Trabalhos Científicos

Título: Vosoritide For Children With Achondroplasia: A 60-Month Update From An Ongoing Phase 2 Clinical Trial

Autores: THALIS BOLZAN (BIOMARIN), LYNDA POLGREEN (THE LUNDQUIST INSTITUTE AT HARBOR-UCLA MEDICAL CENTER, TORRANCE, CA, USA), MELITA IRVING (GUY´S AND ST. THOMAS´ NHS FOUNDATION TRUST, EVELINA CHILDREN´S HOSPITAL, LONDON, UK), JULIE HOOVER-FONG4 (JOHNS HOPKINS UNIVERSITY SCHOOL OF MEDICINE, BALTIMORE, MD, USA), CARLOS BACINO (BAYLOR COLLEGE OF MEDICINE, HOUSTON, TX, USA), JOEL CHARROW (ANN AND ROBERT H. LURIE CHILDREN´S HOSPITAL OF CHICAGO, CHICAGO, IL), VALERIE CORMIER-DAIRE (INSTITUT IMAGINE, UNIVERSITÉ PARIS DESCARTES, HÔPITAL NECKER - ENFANTS MALADES, PARIS, FRANCE), PATRICIA DICKSON (WASHINGTON UNIVERSITY SCHOOL OF MEDICINE, ST. LOUIS, MO), POUL HARMATZ (UCSF BENIOFF CHILDREN´S HOSPITAL OAKLAND, OAKLAND, CA, USA), KEVIN LARIMORE (BIOMARIN PHARMACEUTICAL INC., NOVATO, CA, USA), KALA JAYARAM (BIOMARIN PHARMACEUTICAL INC., NOVATO, CA, USA), ALICE HUNTSMAN LABED (BIOMARIN PHARMACEUTICAL INC., NOVATO, CA, USA), ELENA FISHELEVA (BIOMARIN PHARMACEUTICAL INC., NOVATO, CA, USA), GEORGE JEHA (BIOMARIN PHARMACEUTICAL INC., NOVATO, CA, USA), JONATHAN DAY (BIOMARIN PHARMACEUTICAL INC., NOVATO, CA, USA), JOHN PHILIPS (VANDERBILT UNIVERSITY MEDICAL CENTER, NASHVILLE, TN, USA), RAVI SAVARIRAYAN (MURDOCH CHILDREN´S RESEARCH INSTITUTE, ROYAL CHILDREN´S HOSPITAL VICTORIA, UNIVERSITY OF MELBOUR)

Resumo: Vosoritide is an analogue of C-type natriuretic peptide (CNP), a potent stimulator of endochondral bone growth. We previously reported on a 42-month Phase 2, open-label study conducted to evaluate the safety and efficacy of vosoritide in children with Achondroplasia (ACH) aged 5-14 years. This is an 60 months follow-up update of an extension study. After completion of 8805,6 months observation, 35 children (mean age 8.16 ± 1.57 years, range: 5-11) were enrolled into 4 dose cohorts: Cohort 1 (n=8), Cohort 2 (n=8), Cohort 3 (n=10), and Cohort 4 (n=9) with vosoritide doses of 2.5, 7.5, 15 and 30 956,g/kg/day respectively given subcutaneously for the first 6 months. The dose was escalated to 15 956,g/kg in Cohorts 1 and 2. Children in Cohort 3 and Cohort 4 remained on their initial doses (15 and 30 956,g/kg, respectively). Of the 30 children who rolled over into the extension study, 4 discontinued treatment (3 left the trial, one remained in the study off therapy) and 19 (from Cohorts 1, 2 and 3) completed 60 months of treatment. This is a report of the data from Cohorts 1, 2 and 3 as at the time of this analysis none of the 8 subjects in Cohort 4 had completed 60 months of follow up. All values are mean61617,(SD). No serious AEs were study drug-related. There was a persistent increase in annualized growth velocity (AGV) during a phase of growth when the expected normal pattern is a persistent decrease for both ACH and the general population. The baseline AGV of 3.7561617,(1.28) cm/yr increased after 60 months (n=19) by 1.3561617,(1.07) to 5.0061617,(0.88) cm/yr. The baseline height Z-score of -5.1261617,(1.00) increased by 0.7861617,(0.70) on treatment to -4.3161617,(1.28). There was no worsening of upper-to-lower body segment ratio which decreased by 0.1461617,(0.11) from a baseline of 1.9961617,(0.19) to 1.8861617,(0.2). An increase in urine cGMP, a biomarker of vosoritide pharmacological activity, was sustained after 60 months of therapy._x000D_ Vosoritide was well-tolerated for up to 60 months with growth velocity and biomarker activity being sustained. These data support the continued development of vosoritide for the treatment of children with ACH._x000D_