

Supplementary Appendix

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

Supplement to: Tang JY, Mackay-Wiggan JM, Aszterbaum M, et al. Inhibiting the hedgehog pathway in patients with the basal-cell nevus syndrome. *N Engl J Med* 2012;366:2180-8.

Supplemental Appendix to manuscript "Inhibition of the Hedgehog Pathway in Basal Cell Nevus Syndrome Patients." J. Y. Tang, E. H. Epstein.

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Supplemental Table 1.

Grades 1 and 2 Adverse Events, No. (%)

Adverse Event	Placebo (N=15)	Vismodegib (N=26)	P-Value
Hair Loss	1 (7)	16 (62)	0.004
Muscle Cramps	0 (0)	21 (81)	<0.001
Taste Disturbance	1 (7)	22 (85)	<0.001
>5% Weight Decrease	0 (0)	11 (42)	0.003
GI upset	1 (7)	5 (19)	0.14
Headache	2 (13)	2 (8)	0.59
Acne	1 (7)	3 (12)	0.60
Fatigue	0 (0)	2 (8)	0.25
Rash	0 (0)	2 (8)	0.25
Angioedema	0 (0)	1 (4)	0.42
Common Cold	0 (0)	1 (4)	0.42
Light Sensitivity	0 (0)	1 (4)	0.42

Grades 3 and 4 Adverse Events, No. (%)

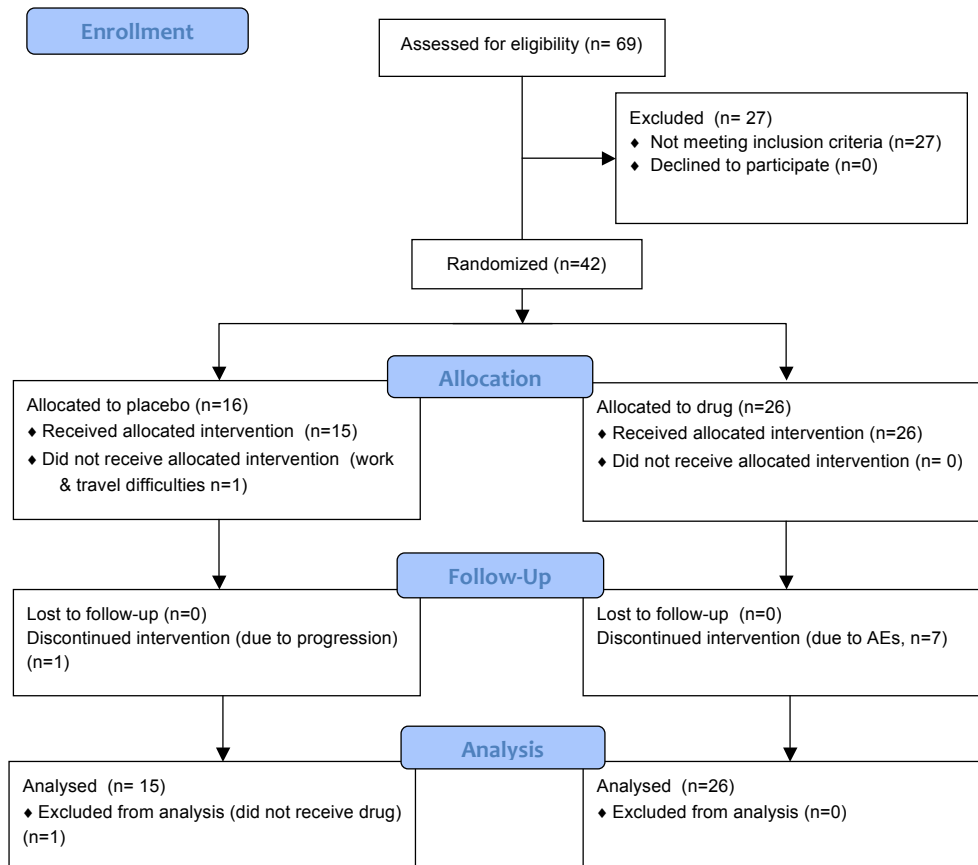
Muscle Cramps	0 (0)	1 (4)	0.42
Atrial Flutter	0 (0)	1 (4)	0.42
Cardiac stent for blocked artery	1 (7)	0 (0)	0.17
Recurrence of metastatic prostate cancer	0 (0)	1 (4)	0.42
Colitis	0 (0)	1 (4)	0.42

Squamous Cell Carcinoma of Larynx	0 (0)	1 (4)	0.42
Knee Replacement Surgery	0 (0)	1 (4)	0.42
Hip Replacement Surgery	0 (0)	1 (4)	0.42
Mysenteric Cyst	0 (0)	1 (4)	0.42
Pneumonia	0 (0)	1 (4)	0.42
Suicide Attempt	0 (0)	1 (4)	0.42
Hysterectomy	1 (7)	0 (0)	0.17

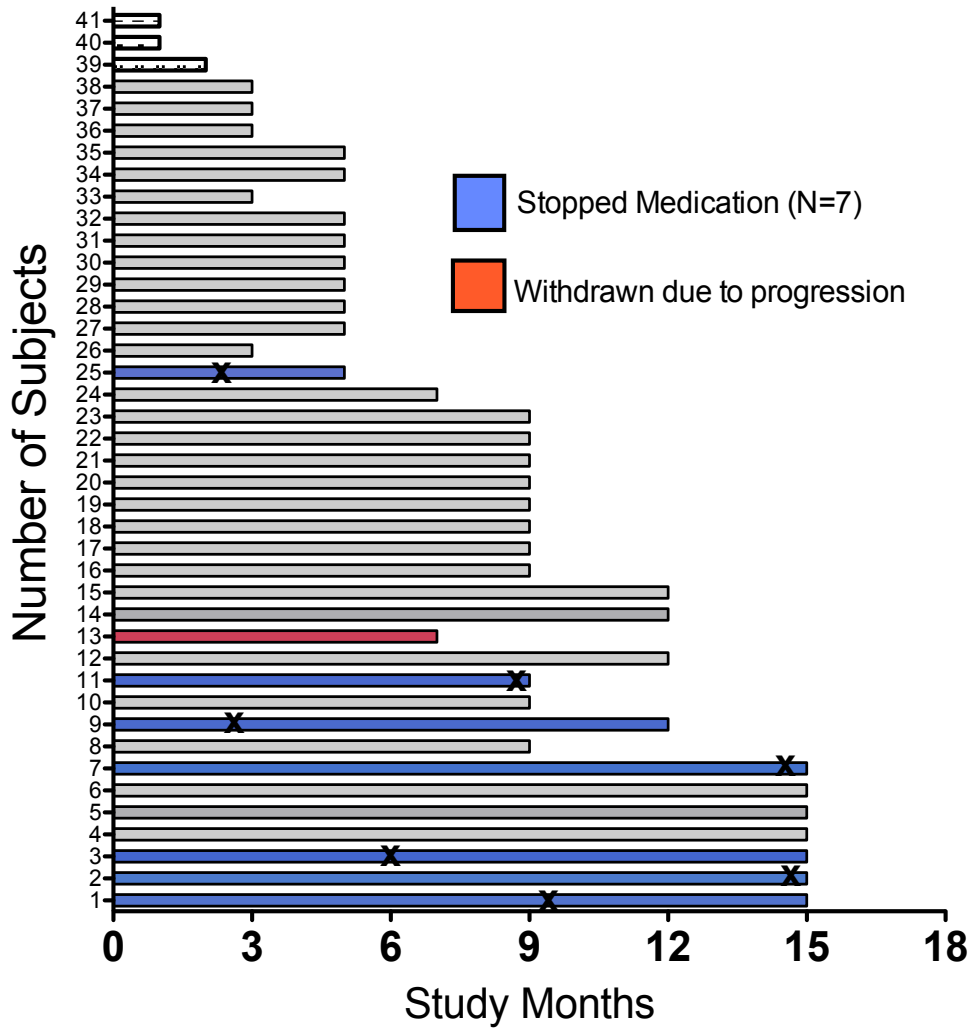
*All grade 3 and 4 events are listed. Grade 1 and 2 events are listed only if investigators considered them to be related to vismodegib treatment. No grade 5 events were reported. The highest grade of event is reported for each patient.

Supplemental Figure 1A. CONSORT diagram.

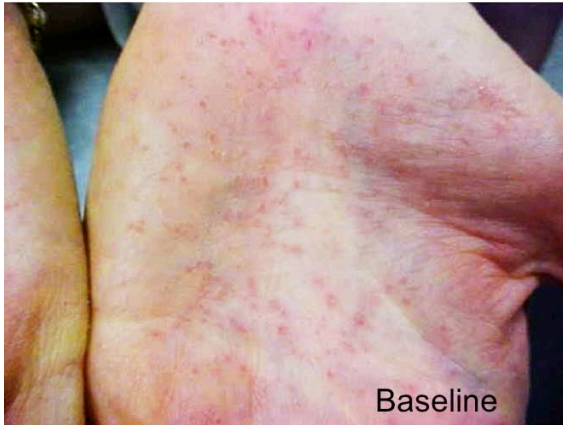
CONSORT 2010 Flow Diagram



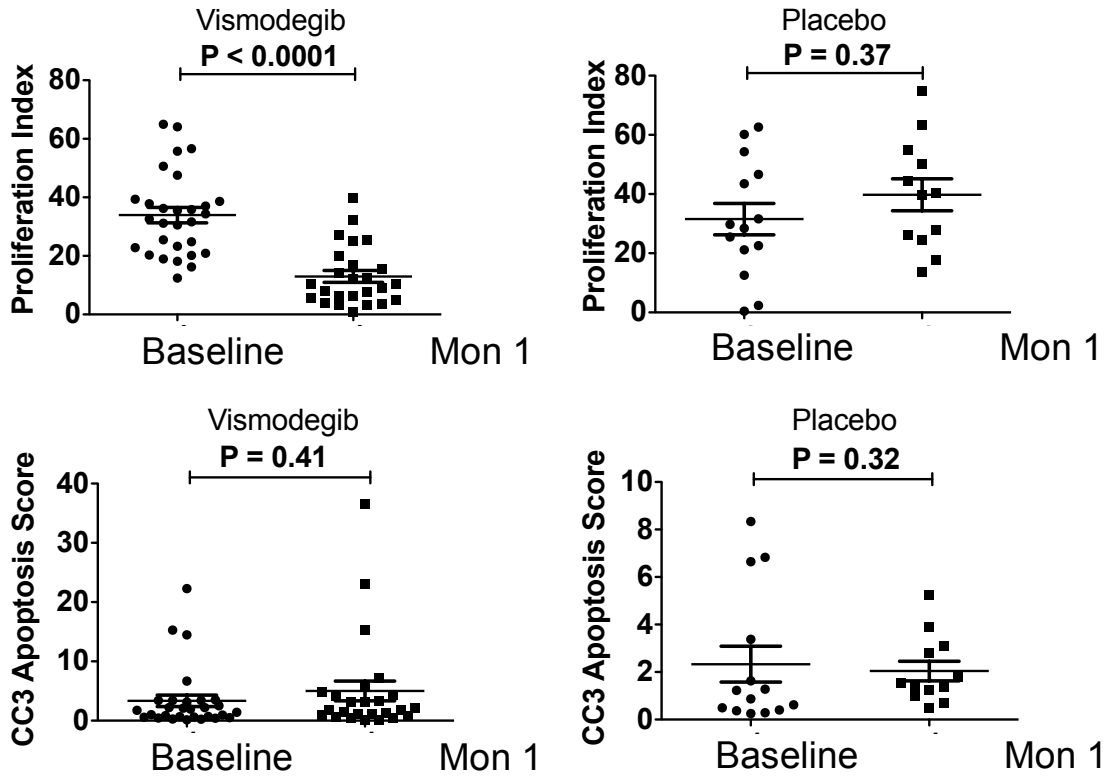
Supplemental Figure 1B. Study enrollment as of data close out (February 17, 2011). X – month in which the subject discontinued medication



Supplemental Figure 2: Multiple palmar pits characteristic of BCNS present at baseline and resolved on vismodegib at month 7.



Supplemental Figure 3: A. Decrease in cellular proliferation (Ki67 index) in 1 month in BCCs from vismodegib treated subjects ($P < 0.001$) and not in BCCs from placebo treated subjects. B. No change in apoptosis after vismodegib (cleaved-caspase 3 score).



Supplemental Figure 4: Existing BCCs return after stopping vismodegib. Back of BCNS subject who took vismodegib for 5 months and was off drug for 10 months (after month 5)

