



Vitamin **D** and
type **2** diabetes

diabetes prevention research matters

Protocol Deviations

And Lessons Learned

Definition

- A **protocol deviation** is any departure from the protocol procedures.
- Deviations may vary from major to minor.
- Protocol deviations should be avoided.

Major Deviations

- Places participants at added risk
- Results in data that cannot be analyzed

Minor Deviations

- No added risk to participant
- Cumulatively result in negative impact on study

What Happens with Deviations?

- Reported to IRB per local procedures by site staff
- Reported to DSMB by CC

Protocol Deviations in D2d to Date

Inclusion/exclusion criteria not met	5
Noncompliance with study procedures	62
Non-compliance with visit schedule	45

Protocol Deviations in D2d to Date

Inclusion/exclusion criteria not met		5
	Safety lab - serum calcium	2
	Safety lab - GFR	1
	Exclusionary medication	2

Protocol Deviations in D2d to Date

Inclusion/exclusion criteria not met		5
	Safety lab - serum calcium	2
	Safety lab - GFR	1
	Exclusionary medication	2

- Both were = ULN
- Query in EDC now fires for $\geq$ ULN
- Sites need to carefully review I/E criteria

Protocol Deviations in D2d to Date

Inclusion/exclusion criteria not met		5
	Safety lab - serum calcium	2
	Safety lab - GFR	1
	Exclusionary medication	2

- GFR calculated centrally by EDC – local lab calculation cannot be used

Protocol Deviations in D2d to Date

Inclusion/exclusion criteria not met		5
	Safety lab - serum calcium	2
	Safety lab - GFR	1
	Exclusionary medication	2

- Both were WelChol (colesevelam)
- See MOP 8.4 for excluded meds list

Protocol Deviations in D2d to Date

Noncompliance with study procedures		62
	30 minute sample outside of window	22
	5-10 minutes outside of window	15
	>10 min	7
	30 min sample not collected	5
	120 minute sample outside of window	21
	5-10 minutes outside of window	16
	>10 min	5
	Screening pregnancy test not done	8
	2nd blood pressure measurement not taken	1
	Weight not collected	1
	Ate snack prior to 2h blood collection	1

Protocol Deviations in D2d to Date

Non-compliance with visit schedule			45
	Randomization visits outside of window		5
		Outside of window by ≤ 4 days	1
		Outside of window by > 4 days	4
	Follow-up visits outside of window		40
		Outside of window by ≤ 4 days	11
		Outside of window by > 4 days	29

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Schedule of Procedures

Point of Contact	Screening ¹	Baseline	Randomization	M03	M06	M09 (Phone)	M12
	Day -49 to - 7	Day -21 to -5	Day 0	Day 76 to 104	Day 166 to 194	Day 256 to 284	Day 346 to 374

- Screening safety labs must be drawn within 7 weeks of randomization
- Baseline OGTT must occur within 3 weeks of randomization

Avoiding Deviations

- o Remediation plan may be requested by local IRB as well as by CC
- o Ensure all staff are adequately trained on protocol and MOP
- o Re-examine visit procedures and checklists
- o Participants must be well informed from the start, with visits scheduled in advance, and with adequate reminders
- o Inclusion/exclusion criteria must be reviewed and signed off by the site Investigator prior to randomization
- o CC will clarify issues as needed – EDC, MOP, RCS, etc.