Supplementary Online Content

The J-David Investigators. Prospective, randomized, open-label, blinded-endpoint trial to examine the effect of active vitamin D on cardiovascular events in hemodialysis patients: Japan Dialysis Active Vitamin D trial (J-DAVID). JAMA. doi:10.1001/jama.2018.17749

Supplement 3. **eTable 1.** Eligibility criteria
eTable 2. Definitions of cardiovascular events
eTable 3. Sample size calculation
eTable 4. Predefined laboratory abnormalities
eTable 5. Blood pressure measurements during follow-up
eTable 6. List of the J-DAVID Investigators
eFigure 1. Definitions of three populations for analysis
eFigure 2. Changes in laboratory data and medications
eFigure 3. Adherence to the assigned treatments
eFigure 4. Study organization of J-DAVID trial

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

Effect of oral alfacalcidol on clinical outcomes in patients without secondary hyperparathyroidism receiving maintenance hemodialysis: the J-DAVID randomized clinical trial

Online-only material

Table of Contents

Page 2	eTable 1	Eligibility criteria
Page 3	eTable 2	Definitions of cardiovascular events
Page 4	eTable 3	Sample size calculation
Page 5	eTable 4	Predefined laboratory abnormalities
Page 6	eTable 5	Blood pressure measurements during follow-up
Page 7-9	eTable 6	List of the J-DAVID Investigators
Page 10	eFigure 1	Definitions of three populations for analysis
Page 11	eFigure 2	Changes in laboratory data and medications
Page 12	eFigure 3	Adherence to the assigned treatments
Page 13	eFigure 2	Study organization of J-DAVID trial

eTable 1. Eligibility criteria

Inclusion criteria
1. Signed informed consent 2. Patients on maintenance hemodialysis for 90 days or longer 3. Men or women aged ≥20 and ≤80 years old 4. No treatment with VDRAs for more than 4 weeks prior to this study 5. Serum calcium level ≤ 10.0 mg/dL 6. Serum phosphate level ≤ 6.0 mg/dL 7. Serum intact PTH level ≤ 180 pg/mL
Exclusion criteria
1. History within 12 weeks of myocardial infarction, stroke, aortic dissection/rupture, amputation of a lower limb, coronary revascularization or bypass surgery, lower limb revascularization or bypass surgery 2. Heart failure of NYHA grade III or IV 3. Respiratory failure with PaO_2 <60 mmHg or SpO_2<90% 4. Life expectancy shorter than 1 year due to known malignant, infectious, or other diseases 5. Abnormal liver function tests exceeding x3 upper normal limits 6. Pregnant or lactating females or females planning to be pregnant 7. History of an allergic reaction to alfacalcidol 8. Participation to other interventional studies within 12 weeks prior to this study 9. Inappropriate for this study as judged by an attending investigator

Abbreviations: VDRAs, vitamin D receptor activators; PTH, parathyroid hormone; NYHA, New York Heart Association; PaO_2, arterial oxygen pressure; SpO_2, oxygen saturation measured by pulse oxymeter.

eTable 2. Definitions of cardiovascular events

Acute myocardial infarction: Clinical signs and symptoms such as chest pain or cardiogenic shock, associated with abnormalities in biomarkers (creatine kinase, troponin, etc.) and/or electric cardiogram (new abnormal Q-wave, ST elevation, etc.) for myocardial infarction.
Congestive heart failure: Congestive heart failure (NYHA grade III or IV) requiring hospitalization, excluding dyspnea due to non-cardiac causes (bronchial asthma, etc.)
Stroke: Rapidly developing clinical signs of neurological deficit attributable to a focal and/or total brain functions, without clear causes than vascular origin, lasting for more than 24 hours or leading to death (if not interrupted by surgical operations or death). Stroke includes subarachnoidal hemorrhage, intracranial hemorrhage, and cerebral infarction, but excludes transient ischemic attack, cerebrovascular disease due to hematological disorders (leukemia, polycytemia vera, etc.), primary brain tumors, and metastatic brain tumors. Stroke secondary to trauma is also excluded.
Aortic dissection/rupture: Clinical symptom of chest pain and/or abdominal pain, and diagnosed with imaging test such as contrast enhanced computed tomography.
Amputation of ischemic limb: Major amputations at ankle joint or proximal as treatment for patients with symptom and/or signs of lower extremity ischemia.
Cardiac sudden death: Unexpected death from a cardiac cause that occurs within one hour of symptom onset (witnessed) or within 24 hours of last being observed in normal health (unwitnessed).

eTable 3. Sample size calculation

The equation we used	$$n \fallingdotseq \left(\frac{Z_{\alpha/2}\sqrt{2PQ} + Z_{\beta}\sqrt{P_1Q_1 + P_2Q_2}}{P_2 - P_1} \right)^2$$ where - P1 and P2 are proportion of patients with outcome in group 1 and group 2, respectively. - P = (P1 +P2)/2 - Q1 = 1 – P1, Q2 =1–P2, Q=1–P - Zα/2 and Zß are percent points of normal distribution - Zα/2=Z0.05/25=1.9600, Zß=Z0.20=0.8416
Initial calculation	Assumptions: - P1 = 0.32 for 4-year follow-up - P2 = 0.32 x 0.8 (20% reduction by treatment) - α = 0.05, ß = 0.20 Then, n = 785 in one group, 1570 in two groups. 30 of loss to follow up were considered. Finally, the target sample size of 1600 in total was determined.
Second calculation	Assumptions; - P1 = 0.28 for 4-year follow-up - P2 = 0.28 x 0.7 (30% reduction by treatment) - α = 0.05, ß = 0.20 Then, n = 461 in one group, 922 in two groups. Loss to follow-up was assumed to be 5%. Then, 971 participants in total will be needed. Finally, the target sample size of 972 in total (486 for each group) was determined.
Estimation of CVD risk in the control group	Estimation based on statistics of mortality; - The proportion of patients who die in one year is approximately 9% in Japan (Ref #1). - The number of composite cardiovascular events is larger than the number of all-cause mortality in cohorts of Japanese hemodialysis patients (Ref #2). - Then, the number of patients who experience cardiovascular events can be estimated approximately 9% per year or 36% in 4 years.
	Estimation based on statistics of incident cardiovascular disease; - Incidence of a composite of acute myocardial infarction and stroke was approximately 4.2% per year in Japan in patients undergoing hemodialysis without prior cardiovascular disease (Ref #3). This number does not include the numbers of coronary interventions before myocardial infarction, amputation of lower limbs, aortic dissection, or congestive heart failure requiring hospitalization. - The risk should be higher in those with prior cardiovascular disease. - We estimated the proportion of patients who experience a composite of cardiovascular disease to be in the range of 7 – 9% in a year, or 28 – 36% in 4 years.
Estimation of treatment effect	In cohort studies of patients undergoing hemodialysis, use of VDRA was associated with; lower risk of all-cause mortality with hazard ratios in the range of 0.55–0.75 (References #4, 5); CVD death with hazard ratio in the range of 0.38–0.58 (References #6); and incident CVD with odds ratio in the range of 0.74–0.87 (References #7).
References	1. Shinzato T, et al. Nephrol Dial Transplant. 1997; 12(5): 889-898. 2. Shoji T, et al. Am J Kidney Dis 2013; 62(3): 568-576. 3. Shoji T, et al. Clin J Am Soc Nephrol 2011; 6(5): 1112-1120. 4. Teng M, et al. J Am Soc Nephrol. 2005;16(4): 1115-1125 5. Naves-Diaz M, et al. Kidney Int. 2008;74(8): 1070-1078 6. Shoji T, et al. Nephrol Dial Transplant. 2004;19(1): 179-184

	7. Shoji T, et al. Ther Apher Dial. 2015 Jun; 19(3): 235-244

eTable 4. Predefined laboratory abnormalities

Measurement	Group	Abnormalities	0M	3M	6M	12M	18M	24M	30M	36M	42M	48M
Number of participants	Intervention			472	466	444	428	408	387	370	349	334
	Control		476	469	462	442	426	407	390	369	356	336
Corrected Calcium	Intervention	Number of reported values	488	471	464	443	422	407	386	369	349	334
		> 10.0 mg/dL	17 (3.5%)	136 (28.9%)	105 (22.6%)	72 (16.3%)	52 (12.3%)	45 (11.1%)	46 (11.9%)	37 (10.0%)	39 (11.2%)	33 (9.9%)
		> 11.0 mg/dL	0 (0.0%)	25 (5.3%)	17 (3.7%)	9 (2.0%)	8 (1.9%)	3 (0.7%)	2 (0.5%)	6 (1.6%)	5 (1.4%)	2 (0.6%)
	Control	Number of reported values	476	467	459	439	422	403	389	367	356	332
		> 10.0 mg/dL	21 (4.4%)	30 (6.4%)	25 (5.4%)	36 (8.2%)	41 (9.7%)	29 (7.2%)	40 (10.3%)	29 (7.9%)	34 (9.6%)	22 (6.6%)
		> 11.0 mg/dL	0 (0.0%)	4 (0.9%)	4 (0.9%)	2 (0.5%)	3 (0.7%)	4 (1.0%)	2 (0.5%)	2 (0.5%)	3 (0.8%)	2 (0.6%)
Phosphate	Intervention	Number of reported values	488	471	464	443	422	407	386	369	349	334
		> 6 mg/dL	0 (0.0%)	88 (18.7%)	91 (19.6%)	101 (22.8%)	84 (19.9%)	73 (17.9%)	85 (22.0%)	65 (17.6%)	62 (17.8%)	64 (19.2%)
		> 7 mg/dL	0 (0.0%)	32 (6.8%)	28 (6.0%)	25 (5.6%)	28 (6.6%)	20 (4.9%)	22 (5.7%)	20 (5.4%)	15 (4.3%)	22 (6.6%)
	Control	Number of reported values	476	467	459	439	422	403	389	367	356	332
		> 6 mg/dL	0 (0.0%)	67 (14.3%)	57 (12.4%)	69 (15.7%)	5 (14.0%)	70 (17.4%)	64 (16.5%)	74 (20.2%)	63 (17.7%)	68 (20.5%)
		> 7 mg/dL	0 (0.0%)	14 (3.0%)	11 (2.4%)	27 (6.2%)	20 (4.7%)	20 (5.0%)	19 (4.9%)	20 (5.4%)	15 (4.2%)	19 (5.7%)
Intact PTH	Intervention	Number of reported values	488	427	421	402	386	377	356	337	323	314
		> 240 pg/mL	0 (0.0%)	3 (0.7%)	7 (1.7%)	8 (2.0%)	17 (4.4%)	16 (4.2%)	23 (6.5%)	34 (10.1%)	35 (10.8%)	45 (14.3%)
		> 500 pg/mL	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	1 (0.3%)	2 (0.6%)	1 (0.3%)	1 (0.3%)	3 (1.0%)
	Control	Number of reported values	476	432	422	404	391	381	366	344	336	313
		> 240 pg/mL	0 (0.0%)	19 (4.4%)	19 (4.5%)	33 (8.2%)	37 (9.5%)	46 (12.1%)	46 (12.6%)	4 (12.5%)	41 (12.2%)	43 (13.7%)
		> 500 pg/mL	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (0.8%)	0 (0.0%)	1 (0.3%)	1 (0.3%)	0 (0.0%)

Because of lacking data, the table gives the total number of participants, the number of reported values, the number of abnormal values, and the percentage of abnormal values out of the reported values across the visits by the treatment group.

eTable 5. Blood pressure measurements during follow-up

Visit			0M	3M	6M	12M	18M	24M	30M	36M	42M	48M
Intervention group	*Number of participants*		*495*	*488*	*471*	*465*	*443*	*427*	*407*	*387*	*370*	*349*
	SBP	*N of measured values*	*488*	*469*	*462*	*440*	*422*	*403*	*384*	*365*	*347*	*332*
		25th percentile (mmHg)	130	134	131	134	132	133	131	132	130	133
		Median (mmHg)	145	149	146	148	147	146	147	148	146	147
		75th percentile (mmHg)	160	164	160	162	160	160	161	164	163	160
	DBP	*N of measured*	*486*	*467*	*460*	*437*	*421*	*402*	*383*	*364*	*347*	*332*
		25th percentile (mmHg)	67	70	67	70	67	68	66	67	66	67
		Median (mmHg)	74	76	75	78	74	76	76	77	75	76
		75th percentile (mmHg)	82	84	84	84	83	86	85	85	85	84
Control group	*Number of participants*		*481*	*476*	*469*	*462*	*442*	*426*	*407*	*390*	*369*	*356*
	SBP	*N of measured values*	*476*	*467*	*459*	*435*	*415*	*397*	*384*	*363*	*349*	*326*
		25th percentile (mmHg)	134	132	131	132	130	132	130	132	132	132
		Median (mmHg)	148	147	144	148	144	147	146	147	145	148
		75th percentile (mmHg)	160	162	159	164	159	160	160	161	160	165
	DBP	*N of measured values*	*475*	*466*	*458*	*433*	*415*	*397*	*383*	*363*	*349*	*325*
		25th percentile (mmHg)	68	68	66	68	66	66	66	67	66	68
		Median (mmHg)	74	75	74	76	73	74	73	75	75	75
		75th percentile (mmHg)	83	84	81	84	82	84	83	84	83	85

This table gives the numbers of participants, the number of participants with measured values, and the median, 25th and 75th percentiles levels of SBP and DBP at each visit for each group.

Abbreviations: N, number; SBP, systolic blood pressure; DBP, diastolic blood pressure.

eTable 6. List of the J-DAVID Investigators

Steering Committee:

Tetsuo Shoji* (Osaka City University, Osaka), Masaaki Inaba (Osaka City University, Osaka), and Yoshiki Nishizawa (Osaka City University, Osaka)

**Principal investigator*

Executive Committee:

Tadao Akizawa (Showa University School of Medicine, Tokyo), Ryoichi Ando (Japanese Red Cross Musashino Hospital, Tokyo), Masanori Emoto (Osaka City University, Osaka), Rieko Eriguchi (Fukuoka Renal Clinic, Fukuoka), Akira Fujimori (Konan Hospital, Hyogo), Masafumi Fukagawa (Tokai University, Kanagawa), Tetsuya Hashimoto (Tojinkai Hospital, Kyoto), Hideki Hirakata (Japanese Red Cross Fukuoka Hospital, Fukuoka), Hirokazu Honda (Showa University, Tokyo), Tatsuo Hosoya (Jikeikai University School of Medicine, Tokyo), Daijo Inaguma (Japanese Red Cross Nagoya Daini Hospital, Aichi), Toru Inoue (Higasikouri Hospital, Osaka), Yoshitaka Isaka (Osaka University Graduate School of Medicine, Osaka), Kunitoshi Iseki (University Hospital of the Ryukyus, Okinawa), Mari Ishida (Tokai University Hachioji Hospital, Tokyo), Eiji Ishimura (Osaka City University, Osaka), Noritomo Itami (Nikko Kinen Hospital, Hokkaido), Chiharu Ito (Haga Red Cross Hospital, Tochigi), Minoru Ito (Yabuki Clinic, Yamagata), Noriyuki Iwamoto (Tojinkai Hospital, Kyoto), Ryusuke Kakiya (Meijibashi Hospital, Osaka), Toshitaka Kakuta (Tokai University Hachioji Hospital, Tokyo), Toru Kawai (Chuou Naika Clinic, Hiroshima), Hideki Kawanishi (Tsuchiya General Hospital, Hiroshima), Shuzo Kobayashi (Shonan Kamakura General Hospital, Kanagawa), Kazutaka Kukita (Sapporo Hokuyu Hospital, Hokkaido), Junko Kumagai (Omachi Tsuchiya Clinic, Hiroshima), Eiji Kusano (JCHO Utsunomiya Hospital, Tochigi), Kiyoshi Maekawa (Fujiidera Shirasagi Clinic, Osaka), Ikuto Masakane (Yabuki Hospital, Yamagata), Hiroya Masaki (Kansai Medical University Takii Hospital, Osaka), Mikio Okamura (Kayashima Ikuno Hospital, Osaka), Jun Minakuchi (Kawashima Hospital, Tokushima), Koji Mitsuiki (Japanese Red Cross Fukuoka Hospital, Fukuoka), Takashi Mizukuchi (Kochi Takasu Hospital, Kochi), Satoshi Morimoto (Tokyo Women's Medical University, Tokyo), Yoshihiro Motomiya (Suiyukai Clinic, Nara), Takeshi Nakanishi (Hyogo College of Medicine, Hyogo), Tatsuya Nakatani (Osaka City University, Osaka), Tomohiko Naruse (Kasugai Municipal Hospital, Aichi), Shigeo Negi (Wakayama Medical University, Wakayama), Mitsushige Nishikawa (Kansai Medical University, Osaka), Kosaku Nitta (Tokyo Women's Medical University, Tokyo), Tetsuya Ogawa (Tokyo Women's Medical University Medical Center East, Tokyo), Seiji Ohira (Sapporo Kita Clinic, Hokkaido), Takayasu Ohtake (Shonan Kamakura General Hospital, Kanagawa), Senji Okuno (Shirasagi Hospital, Osaka), Toshihiko Ono (Tojinkai Hospital, Kyoto), Kazumichi Ota (Kochi Takasu Hospital, Kochi), Shigeru Otsubo (Sangenjaya Hospital, Tokyo), Toshinobu Sato (JCHO Sendai Hospital, Miyagi), Yuzuru Sato (Sato Junkankika Naika, Ehime), Takashi Shigematsu (Wakayama Medical University, Wakayama), Toshitsugu Sugimoto (Shimane University Faculty of Medicine, Shimane), Masashi Suzuki (Shinrakuen Hospital, Niigata), Tsutomu Tabata (Inoue Hospital, Osaka), Yoshio Taguma (JCHO Sendai Hospital, Miyagi), Hideki Tahara (Osaka City University, Osaka), Yoshiaki Takemoto (Osaka City University, Osaka), Kenji Tanaka (Suiyukai Clinic, Nara), Masaru Tanaka (Tanaka Kitanoda Hosipital, Osaka), Hideki Tanida (Yabuki Hospital, Yamagata), Masatomo Taniguchi (Kyushu University, Fukuoka), Yoshihiro Tominaga (Japanese Red Cross Nagoya Daini Hospital, Aichi), Yoshiharu Tsubakihara (Graduate School of Health Care Sciences, Jikei Insutitute, Osaka), Yoshihiro Tsujimoto (Inoue Hospital, Osaka), Kazuhiko Tsuruya (Graduate School of Medical Sciences, Kyushu University, Fukuoka), Yuzo Watanabe (Kasugai Municipal Hospital, Aichi), Kunihiro Yamagata (Faculty of Medicine, University of Tsukuba, Ibaraki), Tomoyuki Yamakawa (Shirasagi Hospital, Osaka), Shozo Yano (Shimane University, Shimane), Keigyou Yoh (University of Tsukuba, Ibaraki), Keitaro Yokoyama (Jikeikai University School of Medicine, Tokyo), Noriaki Yorioka (Hiroshima Kidney Organization, Hiroshima), Mitsuru Yoshimoto (Ohno Memorial Hospital, Osaka), and Kenji Yuasa (Kochi Takasu Hospital, Kochi).

eTable 6. List of the J-DAVID Investigators (continued)

Data Center:
Yoshinobu Hirayama[1)] (Osaka City University, Osaka), Taisuke Hojo[2)] (Osaka City University, Osaka), Toshiyoshi Tominaga[3)] (Osaka City University, Osaka), Yuichi Kato [4)] (Osaka City University, Osaka), Hisako Fujii[5)] (Osaka City University, Osaka)
1) 2008-2010, 2) 2010-2012, 3) 2012-2014, 4) 2014-2017, 5) 2008-2017

Statistical Team and Allocation:
Mitsuru Fukui* (Osaka City University, Osaka)
**Chief*

Event Evaluation Committee:
Hiroki Hase* (Toho University, Tokyo), Minoru Yoshiyama (Osaka City University, Osaka), and Yuji Ikari (Tokai University School of Medicine, Kanagawa)
**Chief*

Independent Data Monitoring Committee:
Shinichiro Ueda* (University of the Rryukus, Okinawa), Toyoaki Murohara (Nagoya University, Aichi), Shinichi Nishi (Kobe University, Hyogo)
**Chief*

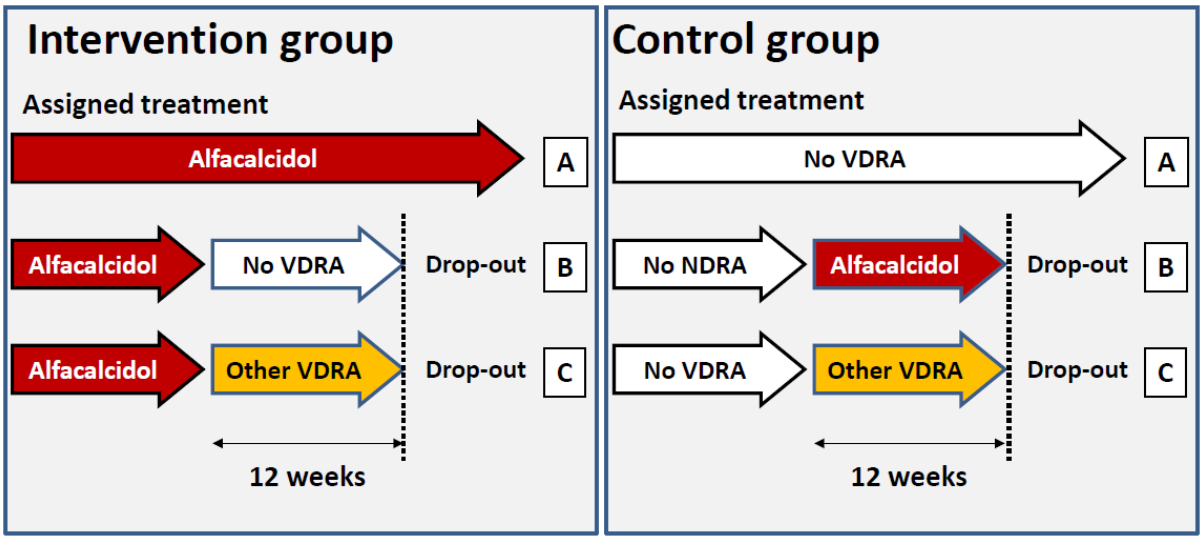
Audit:
Shinichiro Ueda* (University of the Rryukus, Okinawa), Toyoaki Murohara (Nagoya University, Aichi), Shinichi Nishi (Kobe University, Hyogo)
**Chief*

J-DAVID Research Group:
The following list indicates J-DAVID study sites by prefecture from which 1 or more participants were enrolled, excluding the institutions of the Executive Committee members.
Aichi prefecture – Kazuhiro Fujisawa (Kasugai Central Clinic), Sumie Tawada (Kojukai Kasugai Hospital), Satoshi Yamaguchi (Seto Kyoritsu Clinic);
Chiba prefecture – Yasuho Kimura (Shin Kashiwa Clinic);
Fukushima prefecture – Hirofumi Nakano (Kashima Hospital);
Fukuoka prefecture – Itsuko Ishida (Harasanshin Hospital Gofukumachi Jin Clinic), Tetsuo Komota (Komota Clinic), Dai Matsuo (Hirao Clinic), Hiroaki Takamura (Hara Hospital);
Gunma prefecture – Kyoko Ito (Heisei Hidaka Clinic);
Hokkaid prefecture – Nobuo Hashimoto (H・N・Medic), Hironori Ishida (Kitasaito Hospital), Yoshitomo Itami (Higashi Muroran Satellite Clinic), Hirofumi Kon (KKR Sapporo Medical Center), Fumiaki Kumagai (Tomakomai Nissho Hospital);
Hyogo prefecture – Takuma Mabuchi (Tanaka Wadayama Clinic), Furuta Minoru (Aoi Hospital), Shiro Okajima (Tanaka Iin), Noriko Tanaka (Hojo Tanaka Hospital);
Ibaraki prefecture – Takashi Ishizu (Tsukuba Central Hospital), Takashi Ishizu (Central Jin Clinic Ryugasaki), Hiroshi Kikuchi (Kikuchi Medical Clinic), Masakazu Otsuka (Tokiwa Clinic), Atsushi Ueda (Namegata District General Hospital);
Kanagawa prefecture – Naoto Ishida (Seichi Clinic), Mikako Nagaoka (Honatsugi Medical Clinic), Ayaka Tanaka (Bousei Oone Clinic);
Kochi prefecture – Yasukazu Sen (Kochi Takasu Hospital Aki Clinic);
Kyoto prefecture – Naoto Adachi (Mabuchi Clinic), Masaki Koyama (Nishijin Hospital);
Miyagi prefecture – Kosei Kurosawa (Izumi Kurosawa Clinic), Akira Yuza (Dainohara Internal Medicine Clinic);
Oita prefecture – Kazuhiro Matsuyama (Matsuyama Iin Oita Nephrology Clinic), Makoto Matsuyama (Oita Nakamura Hospital);
Okayama prefecture – Masaki Fukushima (Shigei Medical Research Hospital);
Okinawa prefecture – Akira Higa (Shuri Jokamachi Clinic Daini), Kentaro Kohagura (University Hospital of the Ryukyus);

eTable 6. List of the J-DAVID Investigators (continued)

Osaka prefecture – Kaori Adachi (Kitatatsumi Shirasagi Clinic – Shirasagi Minami Clinic), Kiyoshi Goto (Ono Naika), Yuka Hosomi (Inoue Hospital), Noriko Kambara (Kanbara Hospital), Hironori Kawamura (Kawamura Clinic), Eiji Kimoto (Meijibashi Hospital), Satoshi Mikami (Higashikouri Hospital), Michiko Miura (Nagai Clinic), Harumi Nagayama (Nagayama Clinic), Koji Nakanishi (Nakanishi Clinic), Sei Nakatani (Ikuno Aiwa Hospital), Yasue Obi (Obi Clinic), Shigeki Okada (Okada Clinic), Mikio Okamura (Ohno Memorial Hospital), Nobuaki Okuda (Okuda Clinic), Senji Okuno (Shirasagi Clinic), Mayumi Sakurai (Jurakukai Clinic), Hidekazu Shimizu (Onoyama Clinic), Shigeichi Shoji (Shirasagi Hosipital), Kenzo Suzuki (Kadoma Clinic Aiwa Clinic), Akiko Tanaka (Tanaka Habikino Clinic), Keiko Tanaka (Kitahanada Clinic), Hitoshi Tanishita (Hanwa Memorial Hospital), Takeshi Wakikawa (Sakai Onshinkai Hospital), Ibuki Yajima (Ibuki Clinic), Yoshiaki Yamada (Arisawa General Hospital), Yasuo Yamakoshi (Ishikiriseiki Hospital), Shozo Yodoi (Yodoi Hospital), ;
Shimane prefecture – Yasutoshi Himeno (Himeno Clinic), Kazushi Shigeno (Ohda Himeno Clinic), Keiko Suzuki (Otsuka Clinic);
Tochigi prefecture – Ryuta Sato (Haga Red Cross Hospital);
Tokushima prefecture – Kazuhiko Kawahara (Kamojima Kawashima Hospital);
Tokyo prefecture – Hirokazu Honda (Ebara Clinic), Noritsugu Imamura (Minami-Tamachi Clinic), Naohiko Kato (Shinagawa Jin Clinic), Taku Morito (Towa Hospital), Seizo Murai (Iidabashi-Murai Iin), Shiori Osada (Tokyo Ayase Kidney Center), Jun Shiota (Kichijoji Asahi Hospital), Shinya Suganuma (Kidney Clinic Setagaya), Daijiro Uetake (Toyosu Kidney Dialysis Clinic), Ryo Yamamoto (Tateishi Jin Clinic);
Wakayama prefecture – Akio Kaketaka (Kihoku Clinic), Toshihiro Kodama (Kinokawa Clinic), Naoya Kodama (Kisen KD Clinic), Kunio Koshimura (Kumanoji Clinic), Akefumi Maeda (Kodama Hospital), Sadako Tamai (Taniguchi Hospital), Takuji Ujita (Ujita Circulation Disease Clinic);
Yamagata prefecture – Minoru Ito (Yabuki Hospital), Hideki Tanida (Tendo Onsen Yabuki Clinic).

The members of Steering Committee, Executive Committee, Data Center, Statistical Team, Event Evaluation Committee, Independent Data Monitoring Committee, and Audit were collectively called "J-DAVID Investigators". J-DAVID Research Group played roles in the recruitment and follow-up of participants. This trial was supported by many clinical research coordinators from the following site management organizations; Clinical Support Corporation (Tokyo), EP-Mint Co., Ltd. (Aichi), I'ROM Co., Ltd. (Tokyo), Medical Toyou Co., Ltd. (Kanagawa), Site Support Institute Co., Ltd. (Tokyo), Souken Co., Ltd. (Tokyo).

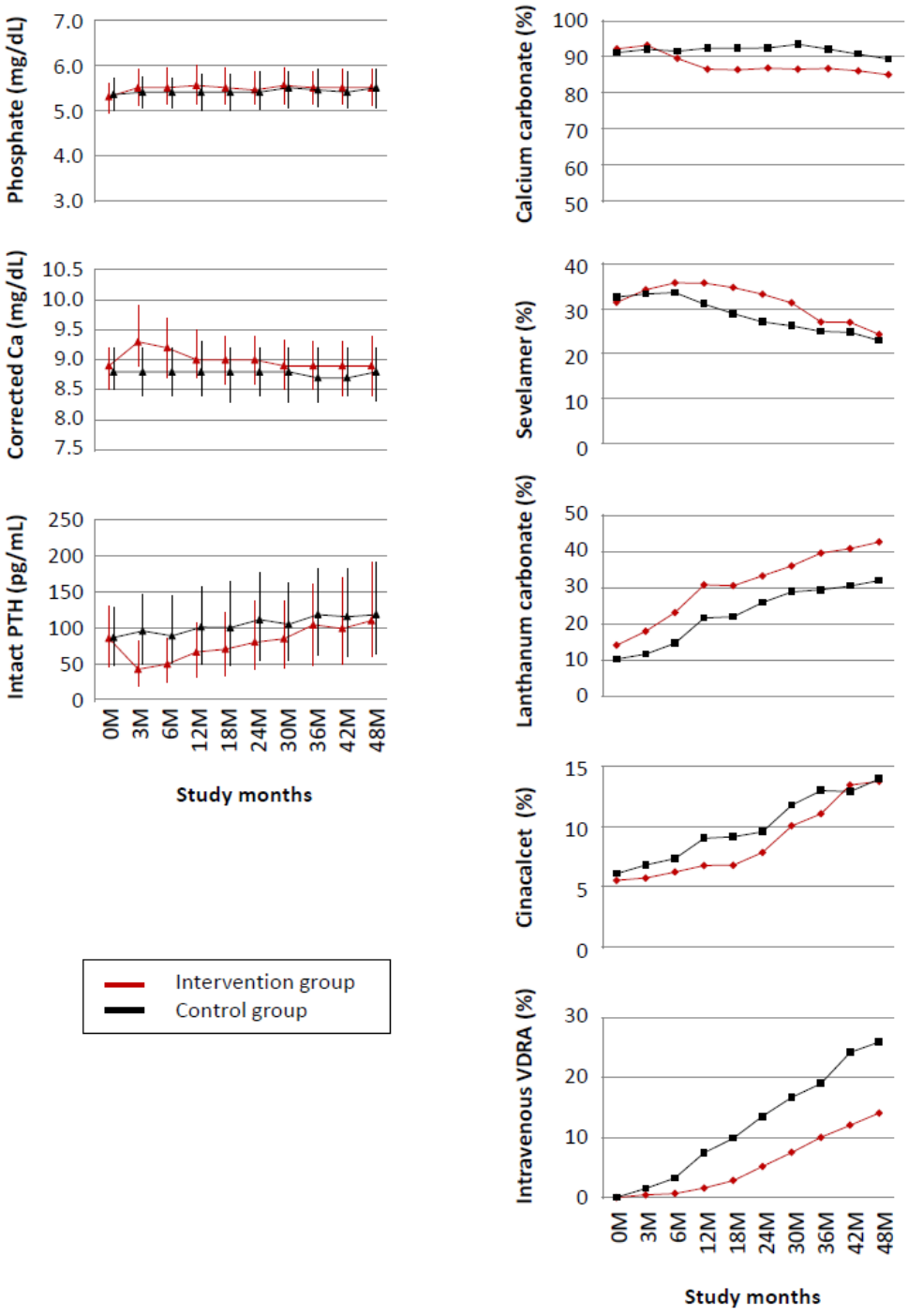


eFigure 1. Definitions of three populations for analysis

1) The full analysis set (FAS) consists of all participants who were randomized, and participants who 'dropped-out' from the assigned treatment are not censored at the time of 'drop-out'.

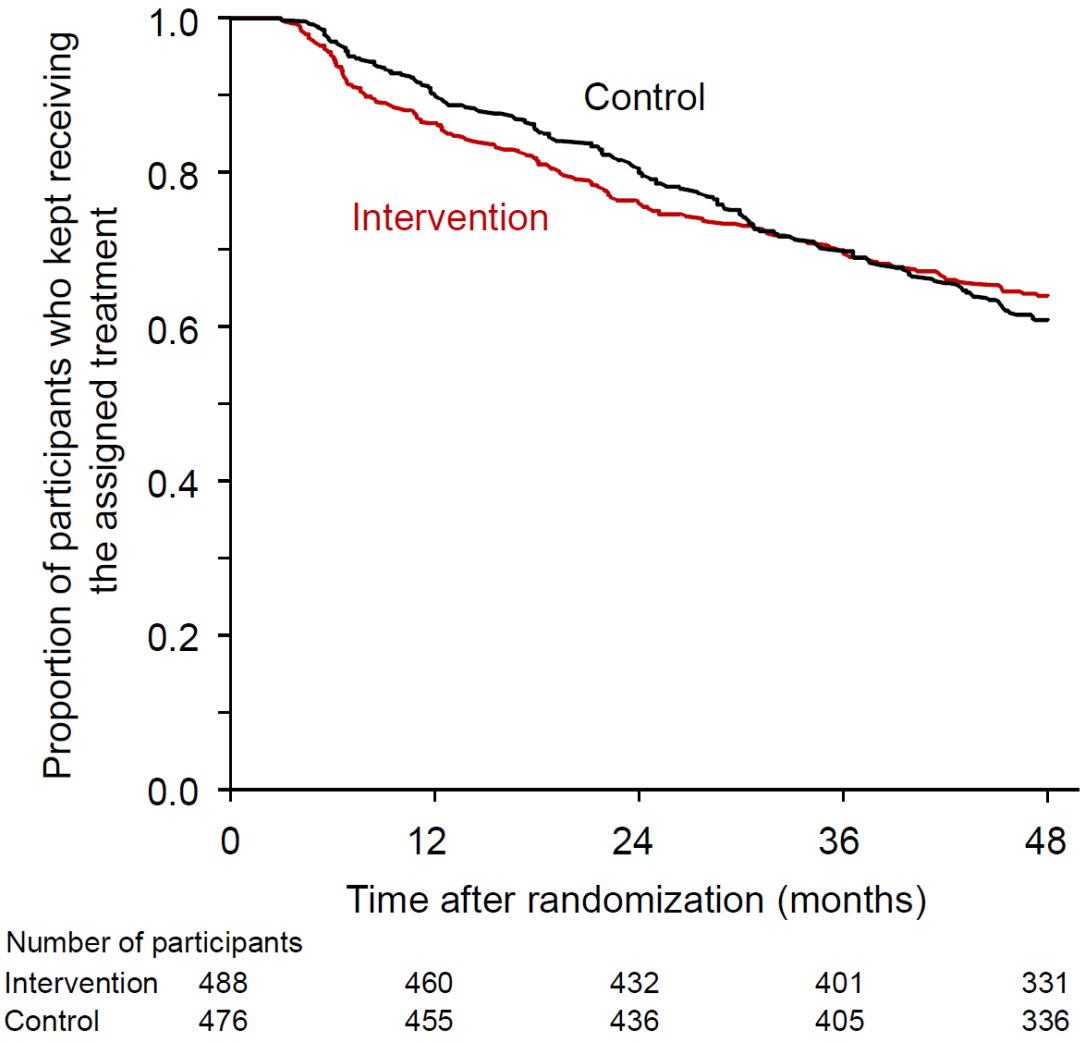
2) The per-protocol set (PPS) consists of all participants who were randomized, but participants (B and C in both arms) are censored at the time of 'drop-out' from the assigned treatment.

3) The modified PPS consists of all participants who were randomized. In the control arm, participants (B and C)are censored at the time of 'drop-out' from the assigned treatment. In the intervention arm, participants who are censored at the time of 'drop-out' from the assigned treatment with oral alfacalcidol, if no VDRA was given in place of alfacalcidol (B). Participants in the intervention arm are not censored at the time of 'drop-out' from the assigned treatment with oral alfacalcidol, if the participants were kept treated with an oral or intravenous VDRA other than alfacalcidol (C); Such patients are censored at the time when any VDRA was not given continuously for more than 12 weeks.

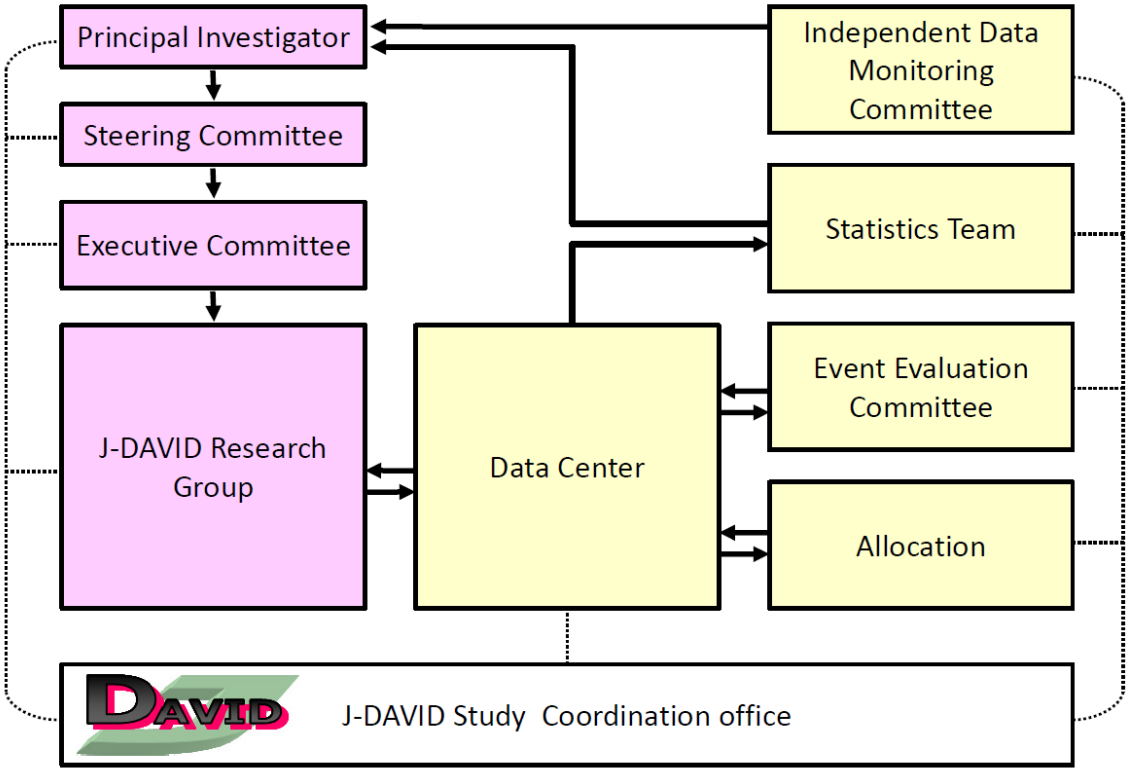


eFigure 2. Changes in laboratory data and medications

Graphs indicate medians (interquartile ranges) for laboratory data and percentages for medication uses in each group. Please see **eTable 4** for the number of participants and the number of reported laboratory values at each visit by treatment group. Data on use of the five medications was obtained for all participants. The numbers of participants at 0M, 3M, 6M, 12M, 18M, 24M, 30M, 36M, 42M, and 48M were 488, 471, 465, 443, 427, 407, 387, 370, 349, and 334 for the intervention group; and 476, 469, 462, 442, 426, 407, 390, 369, 356, and 336 for the control group, respectively. These numbers are based on the visits, and different from number at risk after randomization.



eFigure 3. Adherence to the assigned treatments
The proportions of participants who kept receiving the assigned treatment in the two arms were plotted as a function of time after randomization by the Kaplan-Meier method. Drop-out from the assigned treatment was defined in the text.



eFigure 4. Study organization of this trial