EC Minutes from 12.22.16

Present: Bess Dawson-Hughes, Saul Malozowski, Anastassios Pittas, David Robbins, Clifford Rosen, Patricia Sheehan, Myrlene Staten.

Suggestions for new EC reports

EC agreed that reports should focus on retention and protocol fidelity, especially study pill adherence, outside-of-study medications and diabetes outcomes.

- Page 1, recruitment. Once done, show just SCR, BAS, and RAN, RAN goal, % promised and then retire in archives (unless we want to keep as a reminder of number of RAN per site).
- Page 2, Diabetes Outcomes: Add the number of randomized participants at each site (denominator). If easy, we could do this for all figures.
- Present Kaplan Meir curve for diabetes outcomes monthly.
- Pages 3, 4, recruitment. Show until recruitment is done, then retire in archives.
- Page 5, missed encounters. Rank by site (best to worst).
    - Show new 5.A restricting data to last 6 months.
- Page 6, rank by inactive (to concentrate on those that can be brought back).
- Page 7, 8, 9, 10 recruitment. Once done, retire in the archives.
- Page 11: discontinuation of study pills
    - Show new 11.A restricting data to last 6 months.
- Page 12: discontinuation of study pills
    - Add the overall (%) of participants who have discontinued study pills next to the total number.
    - Show new 12.A restricting data to last 6 months.
    - Details about reason for discontinuation will be shared with sites to encourage re-starting study pills.
- New Page (monthly): Participants currently on diabetes medications without a diagnosis of diabetes.
- *In response to Myrlene's email: Wants to use slide from last DSMB meeting in regards to outcomes projections wants it to look exactly like page 10.

Review of DSMB minutes to be completed at next EC call. The CC will provide suggested response to DSMB comments.

High vitamin D level detected outside of PCP

EC reviewed case in which participant had 25OHD level drawn at PCP visit and was told "it was too high" (91 ng/ml, local reference range is 20-80) and PCP recommended to reduce the current dose of vitamin D in half. No prior Vit D levels available. Currently not taking any additional vitamin supplements other than iron.

Following discussion, the following will be added in the FAQ section of the MOP>

Q: We have a participant (Ms. X) who had a vitamin D level drawn by her PCP and was told it was "higher

than the upper limit of normal." What should we do next?

A: The key factors to consider are participant safety and protocol fidelity. Below is the suggested plan of action. Communication with the PCP, preferably verbally, is essential.

Please note that D2d does **not** follow vitamin D level (i.e., 25OHD) because there is no well-established association between a specific threshold and efficacy/toxicity. For safety, D2d follows serum calcium levels and urine calcium creating levels in each participant. Adverse events (hypercalcemia, hypercalciuria, nephrolithiasis) are rare in D2d and no safety signal has been identified by the study Data Monitoring Committee.

Since Ms. X is still taking study it is presumed she had normal serum/urinary calcium levels at prior D2d visits.

1 Please make sure Ms. X is not taking more than one D2d pill/day and not taking out-of-study supplements with high vitamin D content.
2 Please bring Ms. X back for an UNCO visit to run serum calcium (local lab) and urine calcium creatinine level (sent to the central lab), *while on D2d study pill.*
3 If serum calcium or urine calcium creatinine is elevated, the algorithms in the Data Safety Monitoring Plan (MOP section 14) should be followed.
4 If the values are normal, the site investigator or study physician should speak with the PCP and discuss/convey to the PCP that a “high” 25OHD level is not considered unsafe and recommend for Ms. X to continue taking the D2d pill. Reassure PCP and Ms. X that safety variables will be followed and abnormal values will be shared with the PCP.
5 If serum/urine calcium are normal, but Ms. X and/or PCP are still concerned about the “high” 25OHD level and resistant to continuing study pills as prescribed, the D2d study pill may be reduced to 4 times/week (every other day).