

Sun's out? Tongues out! Improved Vitamin D Replacement Utilizing Oral Thin Film Cholecalciferol in Pediatric Patients Post-HSCT

Allison L. Bartlett, MD¹, Gregory Wallace, DO¹, Stacie McLean, MSN, RN, CPNP¹, Kasiani C. Myers, MD¹, Ashley Teusink-Cross, PharmD, MBA, BCPS¹, Cynthia Taggart, RD, LD¹, Evelyn Nguyen, CRC¹, Adesuwa Ekunwe, CRC¹, Jennifer Bravo, CRC¹, Bhaumik Patel³, Robert Davidson³, Vered Gigi³, Stella M. Davies, MBBS, PhD, MRCP¹ and Sonata Jodele, MD¹

1. Cincinnati Children's Hospital Medical Center, Division of Bone Marrow Transplantation and Immune Deficiency; 2. Cincinnati Children's Hospital Medical Center, Department of Nutrition Therapy; 3. CURE Pharmaceutical, Oxnard, CA



BACKGROUND

- Vitamin D deficiency is common in childhood, pervasive before and after hematopoietic stem cell transplantation (HSCT)¹
- Vitamin D deficiency has been associated with increased incidence of graft versus host disease (GVHD) and decreased survival in patients undergoing HSCT^{1,2}
- Attempts to improve vitamin D deficiency in these patients with additional doses/higher dosing of enteral vitamin D are often not successful^{2,3}
- Numerous barriers impede adequate replacement with conventional vitamin D therapy:
 - Malabsorption secondary to gut GVHD
 - Inability to take capsules
 - Mucositis
 - Kidney disease
 - Liver disease
 - Infection
- Herein, we aim to understand if a novel formulation of vitamin D, delivered as an oral thin film (OTF), can help us achieve therapeutic levels of vitamin D in this vulnerable population



Figure 1. Cholecalciferol Oral Thin Film Strips, each containing 40,000 IU Vitamin D3 (1000 mcg cholecalciferol)

HYPOTHESIS

We hypothesized that a different formulation of cholecalciferol, administered as an oral thin film (OTF), would improve ease of administration, restoring compliance and facilitating therapeutic vitamin D levels in patients who failed to achieve or sustain adequate vitamin D levels with current standard of care.

METHODS

- We enrolled 24 patients (20 evaluable) post-HSCT with 25OHD levels ≤ 35 ng/mL, or not tolerating standard enteral supplementation
- Cholecalciferol OTF strips were provided by CURE Pharmaceutical, each OTF contains 40,000 IU Vitamin D3 (1000 mcg cholecalciferol)
- Patients received dosing of Cholecalciferol OTF based on weight and baseline vitamin D level for twelve weeks while we monitored changes in serum Vitamin D levels, per standard of care
- Dosing was titrated based on response and pharmacokinetics of the individual, in accordance with current standard of care (Figure 2)

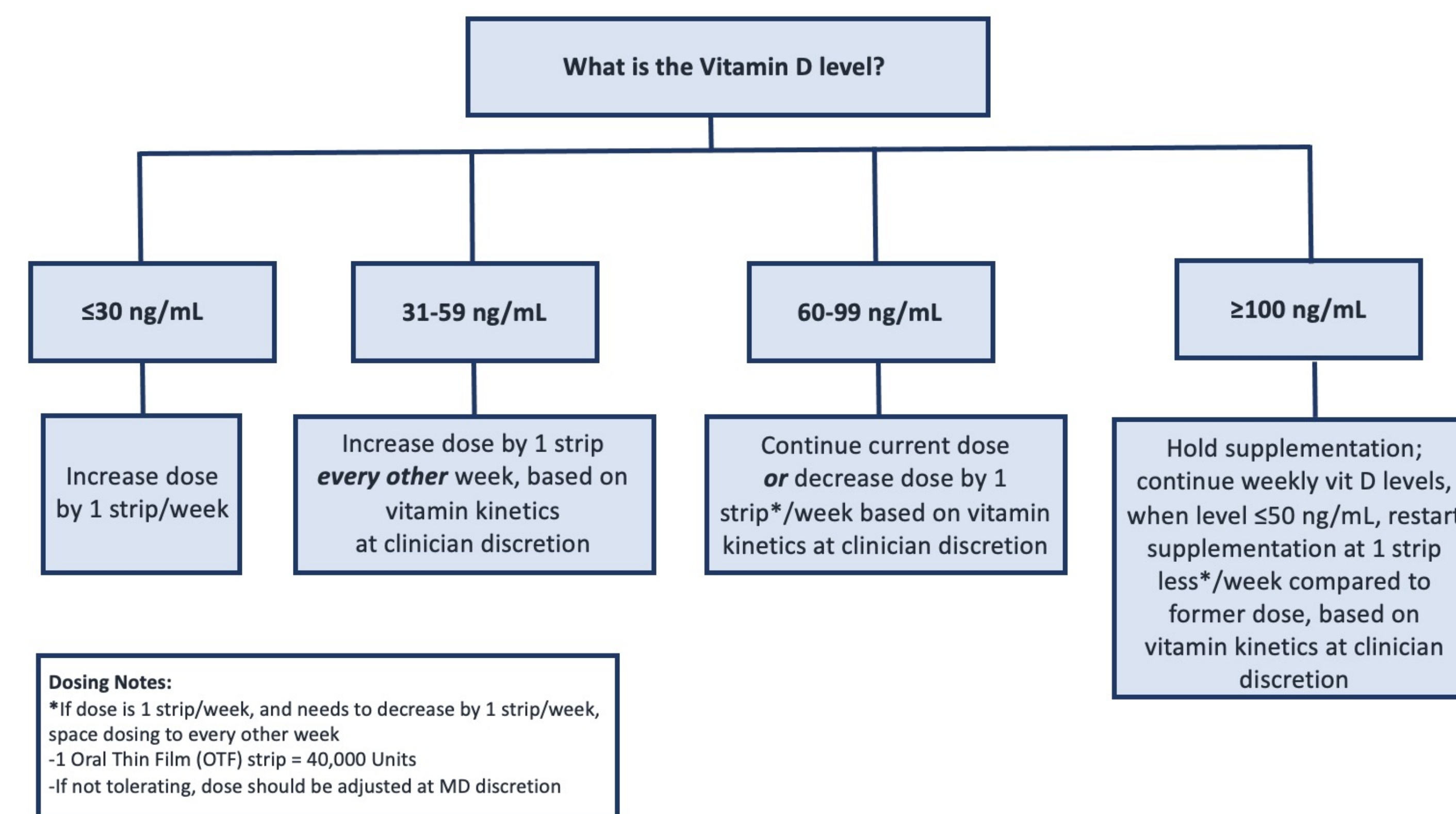


Figure 2. Vitamin D OTF Dosing Schematic

RESULTS

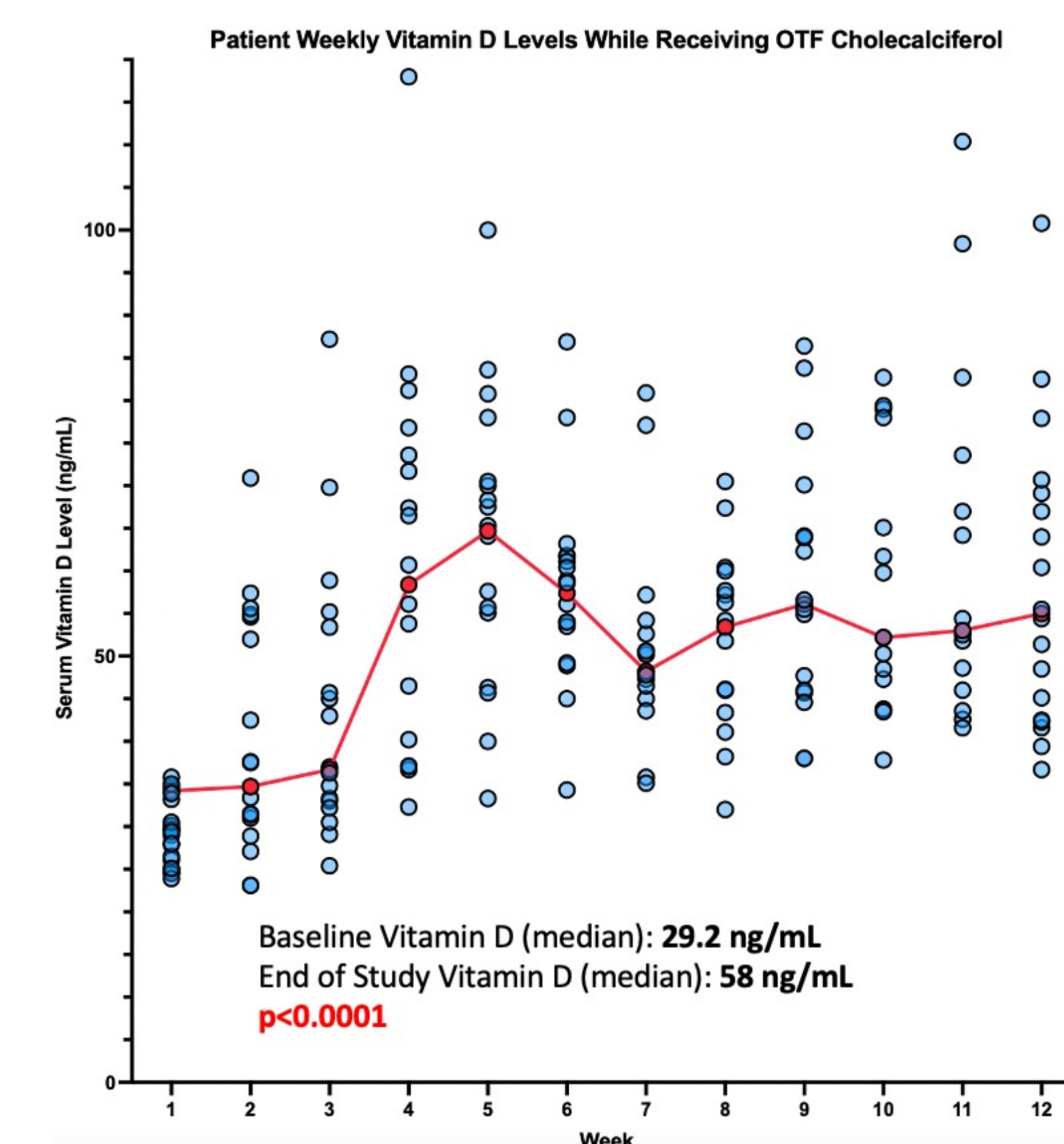


Figure 3(a) Weekly patient vitamin D levels are shown at baseline through 12 weeks on study. Each blue dot represents 1 patient, median values each week shown in red.

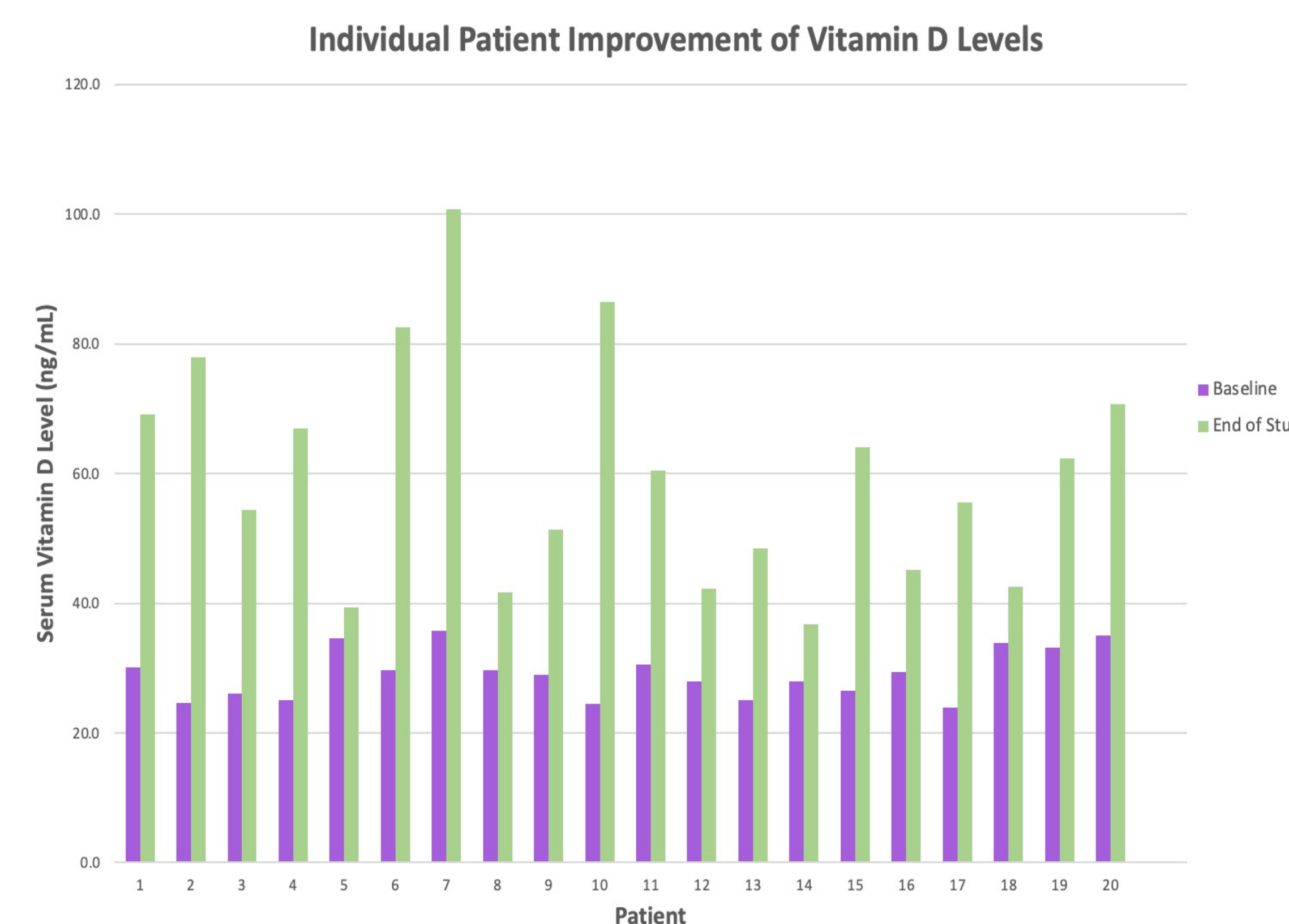


Figure 3(b) Individual patient vitamin D levels are shown at baseline and end of study, demonstrating marked improvement. Median improvement in vitamin D levels was 29.5 ng/mL at the end of study.

DISCUSSION

- Marked improvement in serum vitamin D levels was observed in all patients transitioned from standard of care vitamin D capsules to oral thin film cholecalciferol formulation
- Compliance and tolerance likewise improved, with patients and parents expressing a preference for the strips
- Median age of our cohort was 8 years, range: 1-28 years old
- Dosing varied significantly, from 1 strip monthly to 4 strips weekly
- All patients showed improvement in serum vitamin D levels by week 4 on study
- Median vitamin D level at baseline was 29.4 ng/mL, significantly improved ($p < 0.0001$) to 55.5 ng/mL at the end of study
- No toxicity was observed
- Of 24 patients enrolled, 20 patients were evaluable; 1 patient did not like the taste, 2 patients did not like the texture, 1 non-compliant

CONCLUSIONS

- Vitamin D supplementation delivered as a novel formulation, utilizing oral thin film, is safe, effective and very well tolerated amongst our pediatric population post-hematopoietic stem cell transplantation
- Serum vitamin D levels rose in all patients within 4 weeks
- We noted improved patient compliance and satisfaction with this formulation, as compared to our standard of care, across a wide range of ages

FUTURE DIRECTIONS

- We are eager to explore other therapeutics which might be optimized by this mode of delivery
- We are working with our colleagues in other subspecialties to help improve delivery of care for other patients who face barriers to vitamin supplementation similar to those seen in post-HSCT patients

REFERENCES

- Wallace G, Jodele S, Howell J, et al. Vitamin D Deficiency and Survival in Children after Hematopoietic Stem Cell Transplant. *Biol Blood Marrow Transplant.* 2015;21(9):1627-1631.
- Wallace G, Jodele S, Myers KC, et al. Vitamin D Deficiency in Pediatric Hematopoietic Stem Cell Transplantation Patients Despite Both Standard and Aggressive Supplementation. *Biol Blood Marrow Transplant.* 2016;22(7):1271-1274.
- Wallace G, Jodele S, Myers KC, et al. Single Ultra-High-Dose Cholecalciferol to Prevent Vitamin D Deficiency in Pediatric Hematopoietic Stem Cell Transplantation. *Biol Blood Marrow Transplant.* 2018;24(9):1856-1860.