Preliminary Assessment of Vosoritide for Short Stature in Turner Syndrome: 6-month data from a Clinical Trial

Roopa Kanakatti Shankar, MBBS, MS[1,2], Niusha Shafaei, MSc[1], Anqing Zhang, PhD[3], Kimberly Pitner, MSHS,BSN, RN[1], Niti Dham, MD[1], Andrew Dauber, MD, MMSc[1,2] . [1]Children's National Hospital, Washington DC; [2] The George Washington University School of Medicine

National Clinical Trial Identified Number: NCT05849389

Background

Short-stature homeobox (SHOX) haploinsufficiency associated with increased extracellular signal-regulated kinase (ERK) activity is one of the mechanisms of short stature in Turner syndrome (TS). Vosoritide, a C-type natriuretic peptide (CNP) analog promotes endochondral bone growth by reducing ERK activity. Hence, we hypothesized that vosoritide may increase height in girls with TS.

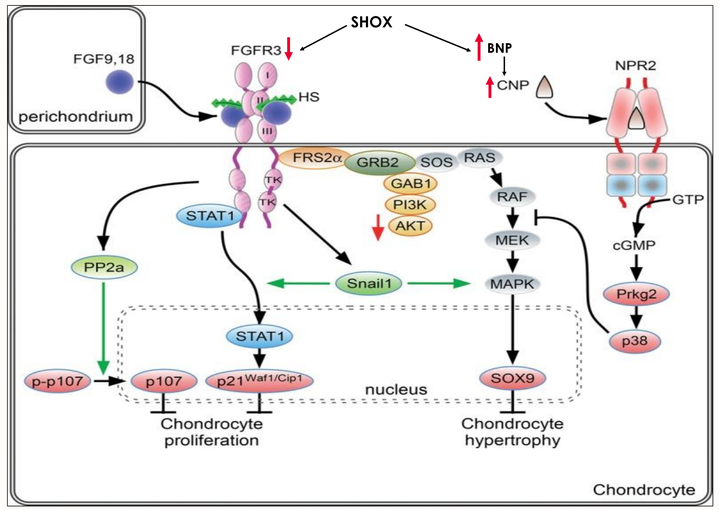


Figure adapted from Ornitz DM et al. Genes Dev. 2015;29(14):1463-1486.

Methods/Design

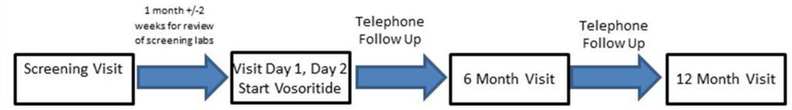
Prospective single center Phase II open label clinical trial of Vosoritide in pre-pubertal girls with TS (ages 3-11years):

Karyotype-confirmed TS < 5%ile for height:

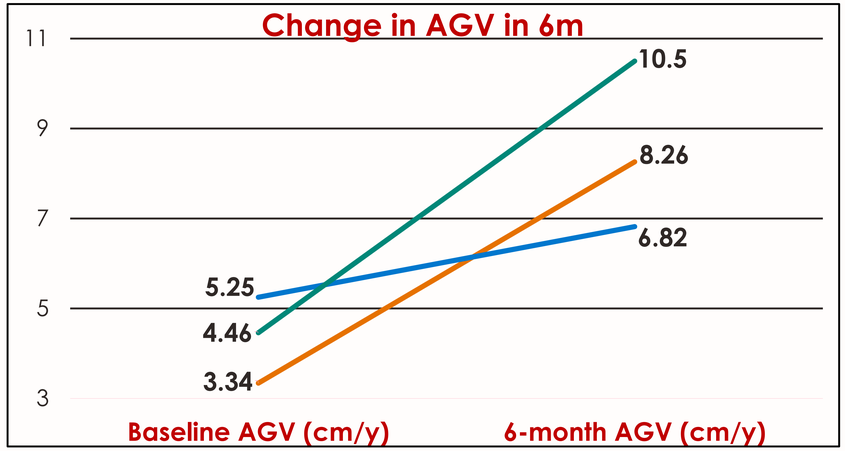
- Naïve to growth hormone (GH) or
- Annualized growth velocity (AGV) after 1 year of treatment: <-1SD on NCGS* response curves
- On GH> a year with 6m AGV <50%ile of US girls for age and sex

*National Cooperative Growth Study

Study Design



Annualized Growth Velocity (AGV) on Vosoritide



Subjects receive daily subcutaneous vosoritide injections (using weight-based dose banding approved for achondroplasia) for 12 months, after discontinuation of GH. The primary outcomes are change in AGV and height SD from baseline, as well as rate of adverse events (AEs).

Results

Of the first 4 subjects enrolled in the trial, one failed screen due to new onset celiac disease and 3 have completed 6 months of treatment.

Subjects with prior GH exposure increased AGV by +4.9 and +1.57 cm/y over the AGV on GH treatment, while the GH naïve subject had an increased AGV +6.04 cm above the baseline at the 6-month visit.

Vosoritide was generally well tolerated, with transient injection site erythema/swelling (Grade 1-2). No subjects discontinued participation due to AEs. There were no serious AEs related to treatment.

Conclusion

This is the first clinical trial of vosoritide therapy in TS and shows promise in increasing AGV in both GH naïve as well as previously GH-treated girls at 6-months. Injections appear well-tolerated. Ongoing enrollment with longer term follow up and additional participant data will shed light on potential utility and safety of vosoritide for short stature in TS.

Acknowledgements

We thank the patients and their families for their participation.

Funding for this study is provided by BioMarin Pharmaceutical Inc.

	Age (years)	50-cell Karyotype	Growth Hormone exposure	Baseline AGV** (cm/y)	6m AGV (cm/y)	Baseline height SD (Day 1 visit)	6m visit height SD	Vosoritide dose in mcg/kg	Other TS-related co-morbidity
1.	9	47,X,del(X)(p22.1)[43],+9 ,del(9)(q12)/46,X,del(X) (p22.1)[7]	yes	3.34	8.26	-2.62	-2.24	15.9	Intrauterine growth restriction
2.	10	45, X	yes	5.25	6.82	-2.14	-1.92	18	Aortic coarctation s/p end to end anastomosis, Scoliosis
3.	6	45,X [47]/46,X, psu idic (X)(p11.23)[3]	no	4.46	10.5	-2.85	-2.35	18.5	Horseshoe kidney

**AGV calculated based on historical data closest to 12 months prior to screening visit