

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

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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

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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 from Europe). A subset of US samples was used to compare IGF-I between regions with lower (Colorado) and higher (Alabama) mean body mass index (BMI). Results: Lower limits (LLs) of RIs calculated from routine results are superimposable to LLs from the original publication for 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

originally published central 95%. However, a striking difference exists in calculated ULs from data of European and US origin: For ages 10-18 years, calculated UL on average was 149.3 ng/mL (34.6%) higher in boys and 94.9 ng/mL (19.8%) in girls from the US. In adults (19-95 years), calculated UL on average was 45 ng/mL (20.3%) higher in males and 29.7 ng/mL (13.8%) in females from the US. Within the US, mean IGF-I was significantly higher in samples from Colorado (lower mean BMI) than in Alabama ($p < 0.0001$) across age- and sex groups, although the difference between the two states was smaller than between each of them and Europe. Conclusion: This study provides evidence that in sufficiently large datasets, both, direct sampling (as in the original publication) and the indirect Hoffmann algorithms provide statistically comparable RI limits and may be considered as accurate representation of results distribution in the disease-free populations. More importantly, we demonstrate that even with tight cross-correlation and continuous monitoring of IGF-I assay performance RIs generated in different populations can be different. Notably, in our extremely large study, the difference between Europe and the US was clinically relevant only at the UL. Although our study cannot reveal the cause of the difference, we suggest using adapted RIs for the US.

Diabetes Mellitus and Glucose Metabolism

CLINICAL AND TRANSLATIONAL STUDIES IN DIABETES

Transcutaneous Magnetic Stimulation: A Novel Treatment of Diabetic Peripheral Neuropathy

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Objective: Transcutaneous Magnetic Stimulation (TCMS) is reported to be an effective treatment in multiple neurologic conditions such as migraine headaches, lower back pain, and post-traumatic peripheral neuropathic pain¹⁻³. The efficacy and safety of TCMS for diabetic peripheral neuropathy is not known. We evaluated whether TCMS is effective and safe in patients with diabetic peripheral neuropathy. **Method:** Eight patients with a previous diagnosis of diabetic peripheral neuropathy and baseline numerical pain-rating scale (NPRS) of 5 or greater in both feet were enrolled. NPRS scale was set from 0 to 10, 0 represents no pain and 10 representing the most severe pain. Each patient was treated with a single session of TCMS applied first on the plantar then the dorsal surface of both feet. Magnetic pulses (1.2 Tesla) were delivered every 6 seconds for 5 minutes in each foot on the plantar and dorsal surfaces, respectively. NPRS was repeated post-treatment over the course of 28-days follow-up period. **Results:** The mean baseline NPRS was 5.8 (± 1.0). Immediately post-treatment, mean NPRS improved to 1.3 (± 1.9), a 77.7 (± 36.5) % decrease. Mean NPRS at 7 and 28 days of follow-up was 2.9 (± 2.8) and 4.1 (± 3.3), respectively. These represent a 53.2(± 42.4) % improvement at 7 days and 30.5(± 52.4) % improvement at 28 days of follow-up compared to baseline NPRS. None of the patients reported significant

discomfort during the treatment, and no major side effects were observed during the study period. **Conclusion:** In this pilot study of patients with diabetic peripheral neuropathy, TCMS appears to be a safe and effective alternative in providing temporary pain relief. Longer and more frequent treatment sessions need to be explored to see if these can increase the effective duration.

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Healthcare Delivery and Education

EXPANDING CLINICAL CONSIDERATIONS FOR PATIENT TESTING AND CARE

Association Between Cancer Related Beliefs and Diabetes Medication Adherence Among Breast Cancer Survivors With Comorbid Type 2 Diabetes

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Introduction: Cancer and diabetes mellitus (DM) are leading causes of death in the United States. Each year, over 245,000 women are diagnosed with breast cancer, and approximately 18% of patients diagnosed have preexisting DM. The presence of a comorbidity, such as DM increases women's mortality risk by 40%. While studies have shown decreased adherence to hypoglycemic medications after cancer diagnosis, the effect of cancer related beliefs on DM medication adherence has not been fully explored. In this study, we evaluated the association between cancer related beliefs and DM medication adherence in survivors of breast cancer.

Hypothesis: Patients with greater positive beliefs about cancer (including personal control, treatment control and understanding) would exhibit greater adherence to DM medication.

Methodology: We enrolled women >55 years with Stage 0-IIIa breast cancer diagnosed in the past 10 years, who had completed chemotherapy and/or were prescribed hormonal therapy and had pre-existing type 2 DM treated with at least 1 oral DM medication. Cancer related beliefs were assessed using the Illness Perception Questionnaire (IPQ). Medication adherence was evaluated using the Medication Adherence Rating Scale (MARS). Adherence was dichotomized at a mean MARS score of ≥ 4.5 . Wilcoxon rank-sum tests were used to examine the relationship between patients' cancer related beliefs and DM medication adherence.