer Risk Groups	Treatment Target	ADT Use and Duration (median)	Age (median)	Comorbidity	Cancer control (Hazard ratio – 1ºendpoint)	Acute G2+ GI Toxicity	Acute G2+ GU Toxicity	Late G2+ GI Toxicity	Late G2+ GU Toxicity	Patient-reported outcomes
CHHiP[1]	3216	5.2 years	Multicenter non-inferiority trial 1ºendpoint: biochemical or clinical failure-free rate Non-inferiority margin: hazard ratio 1.208	7400 in 200 cGy/ 7400 cGy 6000 in 300 cGy/ 7700 cGy 5700 in 300 cGy/ 7300 cGy	IMRT IGRT optional (53% use)	15% LR 73% IR 12% HR	Prostate + proximal SV	97% 3-6 mo. (median 5.5 mo.)	68 years	Diabetes: 11% Hypertension: 40% Inflammatory bowel disease: 4% Previous pelvic surgery: 8% Symptomatic hemorrhoids in past 12 months: 7% Previous TURP: 8%	6000 vs. 7400 cGy: 0.83 (90% CI: 0.64-1.14) 5700 vs. 7400 cGy: 1.20 (90% CI: 0.99-1.46)	25% 38% 38% p<0.0001)	46% 49% 46% (p=0.90)	14% 12% 11% (5-year)	9% 12% 7% (5-year; 7400 vs. 6000 cGy: p=0.07)	Bowel bother: 14%, 15%, 15% Bladder bother: 17%, 17%, 16% Sexual bother: 52%, 52%, 53% (5-year)
HYPRO [2-4]	820	5 years	Multicenter superiority 1ºendpoint: relapse free survival	7800 in 200 cGy/ 7800 cGy 6460 in 340 cGy (3/week) /8700 cGy	IMRT IGRT	26% IR 74% HR	Prostate +/- SV	67% Variable duration (median 32.4 mo.)	71 years 70 years	TURP: 11% (conv), 9% (hypofx) Abdominal surgery: 27%, 23% GI comorbidity: 10%, 9%	0.86 (95% CI: 0.63-1.16)	31% 42% (OR 1.6, 95% CI: 1.19-2.14)	58% 61% (OR 1.12, 95% CI: 0.84-1.49)	18% 22% (3-year; OR 1.19, 95% CI: 0.88-1.59)	39% 41% (3-year OR 1.16, 95% CI: 0.98-1.38)	Not reported
PROFIT [5]	608	6 years	Multicenter non-inferiority trial 1ºendpoint: biochemical-clinical failure	7800 in 200 cGy/ 7800 cGy 6000 in 300 cGy/ 7700 cGy	IMRT or 3-D CRT IGRT required	All IR	Prostate +/- proximal SV	None	71 years 72 years	History of MI: 12% (conv), 9% (hypofx) Diabetes:18%, 16%	0.99 (90% CI: 0.83-1.19)	10% 16% (p=0.003)	27% 27%	11% 7% (p=0.006)	19% 20%	Not reported

Trial	N	Median Follow-Up	Design	Study Arms/ EQD2*	Technique	Cancer Risk Groups	Treatment Target	ADT Use and Duration (median)	Age (median)	Comorbidity	Cancer control (Hazard ratio – 1ºendpoint)	Acute G2+ GI Toxicity	Acute G2+ GU Toxicity	Late G2+ GI Toxicity	Late G2+ GU Toxicity	Patient-reported outcomes
			Non-inferiority margin: hazard ratio 1.32													
RTOG 0415[6]	1115	5.8 years	Multicenter non-inferiority trial 1ºendpoint: disease- free survival Non-inferiority margin: hazard ratio 1.52	7380 in 180 cGy/ 70 7000 in 250 cGy/ 8000 cGy	IMRT or 3-D CRT IGRT required	All LR	Prostate	None	67 years	Not reported	0.85 (95% CI: 0.64-1.14)	10% 11%	27% 27%	14% 22% (p=0.002)	23% 30% (p=0.06)	Not reported
Fox Chase [7,8]	303	5.7 years	Single institution superiority trial 1ºendpoint: biochemical disease-free survival	7600 in 200 cGy/ 7600 cGy 7020 in 270 cGy/ 8400 cGy	IMRT u/s IGRT	66% IR 33% HR	IR: Prostate + proximal SV HR: Prostate + SV + LN	46% (median not reported)	Not reported	Not reported	1.38 (95% CI: 0.79-2.40)	Not reported	Not reported	16% 11% (8-year; p=0.96)	25% 40% (8-year; p=0.24)	IPSS similar early after EBRT
MD Anderson [9,10]	206	5 years 8.4 years^	Single institution superiority trial 1ºendpoint: failure-free survival	7560 in 180 cGy/ 7100 cGy 7200 in 240 cGy/ 8000 cGy	IMRT u/s or kV IGRT	28% LR 71% IR 1% HR	Prostate + proximal SV	24% ≤4 mo. (median not reported)	67 years	Not reported	Not reported	Not reported	Not reported	5% 10% (5-year; p=0.10)	16% 16% (5-year: p=0.98)	Bowel, urinary, and sexual function similar btw arms (p>0.01)
Italian[11]	168	9 years	Single institution superiority trial 1ºendpoint: late toxicity	8000 in 200 cGy/ 8000 cGy 6200 in 310 cGy/ 8100 cGy	3-D CRT	All HR	Prostate + SV	All 9 mo. (median not reported)	75 years	Not reported	0.62 (95% CI: 0.34-1.14)	21% 35% (p=0.07)	40% 45% (p=0.45)	15% 13% (p=0.57)	21% 14% (p=0.68)	Not reported

* a/b=1.5

^ abstract only

1º = primary; ADT = androgen deprivation therapy; btw = between; CI = confidence interval; conv = conventional fractionation; EQD2 = equivalent dose at 200 cGy; EBRT = external beam radiation therapy; G2+ = grade 2 or higher; cGy = centrigray; HR = high-risk; hypofx = hypofractionated; IPSS = International Prostate Symptom Score; IR = intermediate-risk; LN = lymph nodes; LR = low-risk; MI = myocardial infarction; mo. = months; OR = odds ratio; SV = seminal vesicles