Pediatric Endocrinology

PEDIATRIC GROWTH AND ADRENAL DISORDERS

24-Month Efficacy and Safety of Once Weekly and Every Other Week Administration of GX-H9, Hybrid FC-Fused Long-Acting Human Growth Hormone: A Phase 2 Study in Children With Growth Hormone Deficiency

Oleg Malievsksiy, MD, PhD†, Aryaev Mykola, MD†, Nataliya Zelnisna, MD, PhD†, Elena Bolshova, MD, PhD†,
Ganna Senatorova, MD†, György Oroslán, MD, PhD†,
Julia Sharodok, MD‡, Valentina Petekova, MD, PhD‡,
Nataliya Chorna, MD‡, Tamila Sorokman, MD, PhD§,
Seung Yang, MD, PhD‡, Ji-En Lee, MD, PhD‡, Agota Muzsnai, MD, PhD‡, Jin Soon Huang, MD, PhD‡, Sang-Yoon Lee, MD‡,
Hyun-Joo Son, MS§, SuJin Heo, MS§, Minkyu Heo, PhD‡, Yun Jung Choi, PhD‡, Young Chul Sung, PhD‡.

1Bashkir State Medical University, Ufa, Russian Federation, 2Odessa National Medical University, Odessa, Ukraine,
3Ukrainian Scientifically Practical Center of Endocrine Surgery and Transplantation of Endocrine Organs and Tissues, Kyiv, Ukraine, 4Institute of Endocrinology and Metabolism named after Komisarenko NAMS of Ukraine, Kyiv, Ukraine, 5Kharkiv National Medical University, Kharkiv, Ukraine, 6Markusovsky University Hospital, Szombathely, Hungary, 7St. Petersburg State Pediatric Medical University, St. Petersburg, Russian Federation, 8Institute of Pediatric Endocrinology, Moscow, Russian Federation, 9Regional Clinical Children’s Hospital, Ivano-Frankivsk, Ukraine, 1Bukovinian State Medical University, Chernivtsi, Ukraine, 11Kangdong Sacred Heart Hospital, Seoul, Korea, Republic of, 12INHA University Hospital, Inchon, Korea, Republic of, 13St. John’s Hospital and United Hospitals of Northern Buda, Budapest, Hungary, 14Ajou University School of Medical, Suwon City, Korea, Republic of, 15Handok Inc., Seoul, Korea, Republic of, 16Handok, Seoul, Korea, Republic of, 17Genexine Inc., Seongnam, Korea, Republic of.

SAT-LB15

Objectives GX-H9 is a long-acting form of recombinant human GH under clinical development for both adults and children with GHD. In this report, 24-month efficacy and safety of once weekly and every other week (EOW) administration of GX-H9 were evaluated, in addition to Genotropin®, switch-ability to GX-H9 after 12-month of treatment. Methods Subjects were randomly assigned to receive either one of three doses of GX-H9 (0.8 mg/kg/ week, 1.2 mg/kg/week or 2.4 mg/kg every other week) or 0.03 mg/kg/day of Genotropin®. Treatment duration is 24-month for all patients in GX-H9 arms while patients in Genotropin® arm were re-randomized to one of three doses of GX-H9 at the completion of the first 12-month of treatment. Doses of GX-H9 were adjusted throughout the treatment period whenever necessary, based on IGF-1 levels. Results Out of 56 randomized, 54 received either GX-H9 or Genotropin®. Fifty subjects completed the 12-month treatment period. Of 50, 45 subjects completed the next 12-month, comprising 33 patients from GX-H9 and 12 patients who switched from Genotropin®. First year/second year mean±SD annualized height velocity (aHV) for 0.8 mg/kg/week, 1.2 mg/kg/week or 2.4 mg/kg every other week of GX-H9 were 10.50±2.54/9.14±1.96, 11.76±1.96/9.88±1.92 and 11.03±2.92/9.72±1.90 cm/year, respectively. First year mean±SD aHV for Genotropin® was 9.14±3.09 cm/year.

Patients switched to one of the three doses of GX-H9 in the second year showed comparable aHV in the second year (8.73±2.69/7.60±0.90/9.13±1.07 cm/year for 0.8 mg/kg/week, 1.2 mg/kg/week and 2.4 mg/kg/EOW GX-H9, respectively). No significant slow-down of the growth was observed in the second year from patients who received GX-H9 throughout and patients who switched from Genotropin®. Mean change in height SDS after 12 months/24 months of GX-H9 treatment from baseline treatment improved continuously (+1.10/+1.61 and +1.31/+1.89 and +1.15/+1.69 for 0.8 mg/kg/week, 1.2 mg/kg/week and 2.4 mg/kg EOW GX-H9, respectively). First year mean change in height SDS for Genotropin® was +0.92 SDS, and showed comparable improvement in height SDS after switching to GX-H9 weekly arms (+0.76 and +0.79 SDS for 0.8 mg/kg/week and 1.2 mg/kg/week, respectively). Most treatment-emergent adverse events were evaluated as unrelated to the study drug and were mild or moderate in severity. No new safety concerns were observed throughout 24 months of long-term GX-H9 treatment or after switching to GX-H9 from Genotropin®. Conclusions Growth response and safety profile of GX-H9 in children with GHD is comparable to those of daily GH, achieving robust growth rates after 24-month treatment. Subjects switched from Genotropin® in the second year, also showed substantial catch-up growth indicated by improvement in height SDS. GX-H9 has a unique potential to be a convenient long-term GH providing not only weekly but also twice-monthly treatment.

Neuroendocrinology and Pituitary

PITUITARY TUMORS II

An International Simulated Use Study (PRESTO) to Evaluate Nurse Preferences Between the Lanreotide Autogel New Syringe and Octreotide Long-Acting Release Syringe

Daphne T. Adelman, RN†, Xuan-Mai Truong-Thanh, MD‡, Marion Feuilly, PharmD§, Aude Houchard, MPH¶, David Cella, PhD°.

1Northwestern University, Chicago, IL, USA, 2Ipsen Pharma, Boulogne-Billancourt, France.

MON-LB47

Background: A new lanreotide autogel/depot (LAN) syringe was developed based on feedback from a human factors study to improve user experience. Methods: PRESTO was a multinational, simulated-use study in nurses with ≥2 years’ experience injecting LAN or octreotide long-acting release (OCT LAR) in patients with acromegaly and/or neuroendocrine tumors, which aimed to assess injector preference between the LAN new syringe and the current OCT LAR syringe. Participating nurses were invited to test both the LAN new syringe (120 mg) and the current OCT LAR syringe (20 mg or 30 mg), using injection pads. The sponsor was not involved in these sessions. In an anonymous web-based questionnaire, nurses reported overall preference (‘strong’ or ‘slight’; primary endpoint), and rated and ranked the importance of nine attributes for each syringe (1 [not at all] to 5 [very much]). Results: In total, 90 nurses attended injection sessions and completed valid questionnaires. Overall, 97.8% of nurses expressed a preference (85.6% ‘strong’, 12.2% ‘slight’)

doi: 10.1210/jendso/bvaa046 | Journal of the Endocrine Society | A1091
for LAN new syringe (p<0.0001 vs current OCT LAR). Attribute performance ratings were consistently higher for LAN new syringe vs current OCT LAR, with the greatest differences in ‘fast administration’ and ‘confidence the syringe will not be clogged’ (mean [standard deviation]: 2.6 [1.2] and 2.3 [1.5], respectively; p<0.0001). The attribute ranked most important was ‘confidence the syringe will not be clogged’ (24.4%) and least important was ‘convenience of syringe format, including packaging, from preparation to injection’ (34.4%).

Conclusions: The PRESTO study showed that nurses preferred the user experience of the LAN new syringe over the current OCT LAR syringe across all attributes tested.

Tumor Biology
TUMOR BIOLOGY: DIAGNOSTICS, THERAPIES, ENDOCRINE NEOPLASIAS, AND HORMONE DEPENDENT TUMORS
PLK1 as a New Treatment Target for Adrenocortical Carcinoma

Gabrielle Smith, BSc1, Raimunde Liang, MD2, Vasileios Chortis, MD, PhD1, Sana Khan, MD1, Juliane Lippert, BSc1, Constanze Hantel, PhD3, Barbara Altieri, MD, PhD4, Martin Passnacht, MD5, Paul Alexander Foster, PhD3, Cristina Lucia Ronchi, MD, PhD6.
1Institute of Metabolism and System Research, University of Birmingham, Birmingham, United Kingdom, 2Division of Endocrinology and Diabetes, University Hospital of Wuerzburg, Wuerzburg, Germany, 3Institute of Human Genetics, University of Wuerzburg, Wuerzburg, Germany, 4Department of Endocrinology, Diabetes and Clinical Nutrition, University Hospital Zurich, Zurich, Switzerland.

SUN-LB22
Background: Adrenocortical carcinoma (ACC) is an aggressive malignancy with limited medical treatment options. We previously identified polo-like kinase 1 (PLK1) as one of most overexpressed genes in ACC; thus PLK1 represents a potential treatment target for this cancer type. Some PLK1 inhibitors are under evaluation in clinical trials for other solid organ malignancies, and seem to be more effective in TP53 mutated tumours. The aim of this study was to evaluate PLK1 protein levels in a large series of ACC and assess the in vitro efficacy of PLK1 inhibitors in two different ACC cell lines. Methods: 104 formalin-fixed paraffin-embedded ACC tissue samples with available genetic data were investigated. Nuclear PLK1 protein expression was evaluated by immunohistochemistry and a semi-quantitative H-score was calculated. PLK1 expression levels were correlated to clinical and histological parameters. Efficacy of PLK1-specific inhibitor Volasertib (0-200 nM) was tested in the standard NCI-H295R ACC cell line, which presents PLK-1 overexpression and a large TP53 deletion, and in the newly established MUC1 cell line, which bears a frameshift mutation in TP53. Cell proliferation was analysed using DNA fluorescence and cell apoptosis by Caspase Glo 3/7 assay. Results: Nuclear PLK1 expression was classified as high in 59% of ACC samples, with a significant difference noted between TP53-mutated (n=24) and wild-type (n=80) cases (87.5 vs 51%, p<0.01). PLK1 levels did not correlate with either progression-free or overall survival. H295R cells showed a significant time- and dose-dependent reduction of cell proliferation compared to vehicle control after 72h of Volasertib treatment (p<0.005 per trend, p=0.01 by 200nM by non-parametric two-way ANOVA). A less pronounced and non-significant trend towards inhibited proliferation was observed in MUC1 cells. Cell apoptosis was significantly higher in the H295R cells treated with 175nM and 200nM Volasertib when compared to control (p<0.05), while there was no significant difference in MUC1 cells. Conclusion: In this pilot study, we propose PLK1 inhibitors as promising candidates for treatment of a subset of ACC patients that may be pre-selected according to the tumour molecular pattern. We plan to extend functional experiments to further PLK1 inhibitors, including additional ACC cell lines with a different molecular profile.

Neuroendocrinology and Pituitary
ADVANCES IN NEUROENDOCRINOLOGY
Differences in IGF-I Concentrations Between European and US Populations - Consequences for Reference Intervals

Martin Bidlingmaier, MD1, Andre Vaiour, MBA, PhD, D(ABCC)2, Kelly Y. Chun, PhD3, Katharina Schilbach, MD1, Tim Kühlne, PhD4, Seni Diederich, MD1, Thomas Rogge, MD1, Etienne Cavalier, MD, PhD2, Alex Katayev, MD1.
1Klinikum der Universität Muenchen, Munich, Germany, 2Laboratory Corporation of America Holdings, Elon, NC, USA, 3Laboratory Corporation of America Holdings, Agoura Hills, CA, USA, 4Medicover MVZ, Berlin, Germany, 5Diagnos MVZ, Berlin, Germany, 6CHU, Liège, Belgium.

SUN-LB46
Background: IGF-I is the most widely used biomarker for management of GH related diseases. Reproducible assays and method-specific reference intervals (RIs) are crucial determinants of its clinical utility. Assay validation and RIs based on >15,000 subjects were published for the IDS iSYS IGF-I assay (J Clin Endocrinol Metab 2014). We now analyzed distribution of IGF-I results obtained in routine samples analyzed by accredited laboratories in the US and Europe, all using the IDS iSYS assay. Methods: All results from routine IGF-I measurements during the past 5 years in 4 laboratories were included (US lab n=778,173 males/710,752 females; European labs (Germany/Belgium, n=23,220 males/40,183 females). Assay performance across laboratories was confirmed through proficiency testing schemes and exchange of patient samples. We constructed RIs adjusted for age/sex from European and US cohorts separately using a modified Hoffmann approach (Am J Clin Pathol 2015), and compared to the originally published RIs (n=6697 males/8317 females, adults across all ages and sexes, regardless whether IGF-I results were from Europe or the US. For groups with sufficient n, upper limits (ULs) of RIs calculated from European routine data were also not statistically different from the