Supplemental Online Content

Kishan AU, Steigler A, Denham JW, et al. Interplay between duration of androgen deprivation therapy and external beam radiotherapy with or without a brachytherapy boost for optimal treatment of high-risk prostate cancer: a patient-level data analysis of 3 cohorts. *JAMA Oncol*. Published online January 20, 2022. doi:10.1001/jamaoncol.2021.6871

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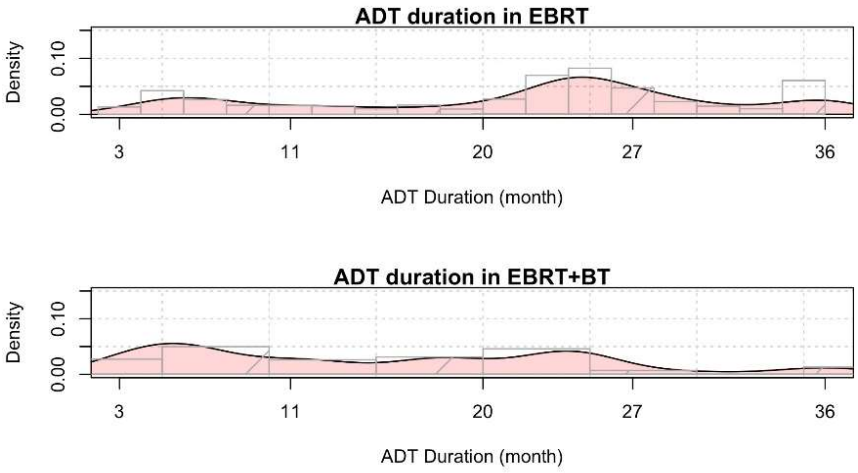
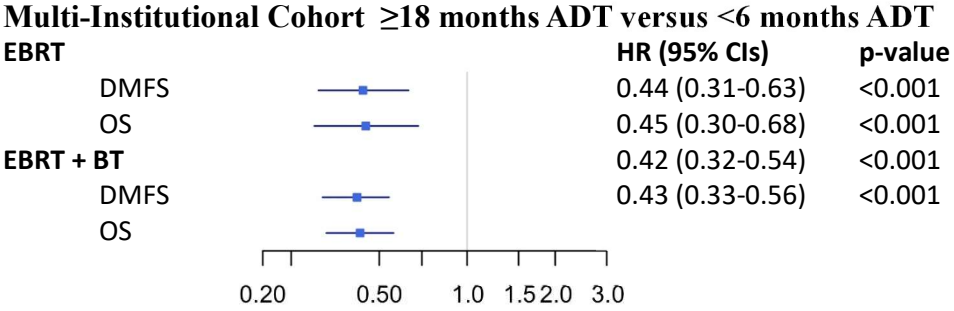
This supplemental material has been provided by the authors to give readers additional information about their work.

eFigure 1. Histograms Depicting Distribution of Use of Various Durations of Androgen Deprivation Therapy in the Multi-Institutional Cohort



Top row shows density histogram for ADT duration in patients receiving external beam radiotherapy (EBRT), bottom row shows density histogram for ADT duration in patients receiving EBRT+brachytherapy boost (EBRT+BT). ADT, androgen deprivation therapy; EBRT, external beam radiotherapy; EBRT+BT, external beam radiotherapy plus brachytherapy boost.

eFigure 2. Associations Between Survival Outcomes and Use of ≥18 months of Androgen Deprivation Therapy versus <6 months of Androgen Deprivation Therapy in the Multi-Institutional Cohort



Forest plots showing associations between distant metastasis-free survival (DMFS) and overall survival (OS) and androgen deprivation therapy (ADT) duration in men receiving external beam radiotherapy (EBRT) or EBRT+brachytherapy boost (EBRT+BT). 95% CI; 95% confidence interval; ADT, androgen deprivation therapy; DMFS, distant metastasis-free survival; EBRT, external beam radiotherapy; EBRT+BT, EBRT+brachytherapy boost; HR, hazard ratio.

eTable 1. Adjusted Cox Models for Distant Metastasis-Free Survival and Overall Survival

ADT Duration (months)	Distant Metastasis-Free Survival		Overall Survival	
	HR (95%CI)	**p-value**	**HR (95%CI)**	**p-value**
EBRT				
(≥6 and <18) *vs.* <6	0.9 (0.61 - 1.31)	0.581	0.9 (0.58 - 1.38)	0.615
≥18 *vs.* <6	0.44 (0.31 - 0.63)	<0.001	0.45 (0.3 - 0.68)	<0.001
≥18 *vs.* (≥6 and <18)	0.49 (0.39 - 0.62)	< 0.001	0.5 (0.39 - 0.65)	< 0.001
EBRT+BT				
(≥6 and <18) *vs.* <6	0.34 (0.25 - 0.45)	<0.001	0.3 (0.22 - 0.41)	<0.001
≥18 *vs.* <6	0.42 (0.32 - 0.54)	<0.001	0.43 (0.33 - 0.56)	<0.001
≥18 *vs.* (≥6 and <18)	1.23 (0.91 - 1.66)	0.171	1.44 (1.04 - 1.99)	0.026

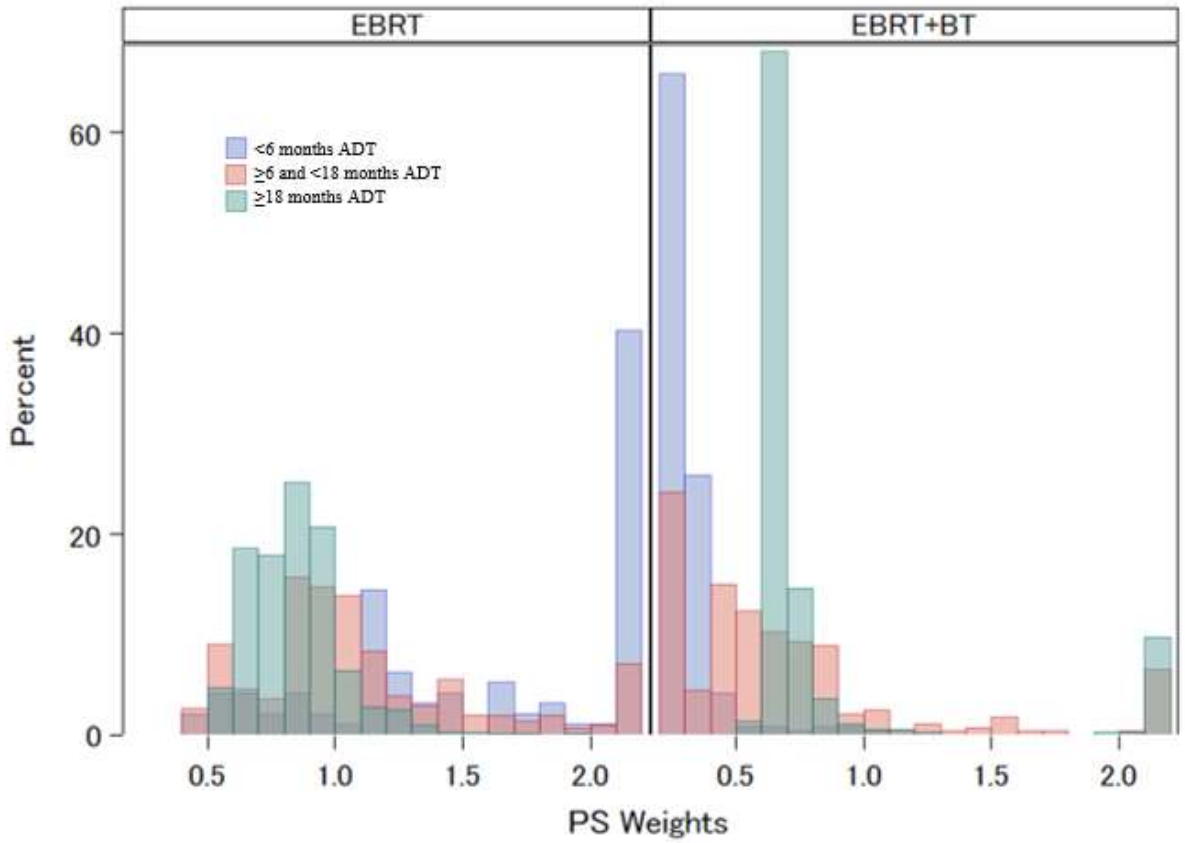
ADT, androgen deprivation therapy; CI, confidence interval; EBRT, external beam radiotherapy; EBRT+BT, EBRT+brachytherapy boost; HR, hazard radio

eTable 2. Adjusted Cox Models for Distant Metastasis-Free Survival and Overall Survival Using Alternative Binning Definitions

ADT Duration (months)	Distant Metastasis-Free Survival		Overall Survival	
	HR (95%CI)	p-value	HR (95%CI)	p-value
Alternative Definition 1: ≤6 vs. >6 and <18 vs. ≥18				
EBRT				
(>6 and <18) *vs.* ≤6	1.23 (0.88 - 1.71)	0.224	1.32 (0.91 - 1.92)	0.144
≥18 *vs.* ≤6	0.54 (0.4 - 0.72)	<0.001	0.58 (0.41 - 0.82)	0.002
≥18 *vs.* (>6 and <18)	0.44 (0.34 - 0.56)	< 0.001	0.44 (0.33 - 0.58)	< 0.001
EBRT+BT				
(>6 and <18) *vs.* ≤6	0.43 (0.31 - 0.59)	<0.001	0.4 (0.28 - 0.57)	<0.001
≥18 *vs.* ≤6	0.53 (0.42 - 0.69)	<0.001	0.56 (0.43 - 0.73)	<0.001
≥18 *vs.* (>6 and <18)	1.25 (0.89 - 1.75)	0.199	1.41 (0.98 - 2.03)	0.065
Alternative Definition 2: ≤6 vs. >6 and ≤18 vs. >18				
EBRT				
(>6 and ≤18) *vs.* ≤6	1.21 (0.87 - 1.67)	0.259	1.3 (0.9 - 1.89)	0.162
>18 *vs.* ≤6	0.53 (0.4 - 0.72)	<0.001	0.58 (0.41 - 0.81)	0.001
>18 *vs.* (>6 and ≤18)	0.44 (0.35 - 0.57)	< 0.001	0.44 (0.34 - 0.58)	< 0.001
EBRT+BT				
(>6 and ≤18) *vs.* ≤6	0.4 (0.3 - 0.53)	<0.001	0.4 (0.28 - 0.57)	<0.001
>18 *vs.* ≤6	0.6 (0.46 - 0.78)	<0.001	0.62 (0.47 - 0.81)	<0.001
>18 *vs.* (>6 and ≤18)	1.5 (1.1 - 2.05)	0.011	1.58 (1.13 - 2.19)	0.007
Alternative Definition 3: <6 vs. ≥6 and ≤18 vs. >18				
EBRT				
(≥6 and ≤18) *vs.* <6	0.89 (0.61 - 1.3)	0.557	0.89 (0.58 - 1.37)	0.599
>18 *vs.* <6	0.44 (0.3 - 0.63))	<0.001	0.45 (0.3 - 0.67)	<0.001
>18 *vs.* (≥6 and ≤18)	0.49 (0.39 - 0.61)	< 0.001	0.5 (0.39 - 0.65)	< 0.001
EBRT+BT				
(≥6 and ≤18) *vs.* <6	0.32 (0.25 - 0.42)	<0.001	0.29 (0.22 - 0.39)	<0.001
>18 *vs.* <6	0.47 (0.36 - 0.62)	<0.001	0.47 (0.36 - 0.62)	<0.001
>18 *vs.* (≥6 and ≤18)	1.46 (1.09 - 1.96)	0.01	1.61 (1.18 - 2.18)	0.003

ADT, androgen deprivation therapy; CI, confidence interval; EBRT, external beam radiotherapy; EBRT+BT, EBRT+brachytherapy boost; HR, hazard radio

eFigure 3. Distribution of Propensity Scores in the Multi-Institutional Cohort, Stratified by Treatment Type and ADT duration



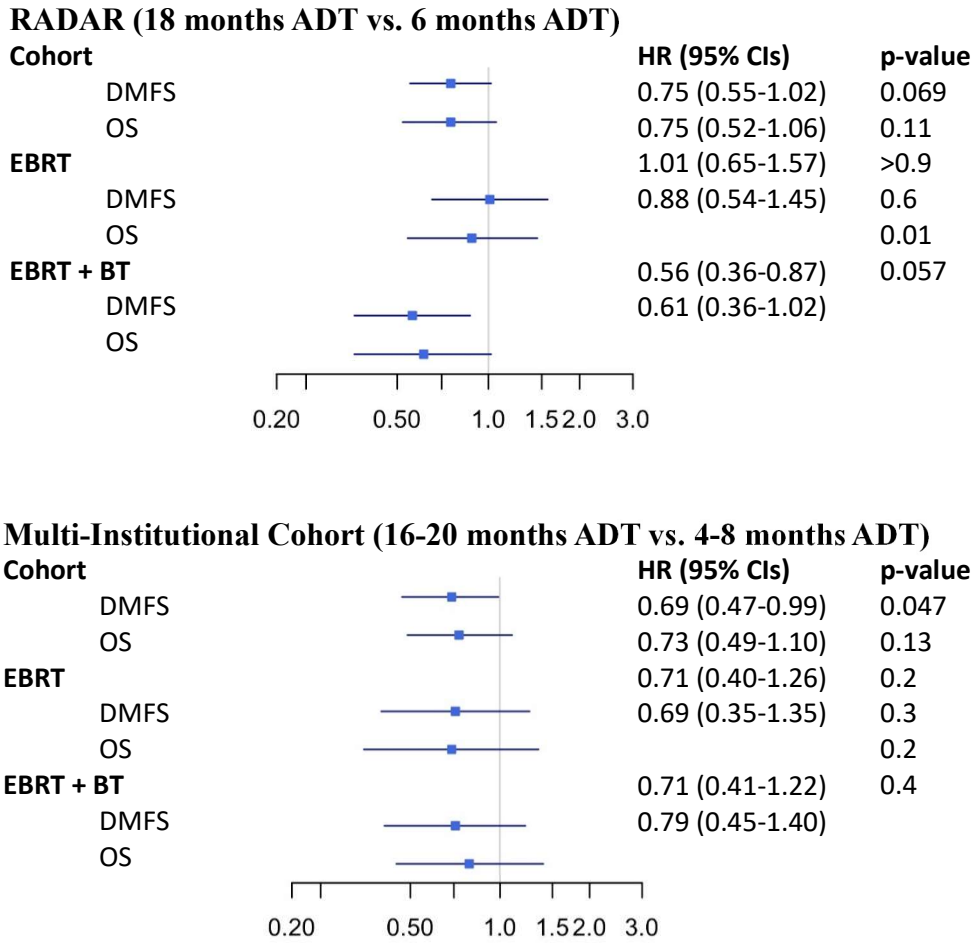
eFigure 3. Distribution of Propensity Scores in the Multi-Institutional Cohort, Stratified by Treatment Type and ADT duration. ADT, androgen deprivation therapy; EBRT, external beam radiotherapy; EBRT+BT, EBRT+brachytherapy boost; PS, propensity score

eTable 3. Adjusted Cox Models for Distant Metastasis-Free Survival and Overall Survival Using A Dichotomization at 12 Months

ADT Duration (months)	**Distant Metastasis-Free Survival**		**Overall Survival**	
	HR (95%CI)	**p-value**		**HR (95%CI)**
EBRT				
≥12 *vs.* <12	0.53 (0.42 - 0.66)	<0.001	≥12 *vs.* <12	0.53 (0.42 - 0.66)
EBRT+BT				
≥12 *vs.* <12	0.47 (0.36 - 0.6)	<0.001	≥12 *vs.* <12	0.47 (0.36 - 0.6)

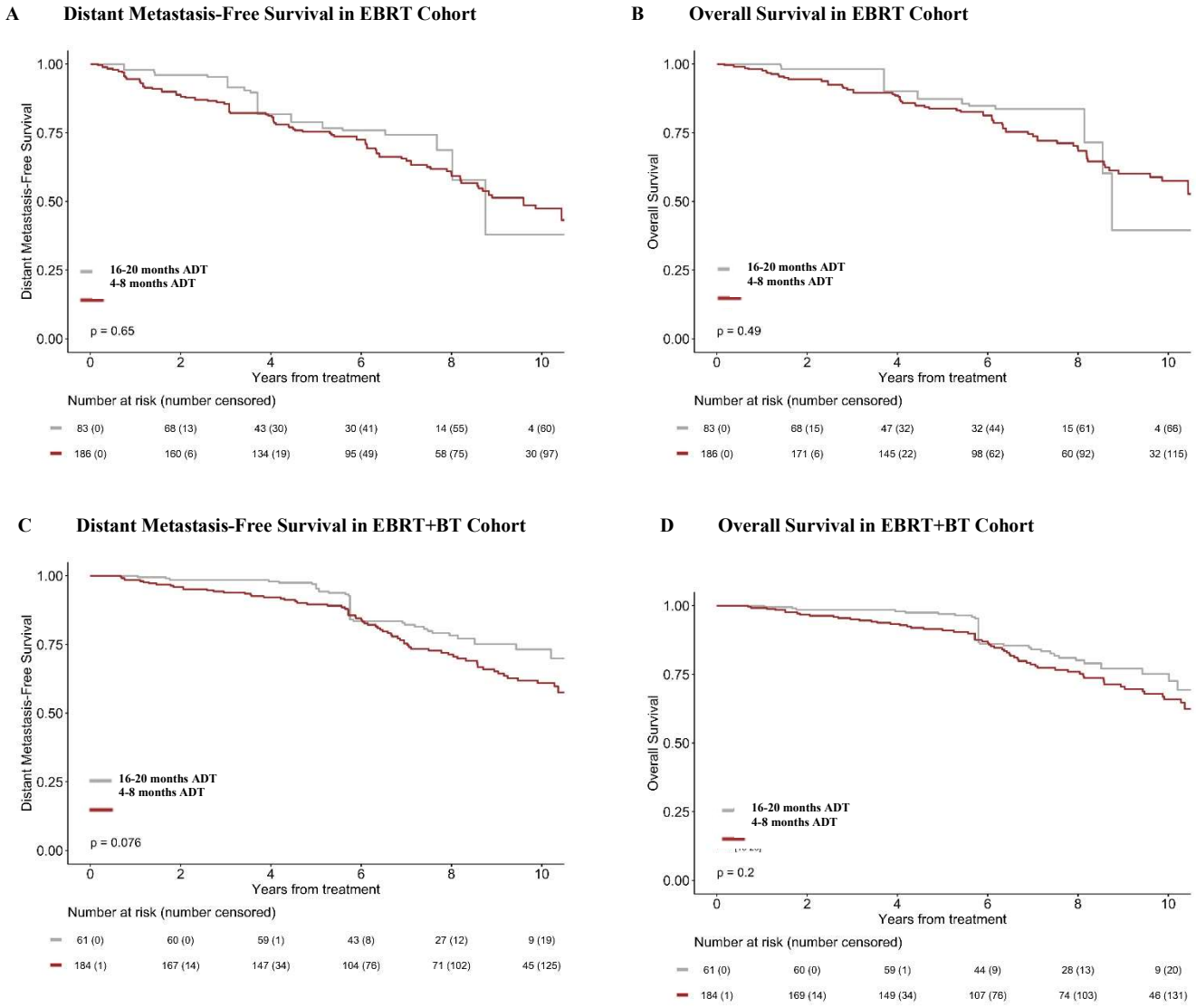
ADT, androgen deprivation therapy; CI, confidence interval; EBRT, external beam radiotherapy; EBRT+BT, EBRT+brachytherapy boost; HR, hazard radio

eFigure 4. Associations Between Survival Outcomes and Use of 18 months of Androgen Deprivation Therapy versus 6 months of Androgen Deprivation Therapy in the RADAR Trial with Comparison to Multi-Institutional Cohort



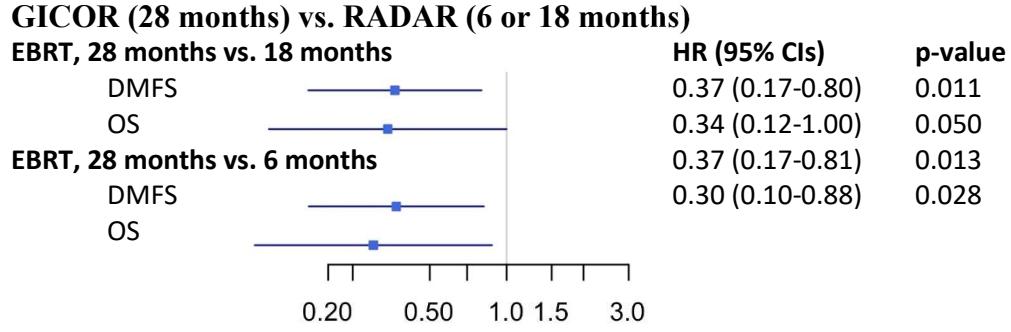
eFigure 4. Associations Between Survival Outcomes and Use of 18 months of Androgen Deprivation Therapy (ADT) versus 6 months of Androgen Deprivation Therapy in the RADAR Trial with Comparison to Multi-Institutional Cohort. Forest plots for patients in the multi-institutional cohort and RADAR. Since ADT duration was not standardized in the multi-institutional cohort, windows of 16-20 months and 4-8 months were chosen to capture patients receiving similar durations to 18 and 6 months, which were protocol-specified for the RADAR trial. 95% CI; 95% confidence interval; ADT, androgen deprivation therapy; DMFS, distant metastasis-free survival; EBRT, external beam radiotherapy; EBRT+BT, EBRT+brachytherapy boost; HR, hazard ratio.

eFigure 5. Distant Metastasis-Free Survival and Overall Survival Outcomes for Men Receiving 4-6 or 16-20 months of Androgen Deprivation Therapy in the Multi-Institutional Cohort



eFigure 5. Distant Metastasis-Free Survival and Overall Survival Outcomes for Men Receiving 4-6 or 16-20 months of Androgen Deprivation Therapy in the Multi-Institutional Cohort. Kaplan-Meier curves for distant metastasis-free survival and overall survival for patients receiving external beam radiotherapy or external beam radiotherapy with a brachytherapy boost. Survival curves were adjusted using an inverse probability treatment weighting approach, wherein propensity scores included treatment type, ln(iPSA), clinical T stage, Gleason grade group, and age at treatment as independent covariates. DMFS, distant metastasis-free survival; EBRT, external beam radiotherapy; EBRT+BT, EBRT+brachytherapy boost; OS, overall survival.

eFigure 6. Associations Between Survival Outcomes and Use of 28 months of Androgen Deprivation Therapy in the GICOR Trial versus 6 months or 18 months of Androgen Deprivation Therapy in the RADAR Trial



eFigure 6. Associations Between Survival Outcomes and Use of 28 months of Androgen Deprivation Therapy in the GICOR Trial versus 6 months or 18 months of Androgen Deprivation Therapy in the RADAR Trial. Forest plots for a cross-trial comparison between the 28 month arm of GICOR and the 6- and 18- month arms of the RADAR trial. 95% CI; 95% confidence interval; ADT, androgen deprivation therapy; DMFS, distant metastasis-free survival; EBRT, external beam radiotherapy; EBRT+BT, EBRT+brachytherapy boost; HR, hazard ratio.