Vascular Calcification Progression: Novel Agents and Future Perspectives

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- Disclosures
- VC progression
- New treatment
- Future perspectives

The views expressed in this presentation are the personal, professional views of Antonio Bellasi and not necessarily those of any stakeholder.

Disclosures: ***speaking honoraria form Amgen, Sanofi, Vifor, Sanifit***

This presentation is only to be used for educational reference purposes

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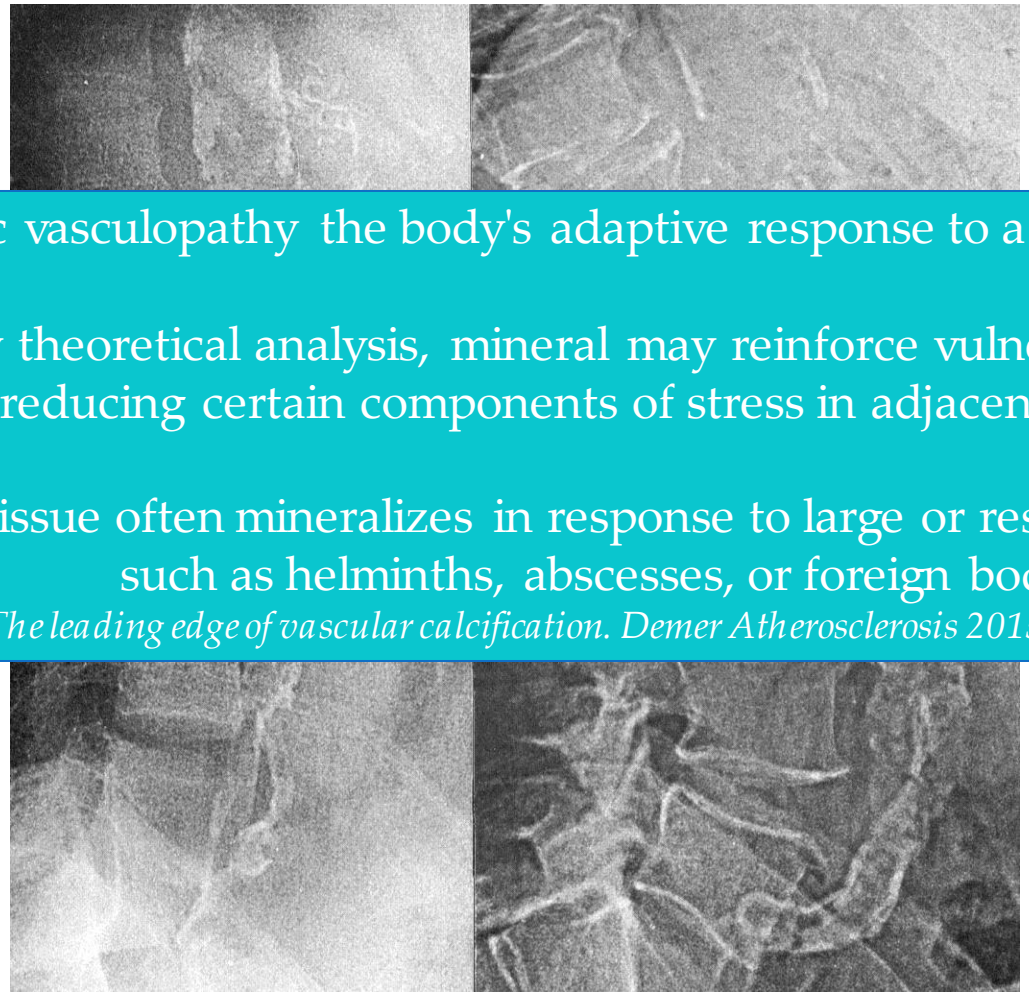
VASCULAR CALCIFICATION: A USEFUL MARKER OF CV RISK?



Is calcific vasculopathy the body's adaptive response to a perceived threat?

(…) By theoretical analysis, mineral may reinforce vulnerable plaque by reducing certain components of stress in adjacent regions.

(..) Soft tissue often mineralizes in response to large or resistant opponents, such as helminths, abscesses, or foreign bodies

The leading edge of vascular calcification. Demer Atherosclerosis 2015; 25:275-277

Bellasi, Papagni, Di Lullo Atherosclerosis. 2018 Dec; 279:88-90

CAC as a marker of risk

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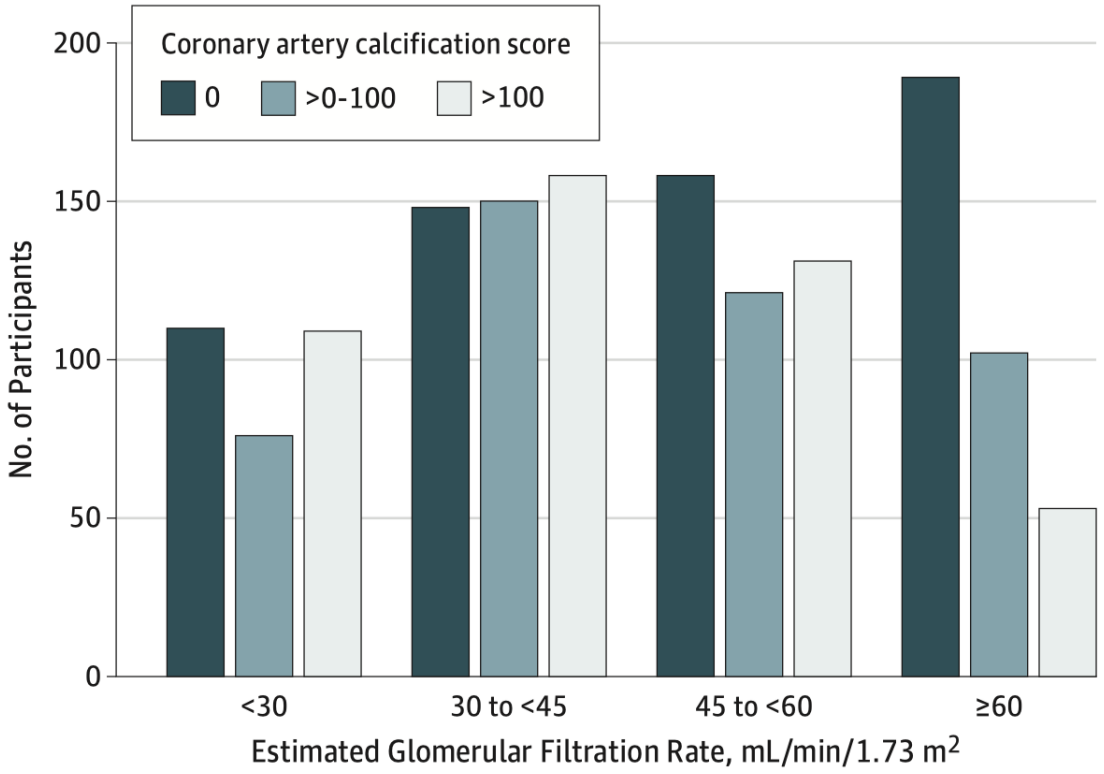
Figure 1. Chronic Renal Insufficiency Cohort Study Participants by Coronary Artery Calcification Score and Estimated Glomerular Filtration Rate



A score of 0 indicates no coronary artery calcification; greater than 0 to 100, moderate calcification; greater than 100, severe calcification.

CRIC study

- ✓ 1541 participants (21 to 74 years of age),
- ✓ average follow-up of 5.9 years
- ✓ 137 all-cause deaths
- ✓ 188 cardiovascular disease events:
  - ✓ 60 cases of myocardial infarction,
  - ✓ 120 heart failures,
  - ✓ 27 strokes

  (patients may have had >1 event)

Chen et al JAMA Cardiol. 2017;2(6):635-643.

CAC as a marker of risk

Chen et al JAMA Cardiol. 2017;2(6):635-643.

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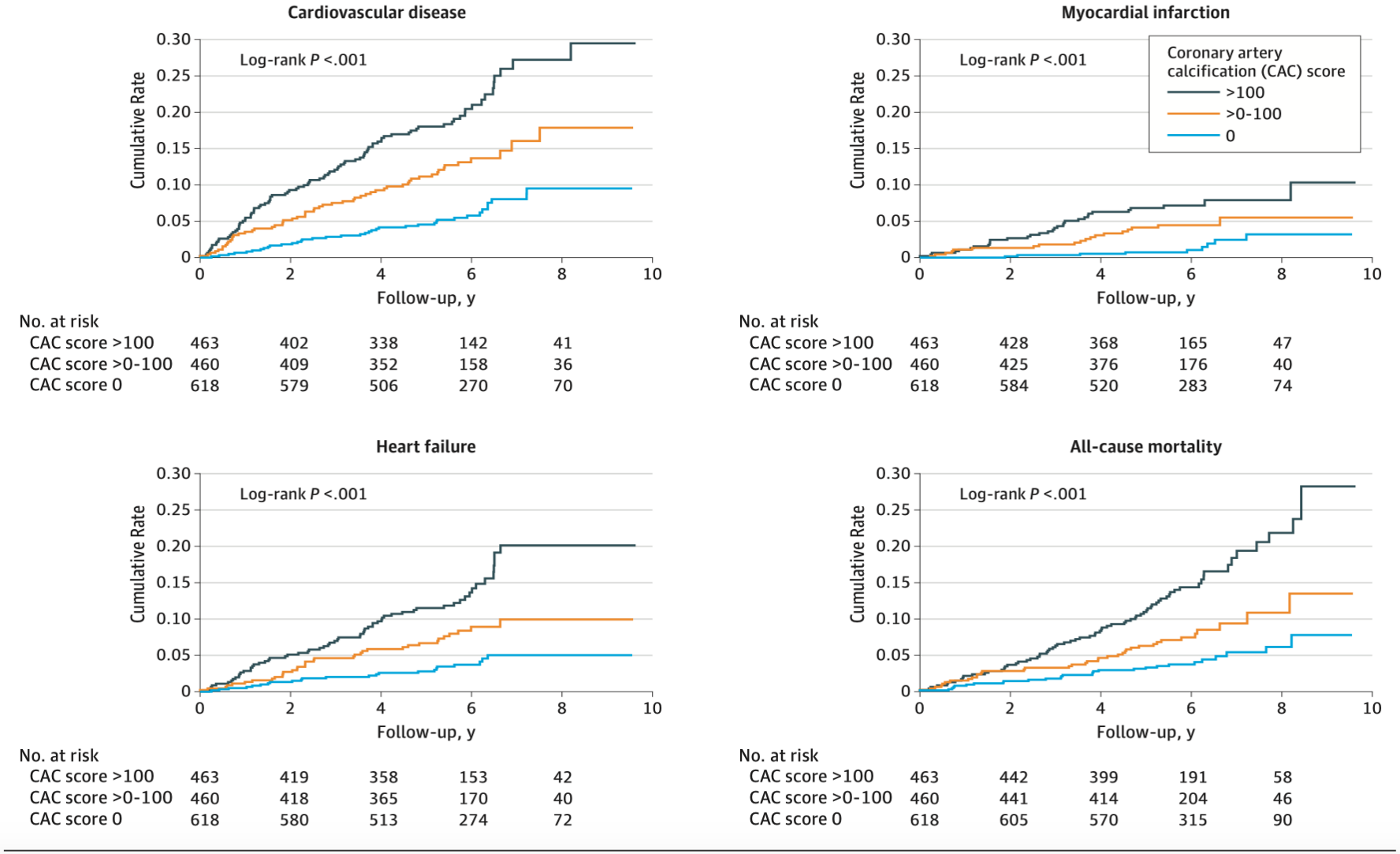
Figure 2. Kaplan-Meier Cumulative Event Rate of Cardiovascular Disease, Myocardial Infarction, Heart Failure, and All-Cause Mortality According to Coronary Artery Calcification Score Among Chronic Renal Insufficiency Cohort Participants Without a History of Cardiovascular Disease



CAC as a marker of risk

Chen et al JAMA Cardiol. 2017;2(6):635-643.

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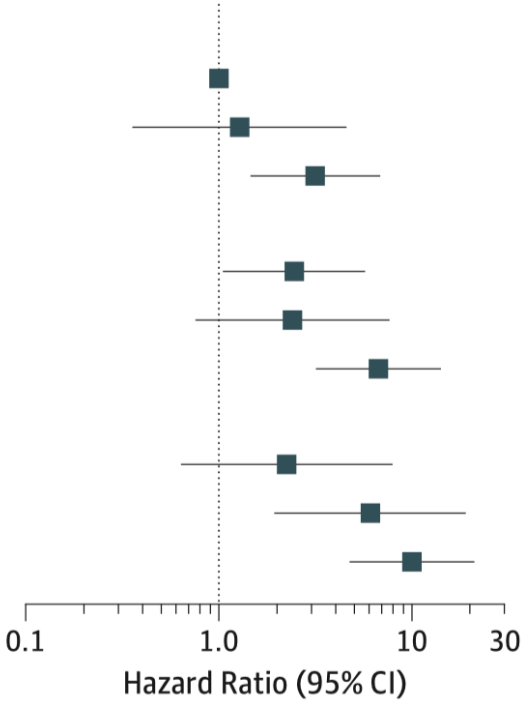
Figure 3. Multivariable-Adjusted Hazard Ratios of Cardiovascular Disease by ACC/AHA Atherosclerotic Cardiovascular Disease Risk Score and CAC Score Among Chronic Renal Insufficiency Cohort Participants Without a History of Cardiovascular Disease

ACC/AHA Atherosclerotic Cardiovascular Disease Risk Score Category	Hazard Ratio (95% CI)
<5.0%	
CAC score 0	1 [Reference]
CAC score >0-100	1.28 (0.36-4.60)
CAC score >100	3.16 (1.46-6.84)
5.0%-7.5%	
CAC score 0	2.45 (1.05-5.71)
CAC score >0-100	2.41 (0.76-7.64)
CAC score >100	6.70 (3.18-14.10)
>7.5%	
CAC score 0	2.25 (0.64-7.93)
CAC score >0-100	6.09 (1.94-19.10)
CAC score >100	10.00 (4.76-21.00)



CAC progression as a marker of risk

China Dialysis Calcification Study (CDCS)
Zhang et al JAMA Network Open. 2023;6(5):e2310909.

The primary outcome was progression of VC at 3 different anatomical sites (coronary artery, abdominal aorta, and cardiac valves) and identification of risk factors for VC progression

Disclosures
VC progression
New treatment
Future perspectives

Table 1. Baseline Participant Characteristics

Characteristic	Participants, No. (%)			*P* value
	Overall (N = 1489)	Hemodialysis (n = 1168)	Peritoneal dialysis (n = 321)	
Follow-up time, median (IQR), y	3.9 (2.9-4.1)	3.9 (2.9-4.1)	3.9 (2.9-4.0)	.38
Length of time receiving dialysis, median (IQR), y	3.7 (2.0-6.1)	3.9 (2.0-6.6)	3.1 (1.9-4.7)	<.001
Age, median (IQR), y	51.0 (41.0-60.0)	52.0 (43.0-61.0)	47.0 (37.0-57.0)	<.001
Sex				
Male	886 (59.5)	724 (62.0)	162 (50.5)	<.001
Female	603 (40.5)	444 (38.0)	159 (49.5)	
BMI, median (IQR)	22.1 (19.9-24.4)	22.2 (19.9-24.7)	21.7 (19.9-23.7)	.001
MAP, median (IQR), mm Hg	102.7 (93.7-111.7)	101.7 (93.0-110.0)	106.7 (97.7-117.0)	<.001
Smoking status				
Never	1055 (70.9)	804 (68.8)	251 (78.2)	<.001
Former or current	434 (29.1)	364 (31.2)	70 (21.8)	
History of diabetes	302 (20.3)	256 (21.9)	46 (14.3)	.003

CAC progression as a marker of risk

Zhang et al JAMA Network Open. 2023;6(5):e2310909.

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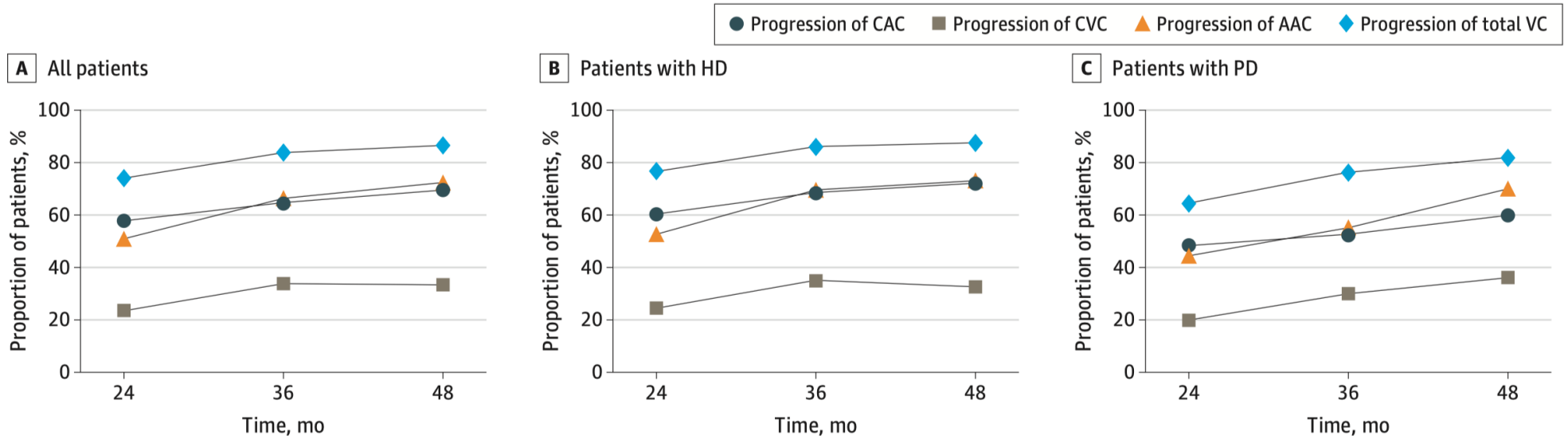
Figure 1. Proportion of Patients With Progression of Calcification During 4-Year Follow-up



AAC indicates abdominal aortic calcification; CAC, coronary artery calcification; CVC, cardiac valve calcification; HD, hemodialysis; PD, peritoneal dialysis; and VC, vascular calcification.

CAC progression as a marker of risk

Zhang et al JAMA Network Open. 2023;6(5):e2310909.

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Table 2. Multivariable Analysis of Factors Associated With Progression of Calcification

Factor	Progression of CAC		Progression of AAC		Progression of CVC	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Dialysis modality (hemodialysis vs peritoneal dialysis)	1.08 (0.76-1.52)	.67	1.11 (0.80-1.55)	.53	0.88 (0.62-1.24)	.45
Length of time receiving dialysis per 1 y	0.93 (0.89-0.97)	.002	0.99 (0.96-1.02)	.41	0.95 (0.91-1.00)	.04
Age per 10 y	1.22 (1.07-1.38)	.003	1.70 (1.52-1.91)	<.001	1.40 (1.25-1.57)	<.001
Sex (male vs female)	1.00 (0.74-1.36)	>.99	0.85 (0.65-1.11)	.24	0.92 (0.69-1.23)	.56
BMI per 1 unit	1.05 (1.01-1.09)	.03	1.02 (0.99-1.06)	.18	1.00 (0.96-1.03)	.79
MAP per 10 mm Hg	1.10 (1.01-1.19)	.04	1.12 (1.03-1.22)	.006	1.02 (0.95-1.11)	.58
Smoking status (former or current vs never)	1.09 (0.77-1.53)	.63	1.59 (1.16-2.19)	.004	0.94 (0.68-1.29)	.68
History of diabetes (yes vs no)	1.22 (0.83-1.78)	.31	1.35 (0.93-1.97)	.12	1.25 (0.91-1.72)	.16
Laboratory values						
Baseline hs-CRP level per log μg/mL	1.06 (0.95-1.18)	.28	1.08 (0.98-1.19)	.14	1.15 (1.04-1.27)	.008
Time-averaged serum calcium level, mg/dL						
<8.40 vs 8.40-10.00	0.76 (0.52-1.11)	.16	0.85 (0.59-1.24)	.40	1.25 (0.83-1.89)	.29
>10.00 vs 8.40-10.00	0.70 (0.46-1.06)	.09	1.23 (0.81-1.87)	.32	0.72 (0.47-1.09)	.12
Time-averaged serum phosphorus level, mg/dL						
>4.49 vs ≤4.49	3.11 (2.11-4.60)	<.001	1.38 (0.97-1.97)	.07	1.39 (0.92-2.08)	.11
Time-averaged iPTH level, pg/mL						
<150 vs 150-600	0.99 (0.69-1.43)	.97	0.84 (0.58-1.20)	.33	0.91 (0.63-1.34)	.65
>600 vs 150-600	1.90 (1.34-2.68)	<.001	1.17 (0.88-1.57)	.28	1.38 (1.03-1.85)	.03
Time-averaged FGF-23 level per log pg/mL	1.13 (1.03-1.23)	.008	1.13 (1.04-1.23)	.004	1.11 (1.02-1.22)	.02
Time-averaged 25-hydroxyvitamin D level per 10 ng/mL	1.02 (0.89-1.15)	.81	0.89 (0.79-1.01)	.07	1.16 (1.03-1.31)	.02
Previous or concomitant medication use						
CPB (yes vs no)	1.33 (1.00-1.76)	.047	0.87 (0.68-1.12)	.28	0.54 (0.42-0.70)	<.001
Non-CPB (yes vs no)	0.74 (0.52-1.06)	.10	0.88 (0.62-1.25)	.48	1.10 (0.76-1.58)	.61
Calcimimetics (yes vs no)	0.92 (0.51-1.64)	.77	1.00 (0.58-1.74)	.99	1.16 (0.69-1.94)	.58
Baseline calcification[a]	1.40 (1.31-1.49)	<.001	2.25 (1.83-2.77)	<.001	0.90 (0.65-1.24)	.51

CAC progression as a marker of risk

Zhang et al JAMA Network Open. 2023;6(5):e2310909.

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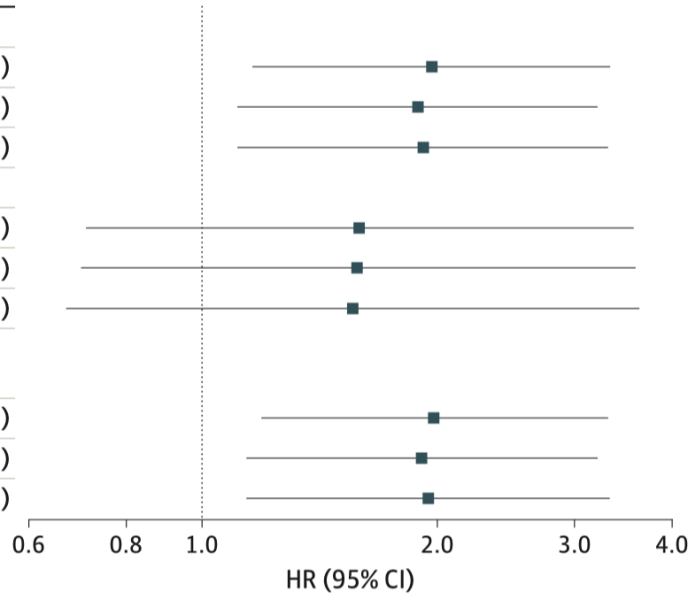
Figure 2. Multivariable Analysis of the Association Between Progression of Coronary Artery Calcification and Occurrence of Clinical Outcomes

Multivariable	HR (95% CI)	*P* value
All-cause death		
Model 1	1.97 (1.16-3.33)	.01
Model 2	1.89 (1.11-3.21)	.02
Model 3	1.92 (1.11-3.31)	.02
CV-related death		
Model 1	1.59 (0.71-3.57)	.26
Model 2	1.58 (0.70-3.59)	.27
Model 3	1.56 (0.67-3.63)	.30
Composite of all-cause death and nonfatal CV events		
Model 1	1.98 (1.19-3.31)	.01
Model 2	1.91 (1.14-3.21)	.01
Model 3	1.95 (1.14-3.33)	.01



Model 1 was adjusted for age, sex, and body mass index (calculated as weight in kilograms divided by height in meters squared). Model 2 was adjusted for all factors in model 1 plus smoking status, history of diabetes, and mean arterial pressure. Model 3 was adjusted for all factors in model 2 plus calcium, phosphorus, intact parathyroid hormone, and fibroblast growth factor 23 levels and calcium-based phosphate binder use. CV indicates cardiovascular; HR, hazard ratio.

CAC progression as a marker of risk

Zhang et al JAMA Network Open. 2023;6(5):e2310909.

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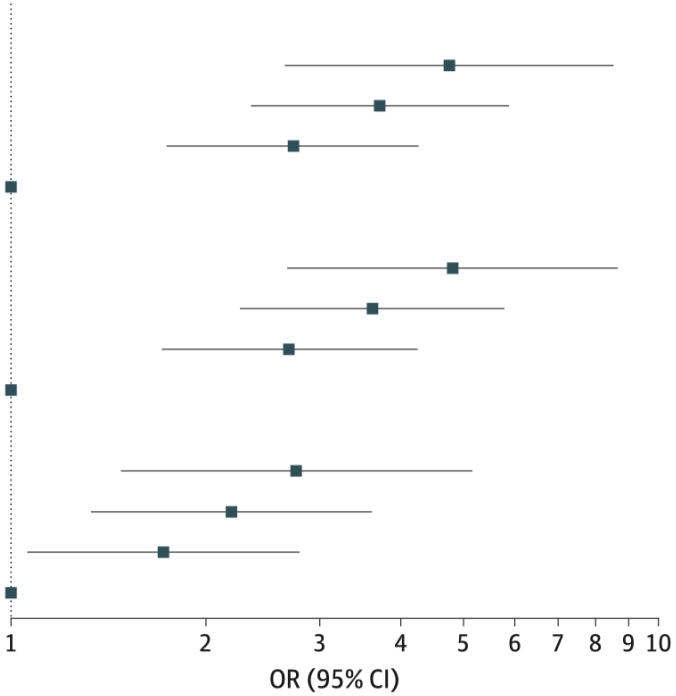
Figure 3. Multivariable Analysis of the Association Between Target Achievement and Progression of Coronary Artery Calcification

Multivariable	OR (95% CI)	*P* value
Model 1		
No targets	4.75 (2.65-8.52)	<.001
1 Target	3.71 (2.35-5.88)	<.001
2 Targets	2.73 (1.74-4.26)	<.001
All targets	1 [Reference]	
Model 2		
No targets	4.81 (2.67-8.66)	<.001
1 Target	3.62 (2.26-5.78)	<.001
2 Targets	2.69 (1.71-4.25)	<.001
All targets	1 [Reference]	
Model 3		
No targets	2.76 (1.48-5.16)	.001
1 Target	2.19 (1.33-3.61)	.002
2 Targets	1.72 (1.06-2.79)	.03
All targets	1 [Reference]	



Model 1 was adjusted for sex, age, and body mass index (calculated as weight in kilograms divided by height in meters squared). Model 2 was adjusted for all factors in model 1 plus smoking status, history of diabetes, and mean arterial pressure. Model 3 was adjusted for all factors in model 2 plus fibroblast growth factor 23 level and calcium-based phosphate binder use. OR indicates odds ratio.

CAC progression as a marker of risk

Bellasi et al Cells 2021 May 3;10(5):1091. doi: 10.3390/cells10051091

- Disclosures
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	Total (n=414)	Alive (n=308)	Expired (n=106)	
Variable	Mean (SD)[n]	Mean (SD)[n]	Mean (SD)[n]	P-Value
Age (years)	**65.3 (14.8)[414]**	**63.1 (14.8)[308]**	**71.5 (12.9)[106]**	**<0.0001**
Male (%)	48.8% [202]	46.4% [143]	55.7% [59]	0.127
Body Weight (Kg)	**70.7(13.7)[414]**	**72.8 (13.3)[308]**	**64.7 (13.0)[106]**	**<0.0001**
ASCVD (%)	**32.6% [135]**	**27.3% [84]**	**48.1% [51]**	**<0.0001**
Diabetes (%)	**28.3% [117]**	**18.8% [58]**	**55.7% [59]**	**<0.0001**
Systolic Blood Pressure (mmHg)	137 (18)[414]	136 (17)[308]	140 (19)[106]	0.056
Diastolic Blood Pressure (mmHg)	76 (9)[414]	76 (8)[308]	76 (10)[106]	0.741
LVMI (g/cm2)	**149 (45)[414]**	**146 (48)[308]**	**158 (34)[106]**	**0.007**
QTc (msec)	407 (32)[414]	406 (34)[308]	410 (26)[106]	0.314
QTd (msec)	26 (11)[414]	27 (11)[308]	25 (11)[106]	0.193
CAC Agatston score (unit)	**273 (728)[414]**	**181 (633)[308]**	**542 (903)[106]**	**0.0002**
CAC strata				**<0.0001**
CAC=0	**31.8 [132]**	**34.7 [107]**	**23.5 [25]**	
CAC 1-100	**44.4 [184]**	**49.0 [151]**	**31.1 [33]**	
CAC 101-400	**8.4 [35]**	**7.7 [24]**	**10.3 [11]**	
CAC 400+	**15.3 [63]**	**8.4 [26]**	**34.9 [37]**	
CAC Agatston score progression	**33.1% [137]**	**26.9% [83]**	**50.9% [54]**	**<0.0001**
Pulse Wave Velocity (m/sec)	**8.7 (2.4)[414]**	**8.5 (1.8)[308]**	**9.4 (3.7)[106]**	**0.012**

CAC progression as a marker of risk

Bellasi et al Cells 2021 May 3;10(5):1091. doi: 10.3390/cells10051091

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VC progression

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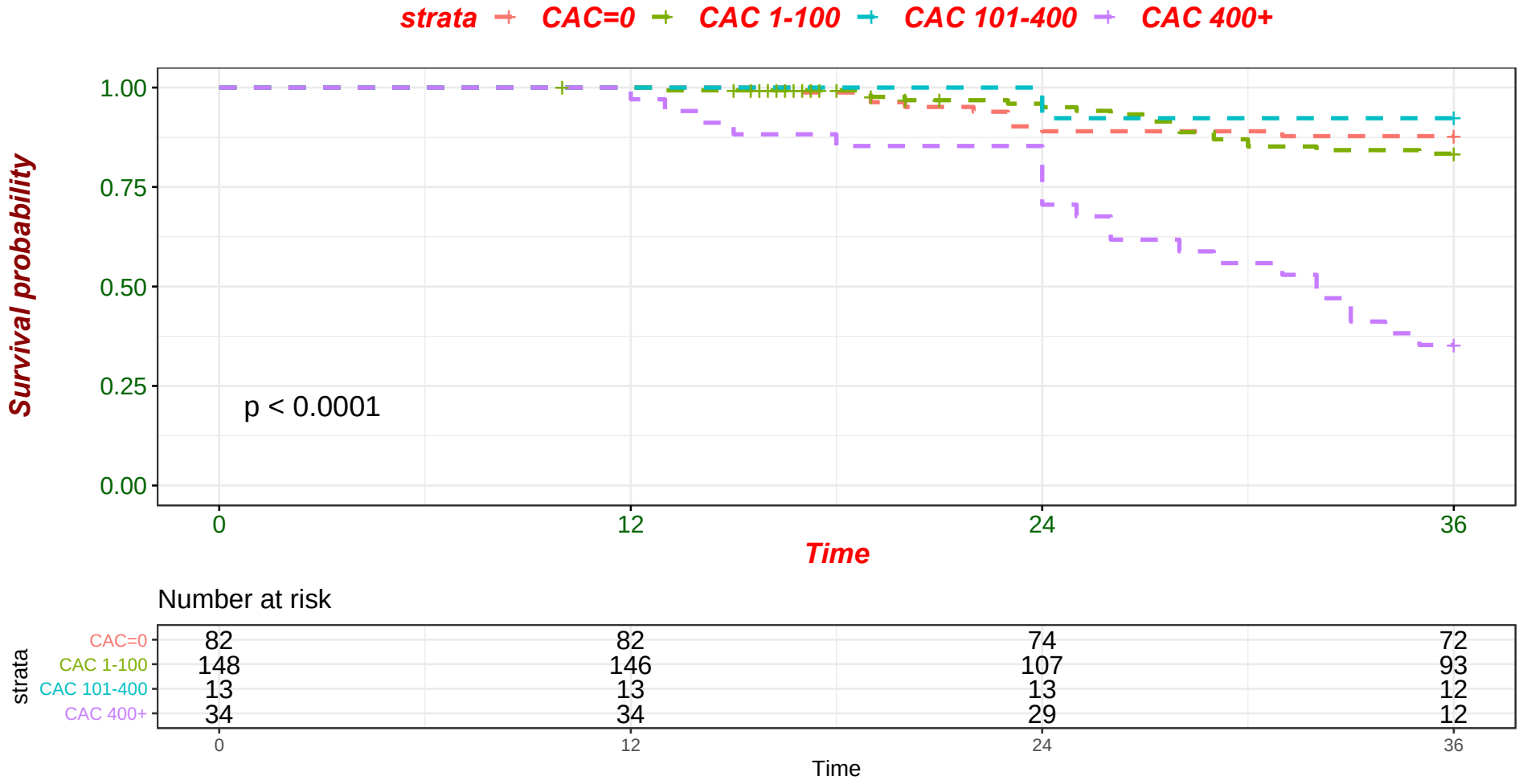
Figure 2B: Survival probability according to CAC burden among non progressors



CAC progression as a marker of risk

Bellasi et al Cells 2021 May 3;10(5):1091. doi: 10.3390/cells10051091

Figure 2C: Survival probability according to CAC burden among progressors

- Disclosures
- **VC progression**
- New treatment
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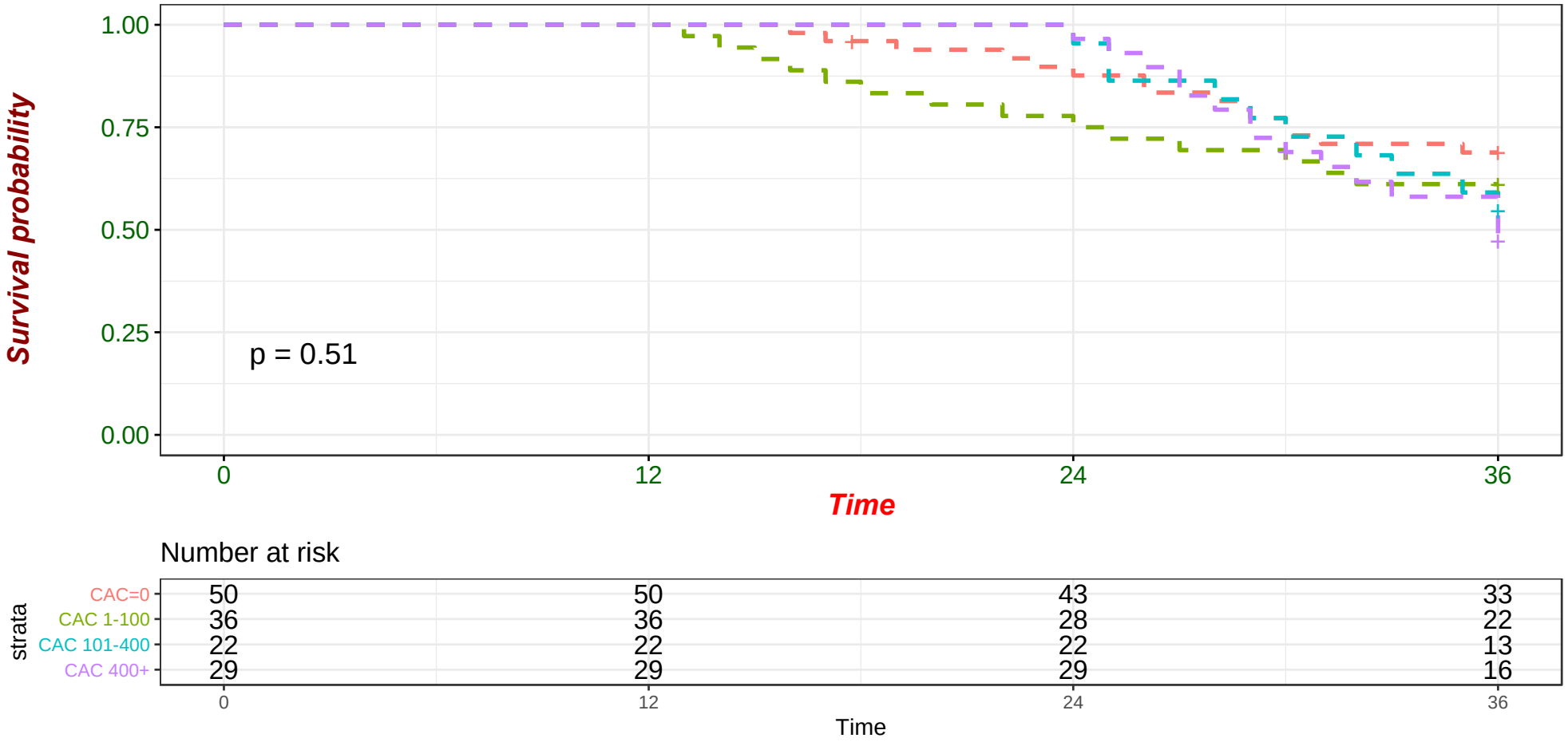

CAC progression as a marker of risk

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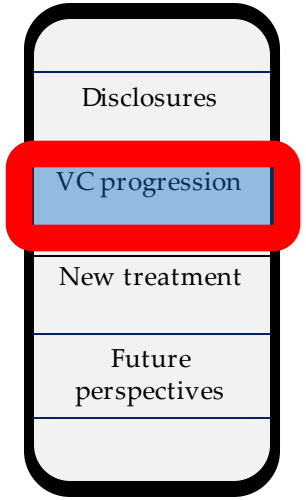


Predictors of all-casue mortality (Cox model) - All subjects n =414 (106 fatalities)				
		95% Confidence interval		
	HR	Lower Boundary	Upper Boundary	Pr(>|z|)
Unadjusted				
Baseline CAC score (log CAC +1) per log increase	1.32252	1.1855	1.4754	<0.001
CAC progression (yes vs no)	4.2082	2.1258	8.3307	<0.001
Interaction term	0.7978	0.6913	0.9207	0.002
Model 1: adjusted for age				
Baseline CAC score (log CAC +1) per log increase	1.3024	1.1671	1.4533	2.34E-06
CAC progression (yes vs no)	4.1393	2.093	8.1863	4.45E-05
Interaction term	0.7939	0.6881	0.9159	0.00156
Model 2: adjusted for model 1 + diabetes + ASCVD + systolic blood pressure				
Baseline CAC score (log CAC +1) per log increase	1.2876	1.1565	1.4335	3.96E-06
CAC progression (yes vs no)	4.2444	2.1608	8.3371	2.71E-05
Interaction term	0.8268	0.7172	0.9531	0.00876
Model 3: adjusted for model 2 + PWV + LVMI				
Baseline CAC score (log CAC +1) per log increase	1.2987	1.171	1.4402	7.34E-07
CAC progression (yes vs no)	5.165	2.6128	10.2101	2.33E-06
Interaction term	0.8019	0.6965	0.9232	0.00213
Model 4 adjusted for model 3 + use of calcium free phosphate binder				
Baseline CAC score (log CAC +1) per log increase	1.1287	1.0114	1.2596	0.03055
CAC progression (yes vs no)	1.9591	0.9214	4.1652	0.08058
Interaction term	0.96	0.8255	1.1164	0.59595

How to modulate VC progression?

Disclosures

VC progression

New treatment

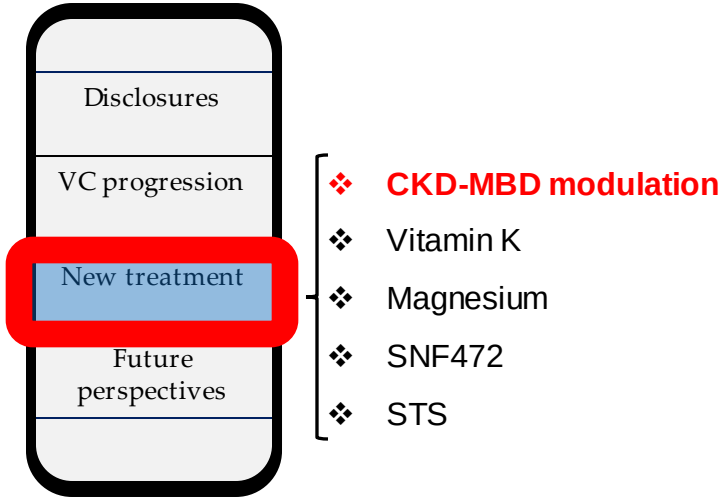
Future perspectives

- CKD-MBD modulation
- Vitamin K
- Magnesium
- SNF472
- STS

How to modulate VC progression?

J Am Soc Nephrol. 2022 May; 33(5): 1011–1032.
Published online 2022 May. doi: 10.1681/ASN.2021101327:
10.1681/ASN.2021101327

PMCID: PMC9063901
PMID: 35232774



Interventions To Attenuate Vascular Calcification Progression in Chronic Kidney Disease: A Systematic Review of Clinical Trials

Chelsea Xu, [1] Edward R. Smith, [1,2] Mark K. Tiong, [1,2] Irene Ruderman, [1,2] and Nigel D. Toussaint [1,2]

(…) interventions were compared with placebo, other comparators, or standard of care. *We reviewed 77 heterogeneous clinical trials (63 randomized)* involving 6898 participants. Therapy involving magnesium or sodium thiosulfate appears the most promising, with consistent findings of attenuation of vascular calcification progression, but *evaluable studies were small and of short duration*. Many other studies had inconclusive or conflicting outcomes (…)

How to modulate VC progression?

OK et al J Am Soc Nephrol 27: 2475–2486, 2016

- Disclosures
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- **CKD-MBD modulation**
- Vitamin K
- Magnesium
- SNF472
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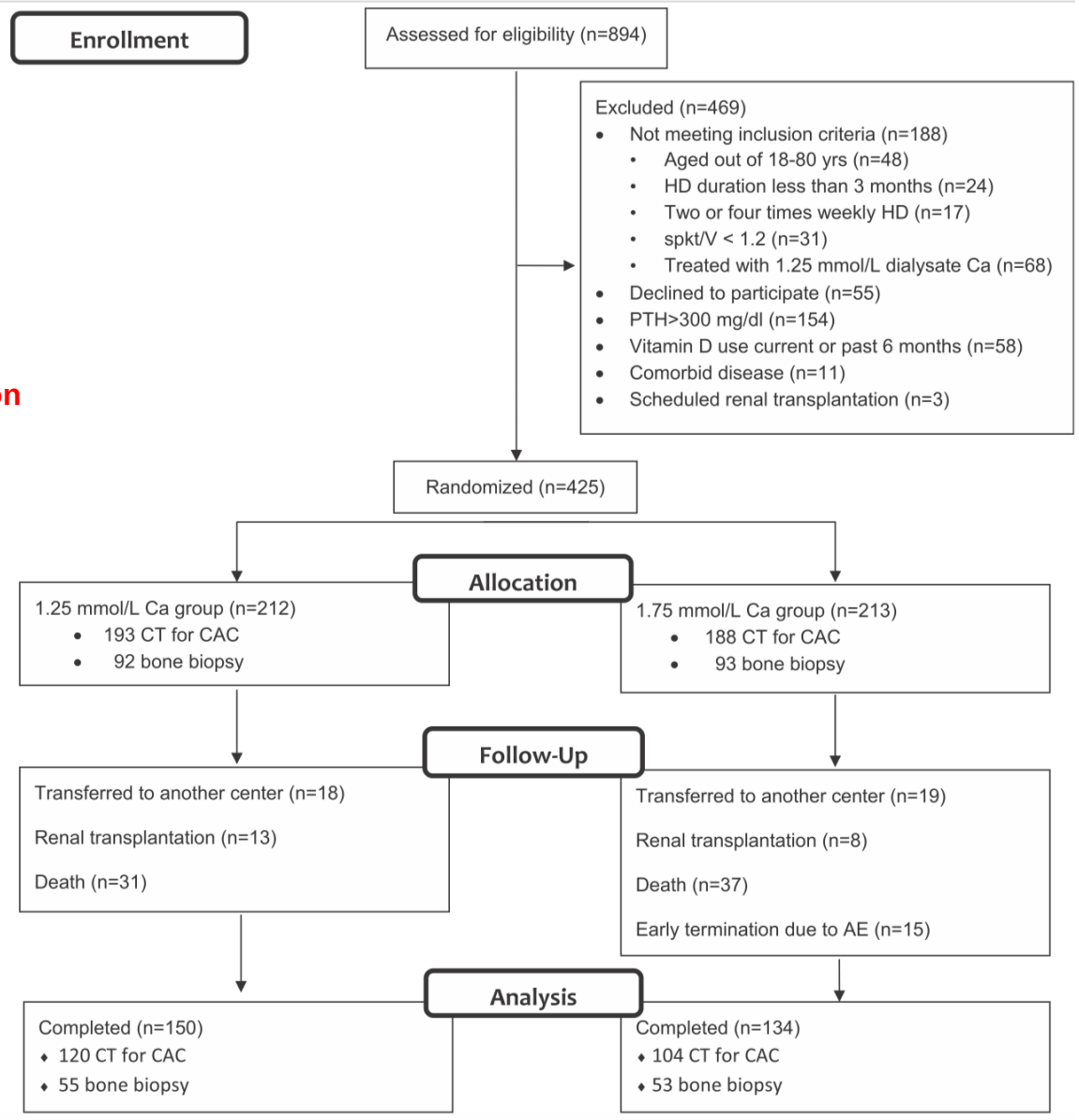

How to modulate VC progression?

OK et al J Am Soc Nephrol 27: 2475–2486, 2016

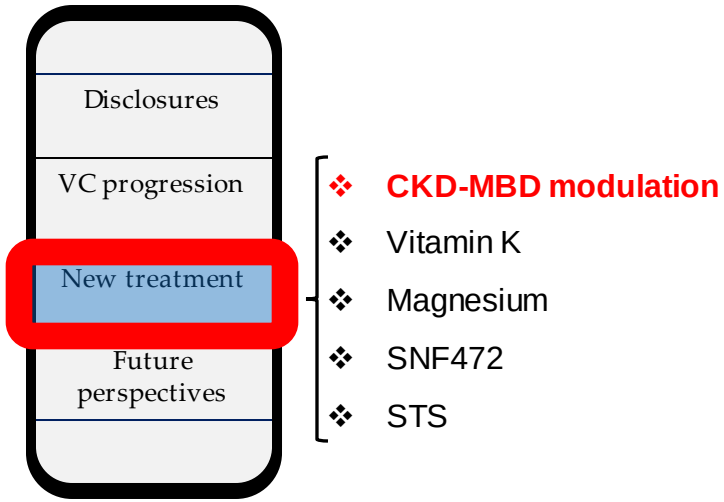

Table 3. CAC scores in treatment groups at baseline and at the end of study

CAC score	1.25 Calcium Group (*n*=120)			1.75 Calcium Group (*n*=104)		
	Baseline	Month 24	*P* Value	Baseline	Month 24	*P* Value
CAC score—Agatston, mean±SD	452±869	616±1086	<0.001	500±909	803±1412	<0.001
CAC score—Agatston, median (interquartile range)	63 (0–504)	99 (0–661)	<0.001	135 (0–586)	258 (10–945)	<0.001
CAC score—volume, mean±SD	351±679	466±821	<0.001	383±698	617±1089	<0.001
CAC score—volume, median (interquartile range)	46 (0–364)	67 (0–530)	<0.001	116 (0–426)	199 (8–728)	<0.001

Table 4. Mean difference in changes of CAC scores between the groups (mean±SD)

Changes in CAC Scores	1.25 Calcium Group (*n*=120)	1.75 Calcium Group (*n*=104)	Mean Difference between Groups (95% Confidence Interval)	*P* Value
Absolute difference				
ΔCAC score—Agatston	160±299	303±624	−138 (−265 to −12)	0.03
ΔCAC score—volume	115±208	234±482	−118 (−214 to −22)	0.01
Transformed difference				
ΔCAC score—Agatston	3.01±3.94	4.79±6.22	−1.77 (−3.13 to −0.42)	0.01
ΔCAC score—volume	2.50±3.38	4.21±5.46	−1.70 (−2.88 to −0.52)	<0.01

How to modulate VC progression?

Disclosures

VC progression

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Future perspectives

- CKD-MBD modulation
- **Vitamin K**
- Magnesium
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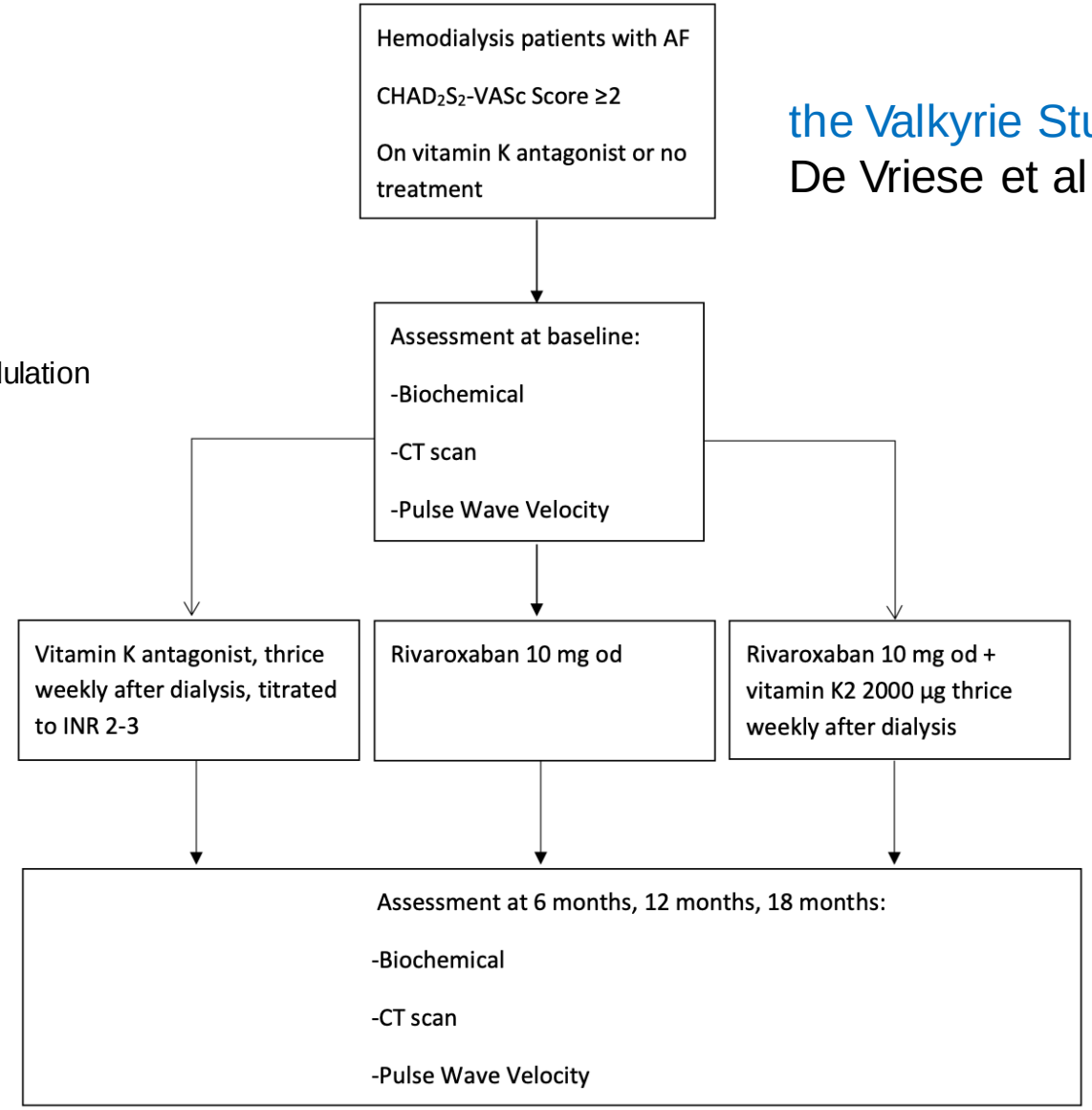
- STS



the Valkyrie Study

De Vriese et al JASN 31: 186–196, 2020

How to modulate VC progression?

the Valkyrie Study

De Vriese et al JASN 31: 186–196, 2020

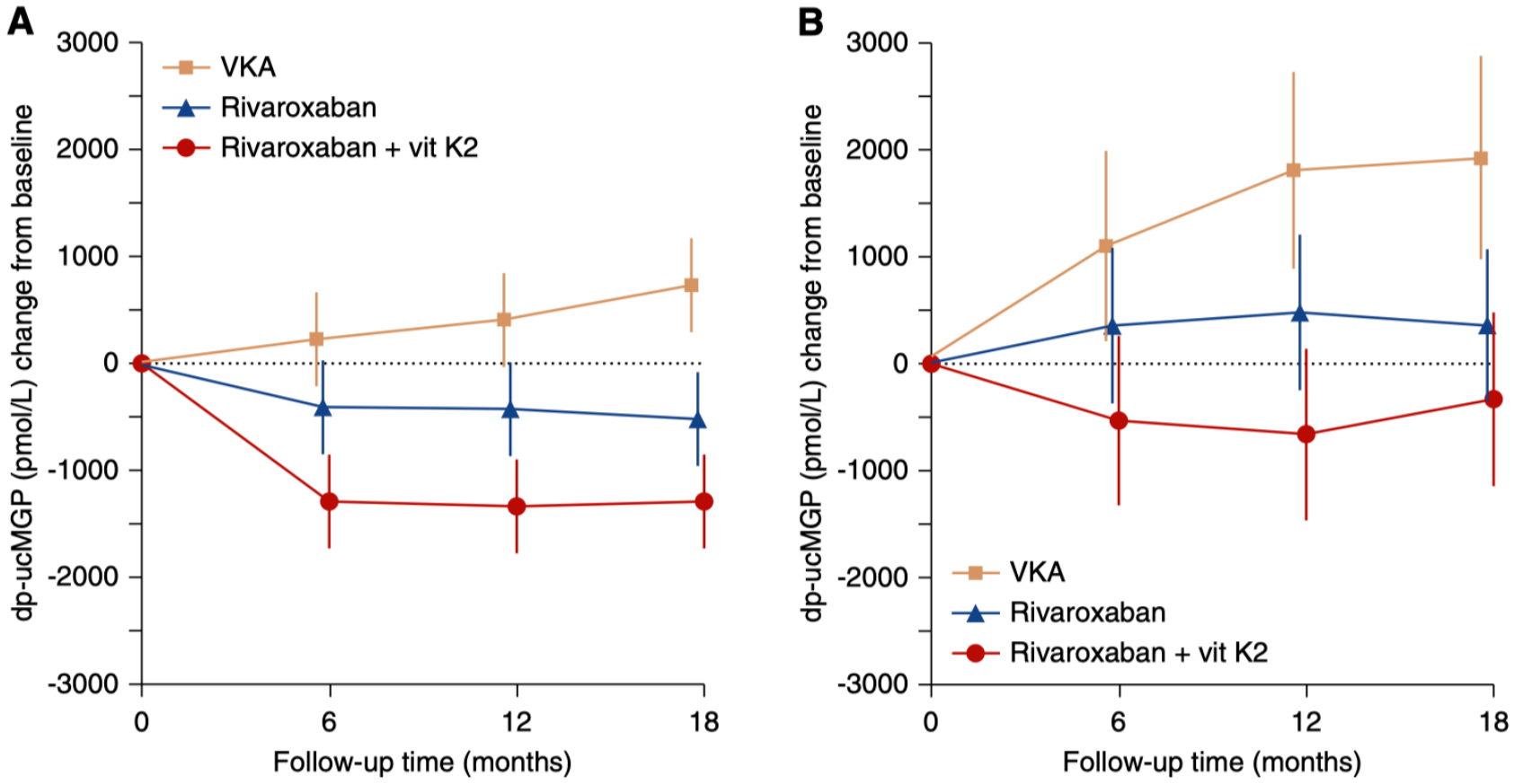
Disclosures

VC progression

New treatment

Future perspectives

- CKD-MBD modulation
- **Vitamin K**
- Magnesium
- SNF472
- STS



How to modulate VC progression?

De Vriese et al JASN 31: 186–196, 2020

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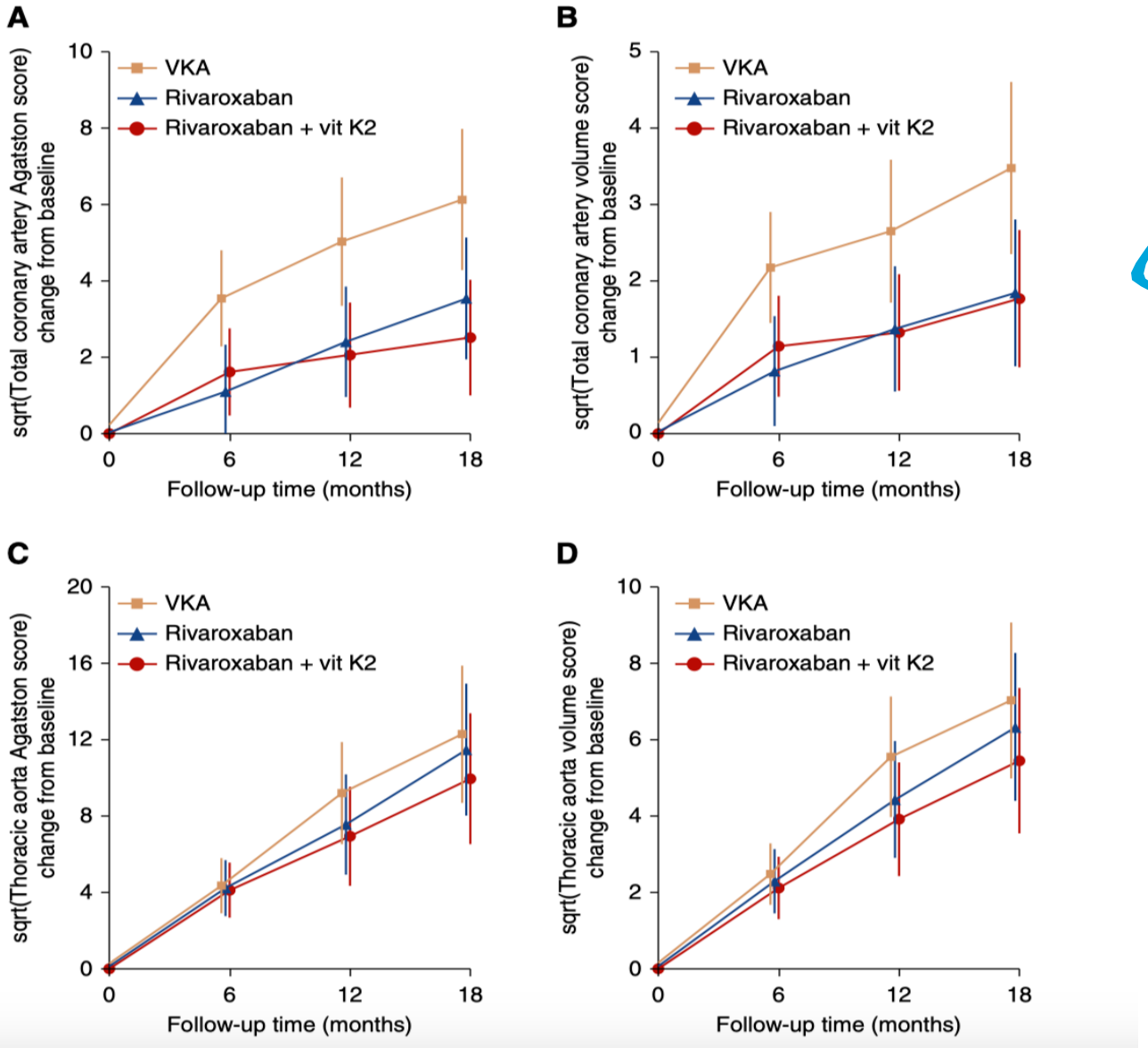

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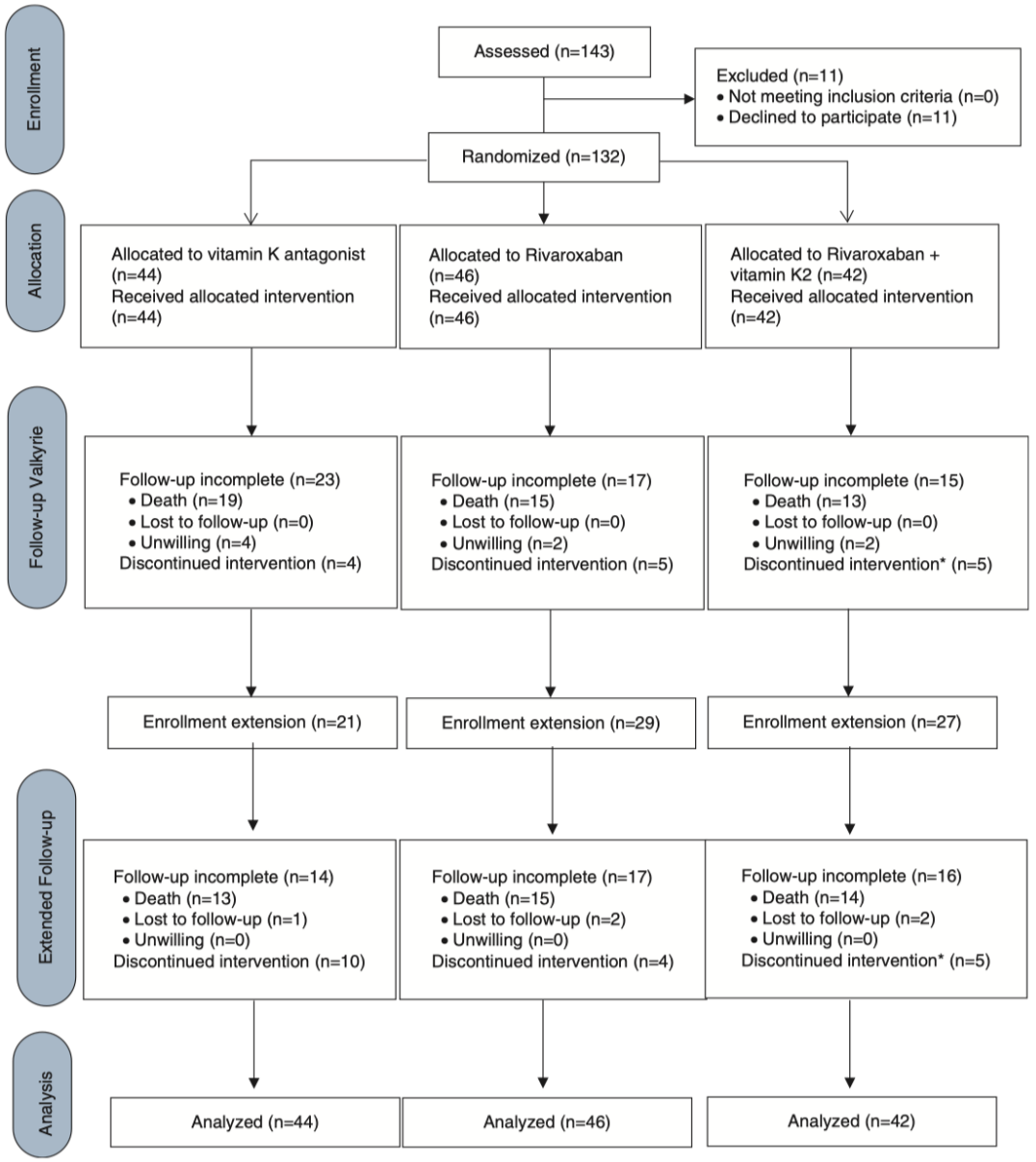

De Vriese et al JASN 32: 1474–1483, 2021

How to modulate VC progression?

De Vriese et al JASN 32: 1474–1483, 2021

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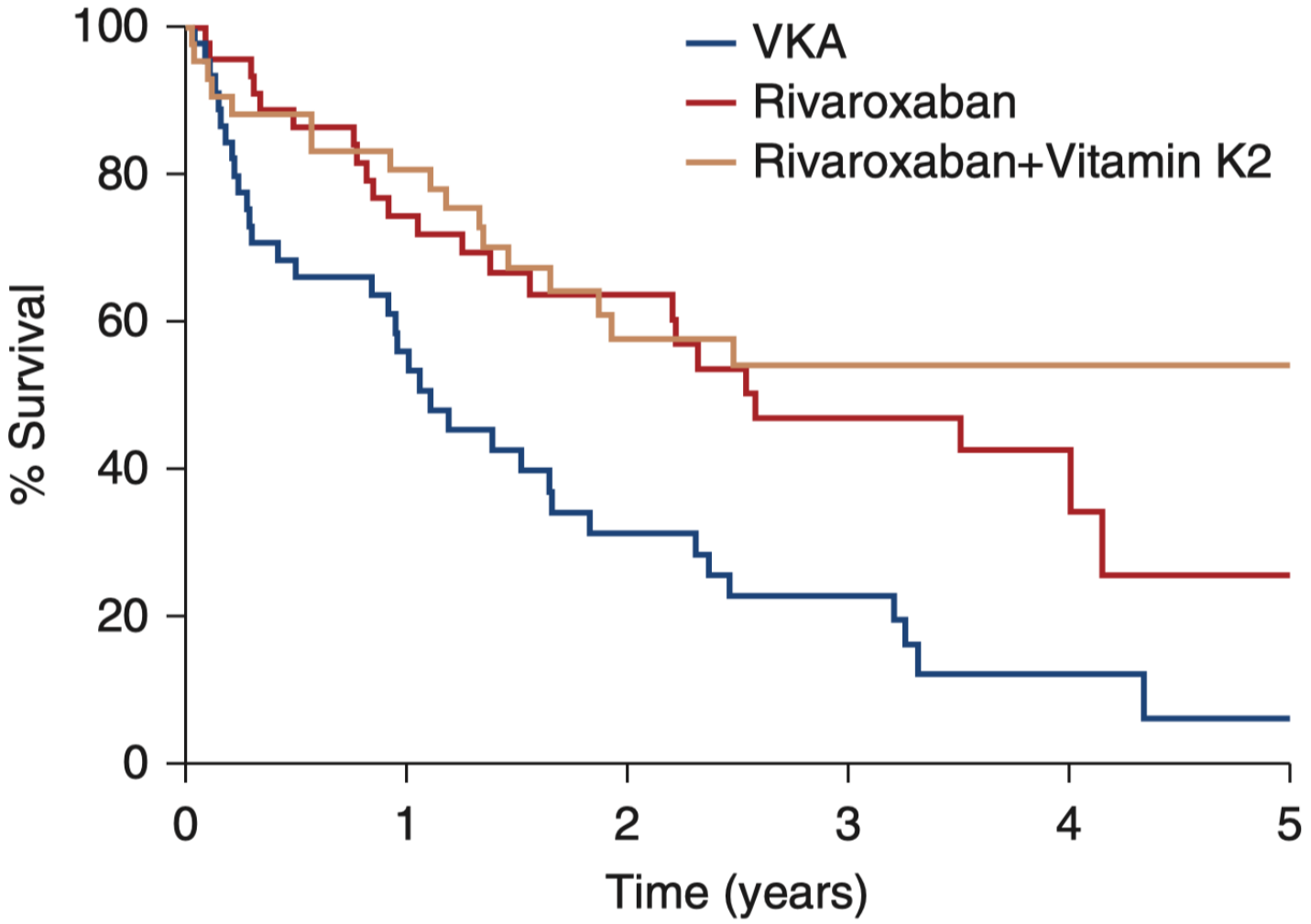

How to modulate VC progression?

Clinical Kidney Journal, 2022, vol. 15, no. 12, 2300–2311

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- New treatment
- Future perspectives

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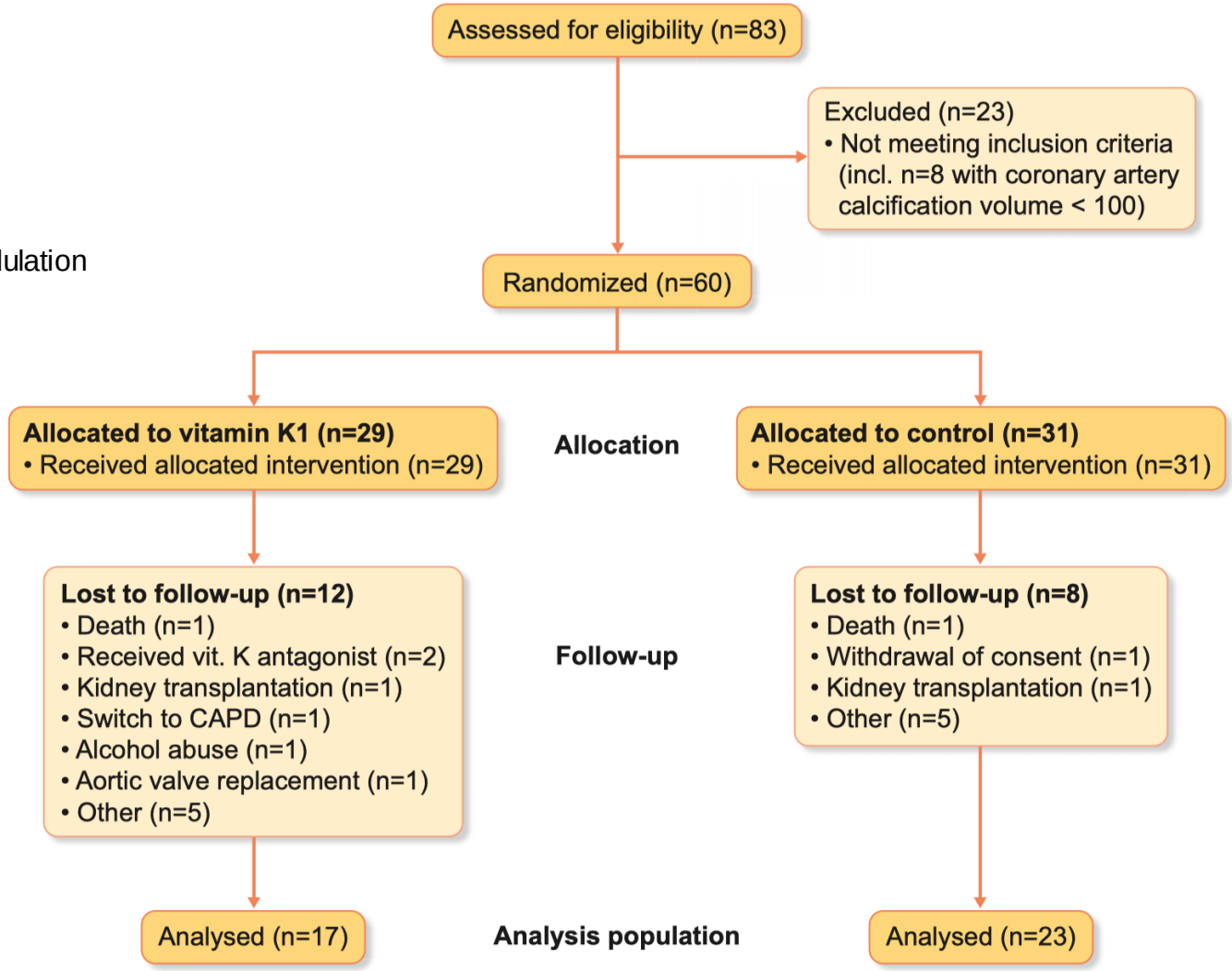

How to modulate VC progression?

Clinical Kidney Journal, 2022, vol. 15, no. 12, 2300–2311

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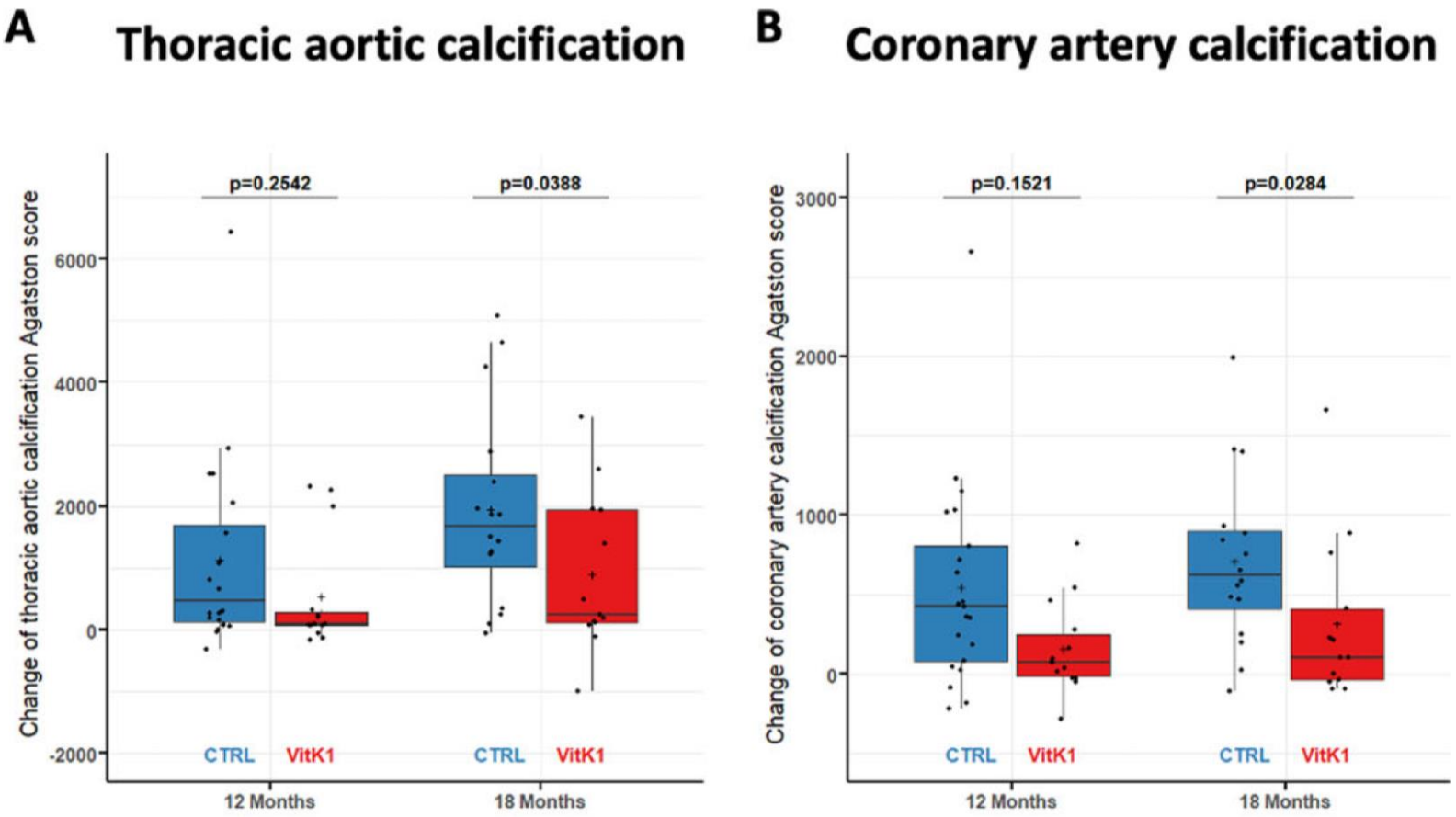
The extent of CAC also increased significantly in both groups between baseline and 18 months



How to modulate VC progression?

Disclosures

VC progression

New treatment

Future perspectives

Vitamin K1 or K2?

- *Eelderink et al American Journal of Transplantation 23 (2023) 520–530:* Effect of vitamin K supplementation on serum calcification propensity and arterial stiffness in vitamin K-deficient kidney transplant recipients: A double-blind, randomized, placebo-controlled clinical trial → *no effect on CPP but positive impact on arterial stiffness*
- *Holden et al Nephrology Dialysis Transplantation (2023) 38: 746–756:* Inhibit progression of coronary artery calcification with vitamin K in hemodialysis patients (the iPACK-HD study): a randomized, placebo-controlled multi-center, pilot trial → *no effect on CAC but higher mortality among treated patients*
- *Oikonomakiet al International Urology and Nephrology (2019) 51:2037–2044:* The effect of vitamin K2 supplementation on vascular calcification in haemodialysis patients: a 1-year follow-up randomized trial → *no effect on aortic calcification*

……On going trials…..

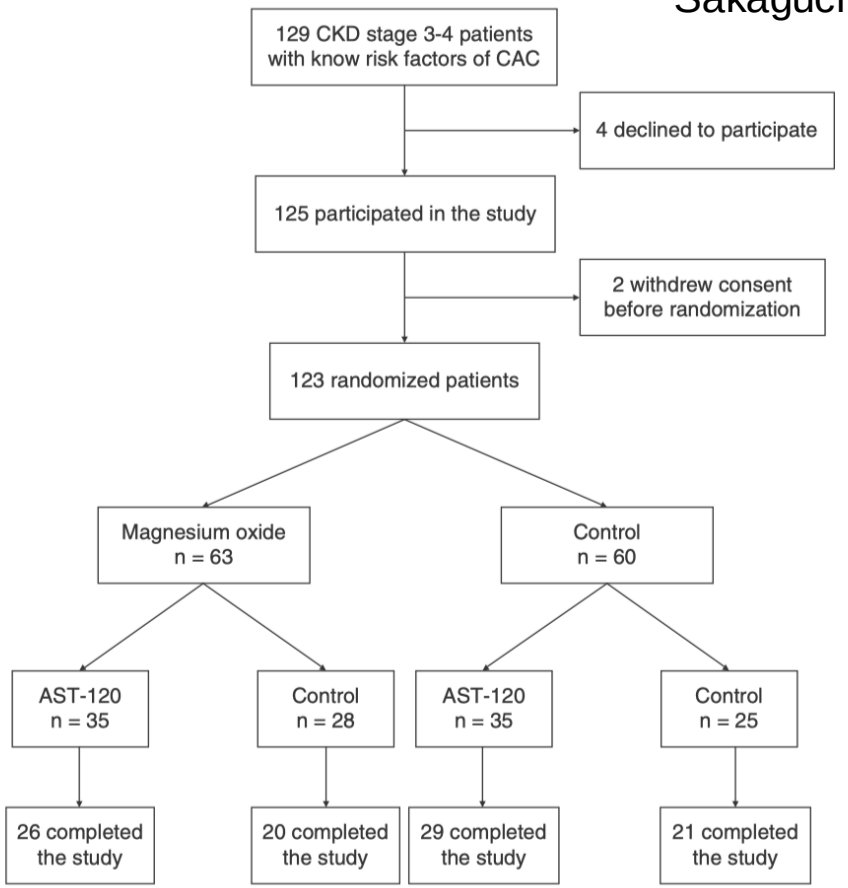
- *Haroon et al. Medicine (2020) 99:36. Treatment to reduce vascular calcification in hemodialysis patients using vitamin K (Trevasc-HDK). A study protocol for a randomized controlled trial*
- *Krueger et al Nephrol Dial Transplant (2014) 29: 1633–1638. Vitamin K1 to slow vascular calcification in haemodialysis patients (VitaVasK trial): a rationale and study protocol*

How to modulate VC progression?

Sakaguchiet al JASN 30: 1073–1085, 2019

- Disclosures
- VC progression
- New treatment
  - ❖ CKD-MBD modulation
  - ❖ Vitamin K
  - ❖ **Magnesium**
  - ❖ SNF472
  - ❖ STS
- Future perspectives

A



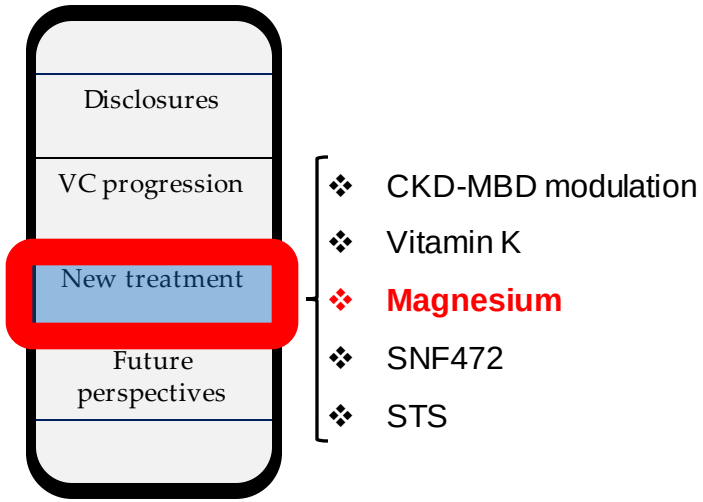
B

		AST-120 arm		
		AST-120	**Control**	Total
Magnesium oxide arm	**Magnesium oxide**	35 (26)	28 (20)	63 (46)
	Control	35 (29)	25 (21)	60 (50)
	Total	70 (55)	53 (41)	123 (96)

Figure 1. A total of 123 patients underwent randomization. (A) Flow chart of the first 125 enrolled patients. (B) The numbers of patients randomized to each group (2×2 factorial design). The numbers in parentheses denote the numbers of patients who completed the study.

How to modulate VC progression?

The study was prematurely terminated after an interim analysis showed that the median change in CAC score was significantly smaller for MgO versus control (11.3% versus 39.5%).



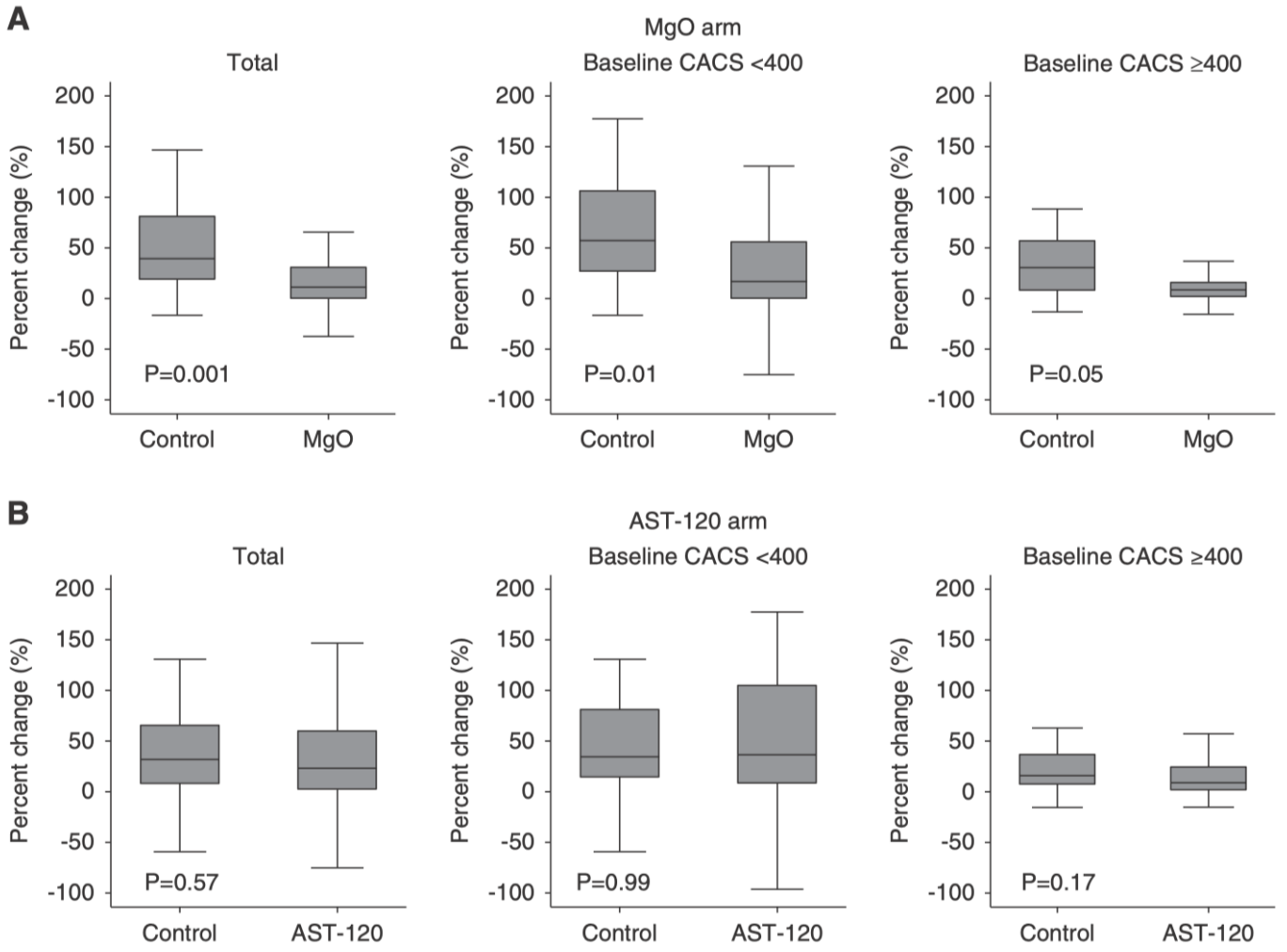


Figure 2. MgO, but not AST-120, retards the progression of CAC. (A) Total patients (*n*=96). (B) Patients with baseline CAC score <400 (*n*=56). (C) Patients with baseline CAC score ≥400 (*n*=40). Percentage changes in CAC scores are compared between groups using the Wilcoxon rank sum test. Data are on the basis of the full analysis set population. CACS, coronary artery calcification score; MgO, magnesium oxide.

Sakaguchiet al
JASN 30: 1073–1085, 2019

How to modulate VC progression?

Bressendorff et al JASN 34: 886–894, 2023.
MAGiCAL-CKD

- Disclosures
- VC progression
- New treatment
- Future perspectives

- CKD-MBD modulation
- Vitamin K
- **Magnesium**
- SNF472
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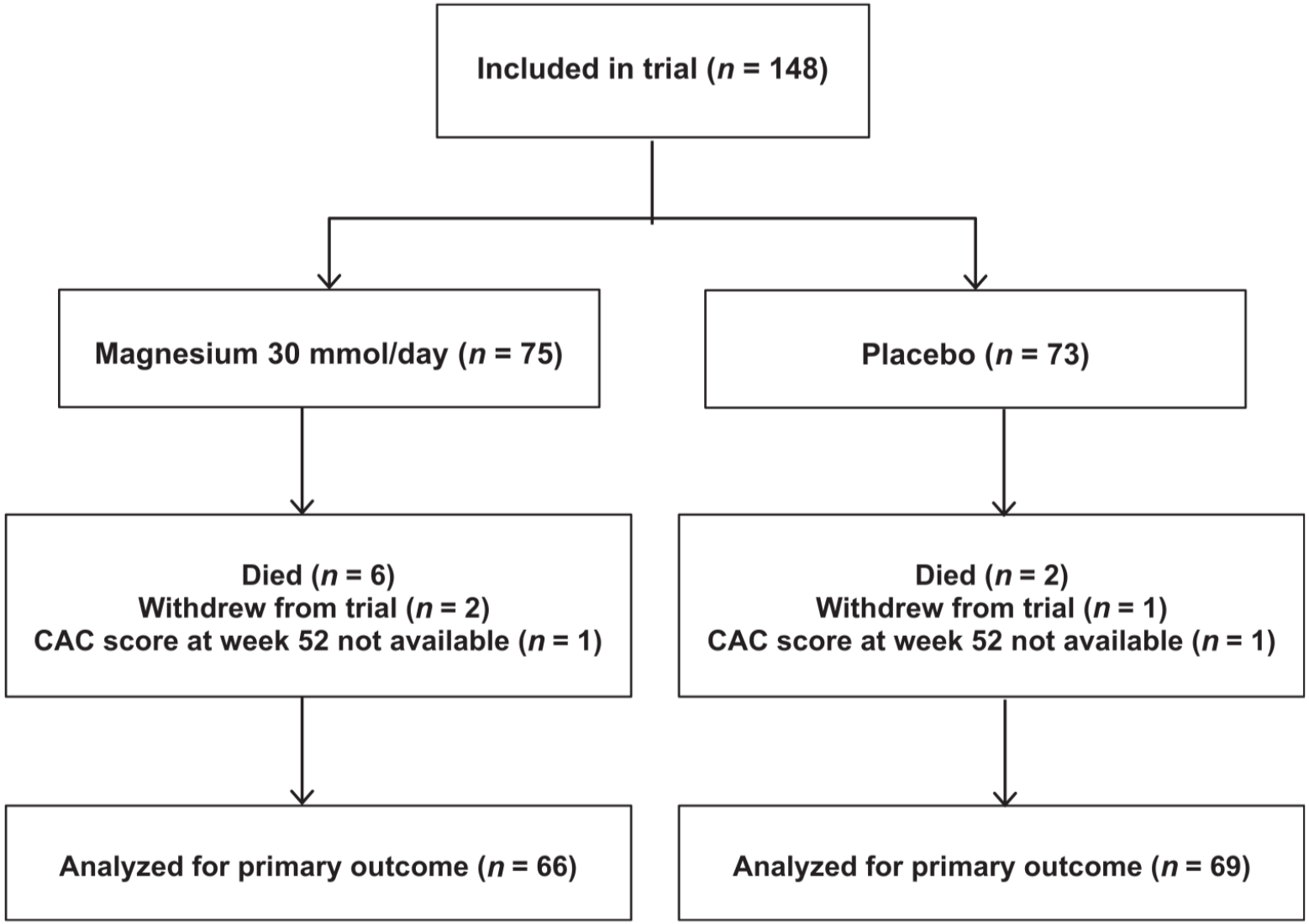
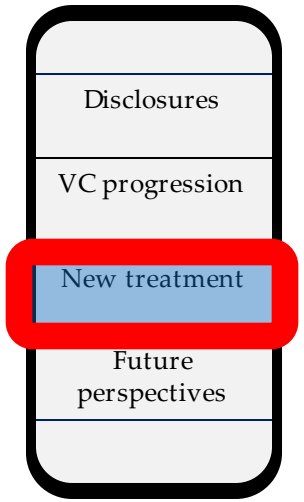


How to modulate VC progression?

Bressendorff et al JASN 34: 886–894, 2023.
MAGiCAL-CKD



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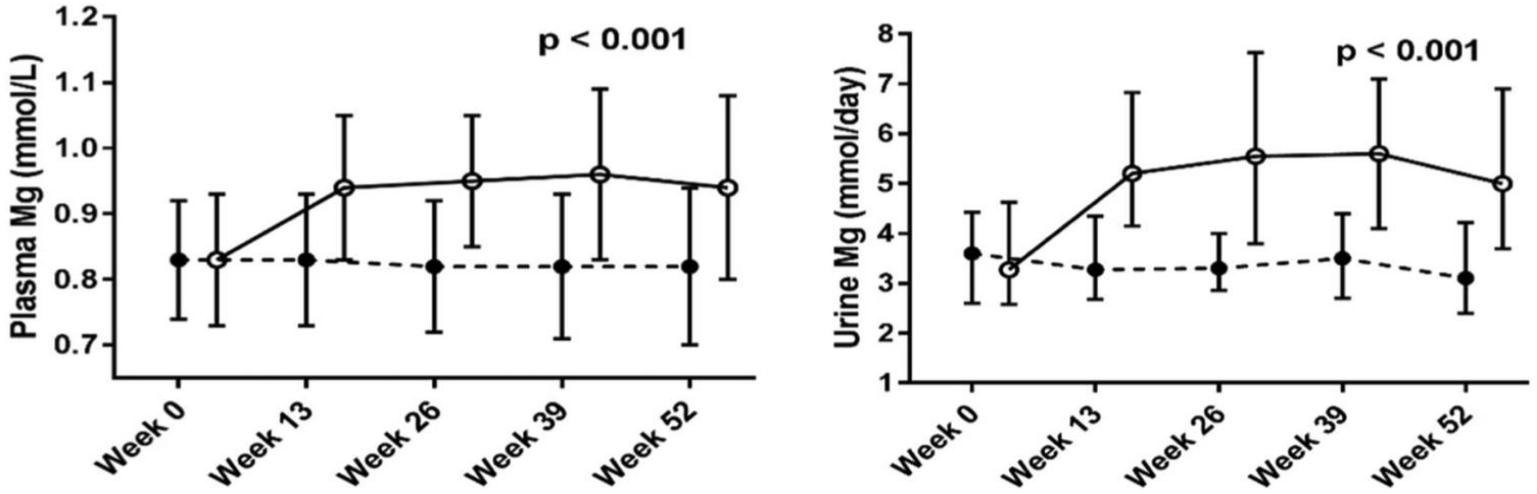

Table 2. Coronary artery calcification scores before and after treatment

Characteristic	CAC Score Week 0 (*n*=66) (Median and Interquartile Range)	CAC Score Week 52 (*n*=69) (Median and Interquartile Range)	Estimated Median Percentage CAC Score Changes Assuming Log-Normal Within-Group Distributions (paired *t*-tests)	Between Groups Difference in Fractional CAC Changes at Week 52 (From ANCOVA Model for Log-Transformed CAC Scores)
Placebo group	247 (21–955)	274 (30–1182)	31.2% (95% CI, 18.5% to 45.2%, *P*<0.001)	
Magnesium group	370 (27–1462)	429 (41–1825)	33.3% (95% CI, 19.9% to 48.2%, *P*<0.001)	
				0.9% (95% CI, –10.2% to 13.4%, *P*=0.438)

Median and interquartile range for subjects with coronary artery calcification scores at week 0 and week 52. Analysis of covariance model adjusted for coronary artery calcification score, age, and prevalent diabetes mellitus at week 0. CAC, coronary artery calcification; ANCOVA, analysis of covariance; CI, confidence interval.

How to modulate VC progression?

Magnesium

……On going trials…..

- Disclosures
- VC progression
- New treatment
- Future perspectives

- *Leenders et al BMJ Open 2022 Nov 21;12(11):e063524. Magnesium in chronic haemodialysis (MAGIC-HD): a study protocol for a randomised controlled trial to determine feasibility and safety of using increased dialysate magnesium concentrations to increase plasma magnesium concentrations in people treated with haemodialysis*
- *Vermeulen et al Trials 2022 Sep 12;23(1):769. Reversal Of Arterial Disease by modulating Magnesium and Phosphate (ROADMAP-study): rationale and design of a randomized controlled trial assessing the effects of magnesium citrate supplementation and phosphate-binding therapy on arterial stiffness in moderate chronic kidney disease*

How to modulate VC progression?

CaLIPSO trial

Bellasi et al Clinical Kidney Journal, 2021:14(1):366–374

Disclosures

VC progression

New treatment

Future perspectives

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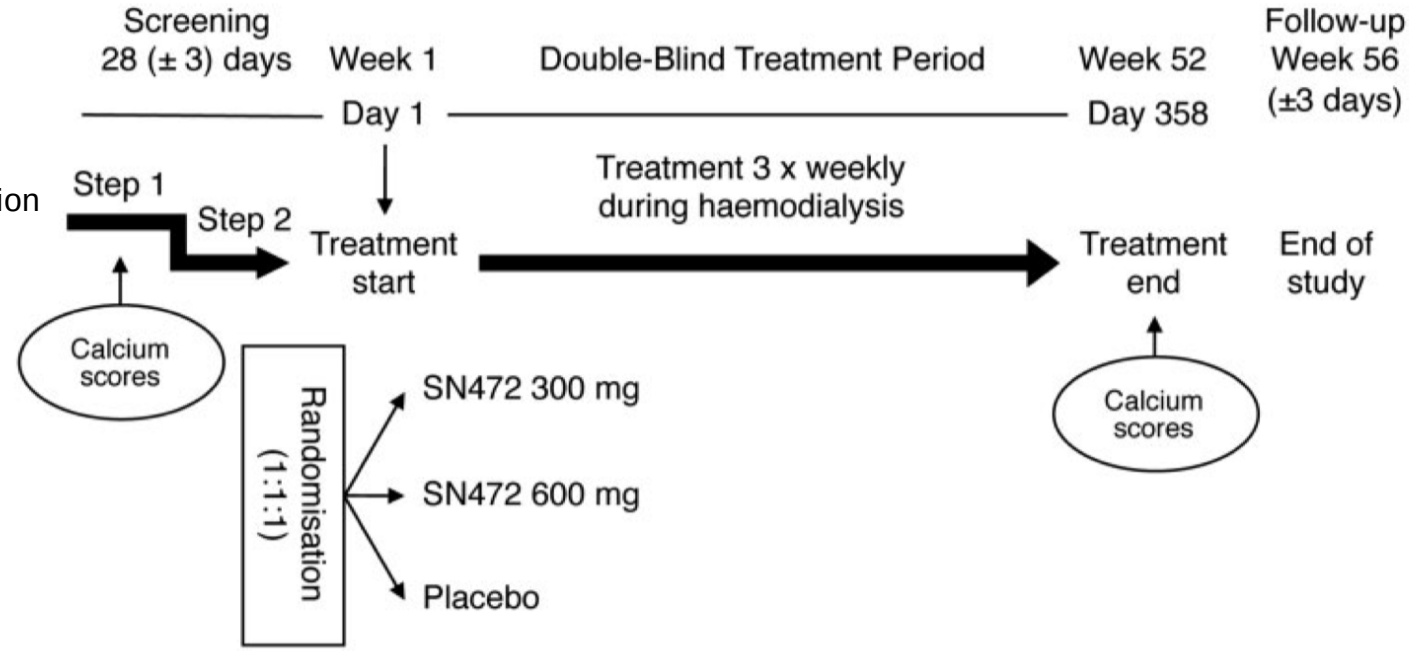

FIGURE 1: CaLIPSO trial flow chart. In Step 1, potential study participants who satisfied the inclusion and exclusion criteria underwent an assessment by MDCT scanner to determine the Agatston score for the coronary artery, as well as dual-energy X-ray absorptiometry for BMD of the total hip and femoral neck. Patients with confirmed calcification of the coronary artery (initially 100–2000 U; later 100–3500 U) at Step 1 entered Step 2 to complete all other screening assessments and confirm all eligibility criteria were met.

How to modulate VC progression?

Disclosures

VC progression

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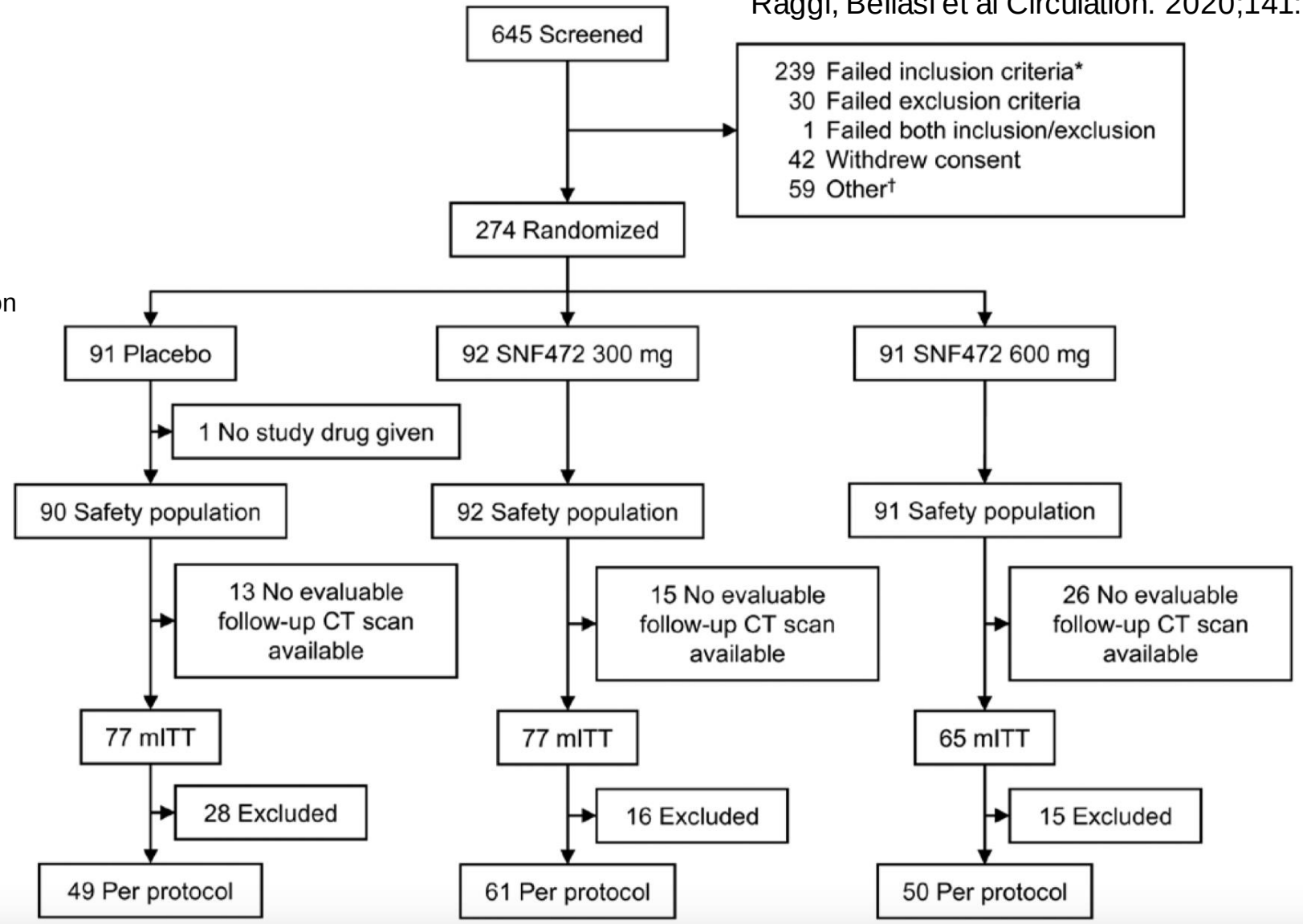
CaLIPSO trial

Raggi, Bellasi et al Circulation. 2020;141:728–739



How to modulate VC progression?

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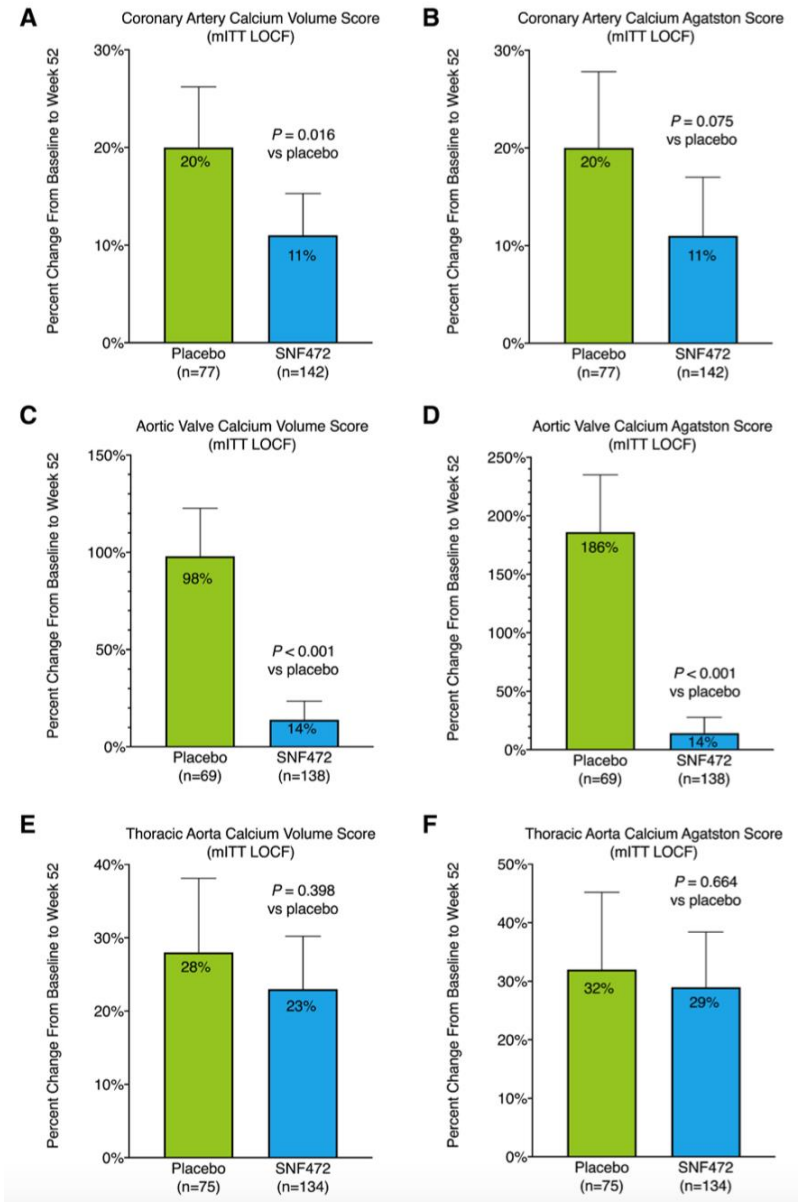

CaLIPSO trial

Raggi, Bellasi et al Circulation. 2020;141:728–739

How to modulate VC progression?

Wen et al. Nephrol Dial Transplant (2023) 38: 733–745

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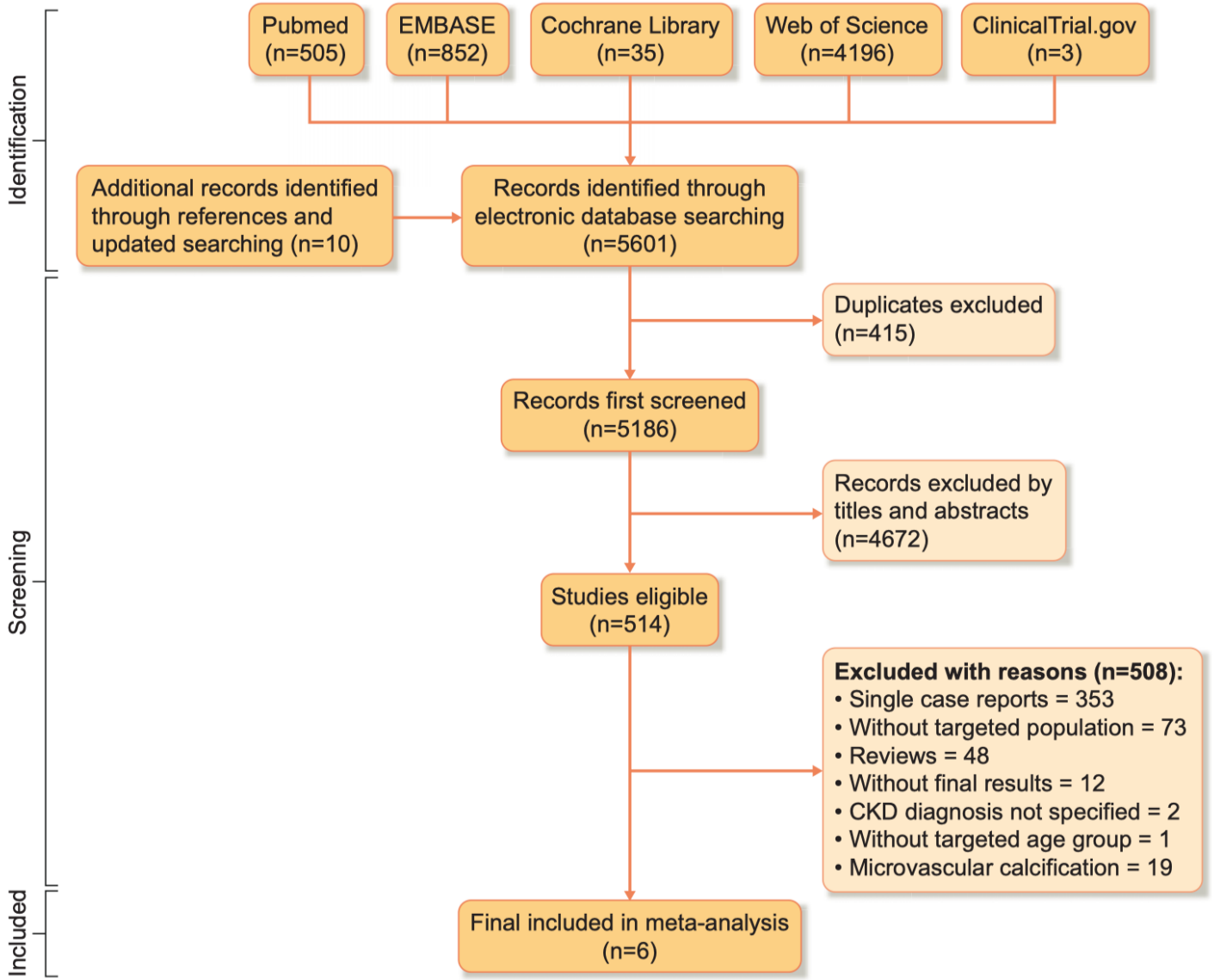

How to modulate VC progression?

Wen et al. Nephrol Dial Transplant (2023) 38: 733–745

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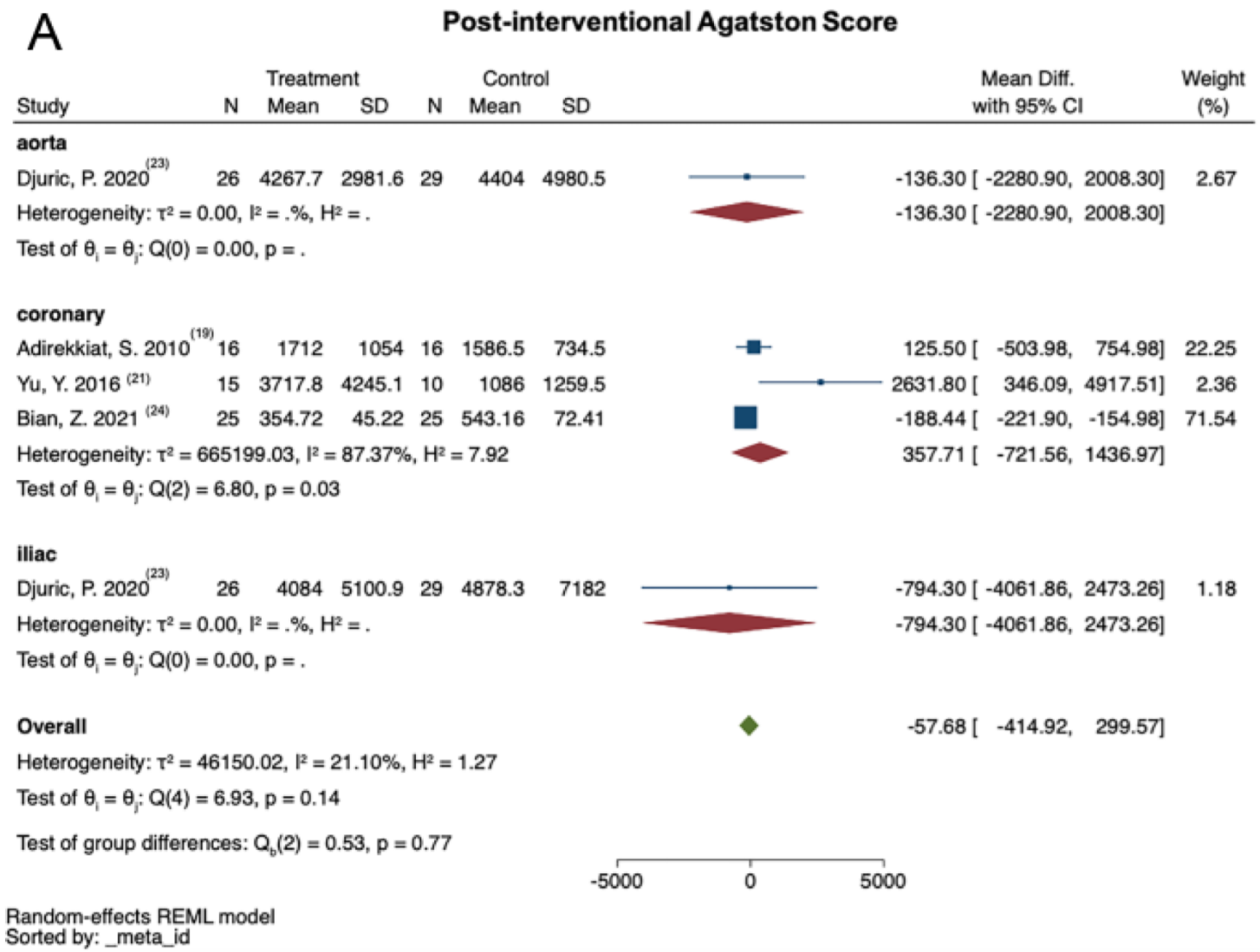
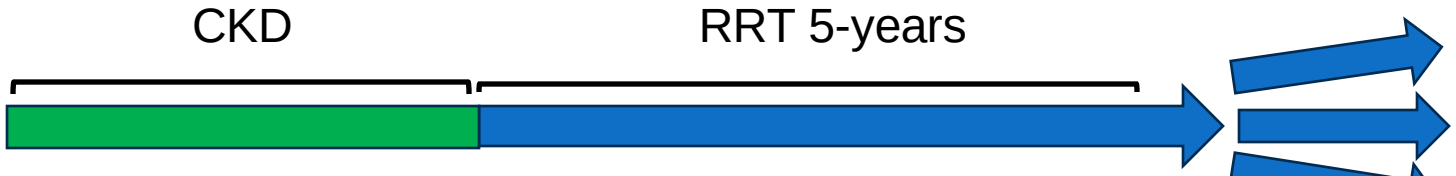


WHAT ARE THE NEXT STEPS?

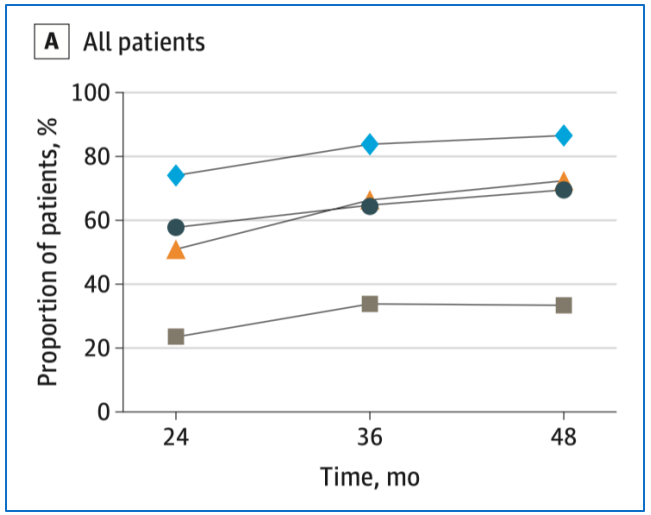
- Define vascular site (CAC vs AoC vs Valvular calcification vs ?)
- Define methodology to assess VC (Agatston vs Volume vs?) and progression (% change vs absolute change vs ?)
- Define patients to be treated:



ERA Registry
(van de Luijtgaarden NDT 2016)

~ 30% Tx
~ 40% HD/PD
~ 30% Death

Zhang et al JAMA Network Open. 2023



WHAT ARE THE NEXT STEPS?

- Define patients to be treated:
  - T50? CPP? Baseline VC

Disclosures

VC progression

Nerw treatment

Future perspectives

WHAT ARE THE NEXT STEPS?

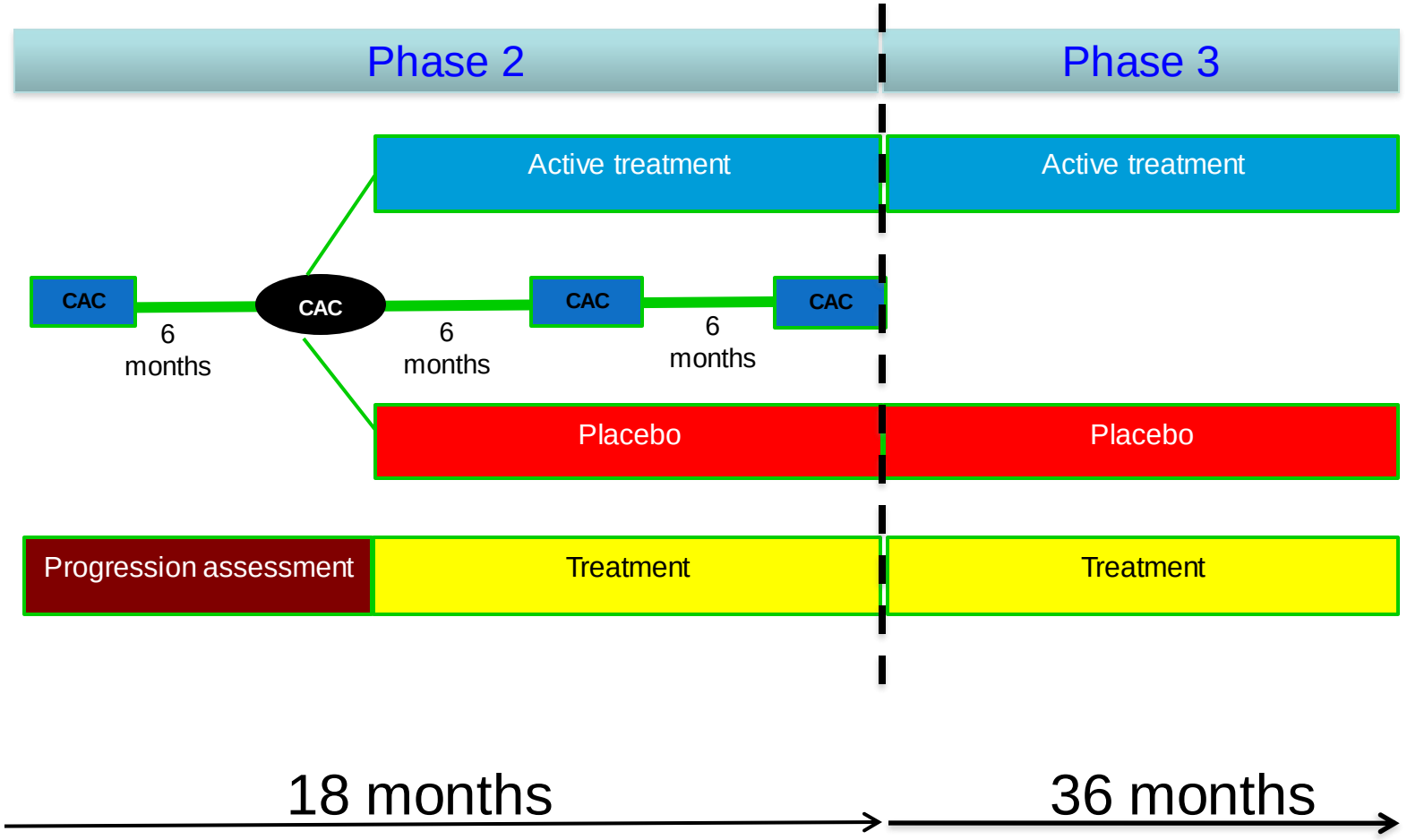
- Hard outcome study?

Disclosures

VC progression

Nerw treatment

Future perspectives



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