

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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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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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