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ICPALM 2023: International speakers

1. Anatomical Pathology

Molecular classification of gastric carcinoma
Corrado DÁrrigo
Poundbury Cancer Institute.

During the past two decades there has been significant improvement of cancer outcomes due, at least in part, to increasing use of biological therapies. This requires the identification of specific subgroup of patients that may benefit from particular targeted treatment. The classical morphological classification of tumours is inadequate to support this transformation of treatment modalities. New molecular classifications have emerged for a number of cancer sites, based on comprehensive analyses of large number of parameters ("multi-omics"). In order to make it accessible to all patients, multi-omics classifications have been implemented into the histopathology diagnostic routine using a handful of on-slide tests.

Such implementation has yet to happen in gastric cancer (GC) and patients access to effective targeted treatment remains limited. We present an overview of the current molecular classification for gastric cancer and a study to assesses the feasibility of implementing a molecular classification based on 4 groups of on-slide tests. These are ISH for EBER (for the identification of GC EBV+), IHC for MLH1 and MSH2 (for the identification of GC MMR-deficient), IHC for E-cadhering and β-catenin (for the identification of GC EMT or epithelial-mesenchymal transformation) and IHC for p53 (for the identification of p53 mutated and p53 wild type GC). The prognostic and predictive implications for GC patients will be discussed.

Rewriting the Her2 testing handbook
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Histopathologists have been providing Her-2 status for breast cancer (BC) patients for over 4 decades. Testing aimed at identifying a small (12-15%) proportion of BC patients that have Her2 gene amplification as a main oncogenic driver in their cancer. Direct blocking of the Her2 receptor with mAb-based therapy is an effective treatment only in patients with Her2 over-expression or amplification.

Recently, targeting Her2 with specific antibodies that deliver cytotoxic payloads inside the tumour cells (ADC or antibody-drug conjugates) has shown effectiveness also in BC that has low level expression of Her2 but lacks amplification. Regulatory approval of this treatment means de facto that the traditional binary classification (positive/negative) has to be replaced with a new ternary classification (high/low/zero) and that the interpretation of the IHC staining needs to be re-focused to recognise the new thresholds.

We developed focused algorithms and training programmes for the interpretation of Her2 IHC in the new diagnostic landscape. We will be discussing the re-evaluation of the scope and parameters for Her2 testing in BC with particular focus on the analytical performance of current tests, the identification of various staining patterns and their significance, the interpretative algorithm and the new (2023) release of the ASCO-CAP and RCPath guidelines.

Surgical pathology of low-grade epilepsy-associated neuroepithelial tumors (LEAT): role of molecular genetic testing and surrogate immunohistochemical markers
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Low-grade epilepsy-associated neuroepithelial tumors (LEAT) is a generic term for CNS WHO grade 1 to 2 or equivalent tumors, with epileptic seizures as the main symptom developing mostly by the age of 15 years, and 88% of patients show a favorable postoperative seizure outcome, representing a clinicopathological concept distinct from the WHO classification of brain tumors. A past survey reported that the majority of LEAT consisted histopathologically of neuronal and mixed neuronal-glial tumors frequently localized in the temporal lobe, with ganglioglioma (GG) and dysembryoplastic neuroepithelial tumor (DNT) being the most common histopathological diagnoses comprising 60 to 90 % of cases. However, disagreement between experts on diagnosing GG and DNT was not uncommon, particularly when specific histological features were not

CP9: Cost-effectiveness of implementation of aspartate aminotransferase elimination from the liver function test panel

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Introduction: Significant savings on reagent costs has been shown by selectively limiting aspartate aminotransferase (AST) testing from routine liver function test (LFT) panel, without affecting patient's outcome. We have eliminated AST from routine LFT panel offered in our Chemical Pathology laboratory in a state hospital, as of November 9, 2021 as part of a strategy for judicious and cost-effective measures. We conducted a clinical audit to evaluate the cost-effectiveness of eliminating AST from the routine LFT panel and introducing an automatic AST reflex testing in our laboratory. *Material & Methods:* This was a retrospective audit, based on monthly workload for LFT and AST as standalone requests, over a 12-months period, starting from the day of introduction of AST removal from routine LFT panel. The cost per test for AST during this audit was RM0.90 (excluding consumables). Saved costs were calculated based on monthly workloads, extracted from our laboratory information system. *Results:* A total of 75,618 AST tests with a total cost of RM68,056.20 were saved throughout the 12-months period after implementing AST elimination from routine LFT panel. *Discussion:* Eliminating AST from the LFT panel resulted in significant cost-savings over a one year-period. We highlighted the cost-saving measure of eliminating AST from the routine LFT panel as an effective measure to reduce overutilisation of laboratory testing, without compromising patient's safety.

CP10: Correlation of HbA1c value between Variant II Turbo HbA1c analyser and D100 HbA1c analyser among diabetic patients with P3 > 5%

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Introduction: Glycated haemoglobin A1c (HbA1c) assay is most widely used in diabetic patients to assess long-term glycaemic control. A P3 peak > 5% with the presence of a variant window on Variant II Turbo HbA1c analyser is not reportable unlike using D100 HbA1c analyser where it is still reportable. We aimed to determine the correlation and agreement between measured HbA1c values that are not reportable on Variant II Turbo HbA1c with that measured on D100 HbA1c. *Materials & Methods:* Blood samples of 40 diabetic patients from Hospital Tengku Ampuan Rahimah (HTAR), Klang was analysed for HbA1c on Variant II Turbo HbA1c analyser (Chemical Pathology Unit, HTAR, Klang) and D100 HbA1c analyser (Chemical Pathology Unit, Hospital Kuala Lumpur). A Bland-Altman plot and linear regression analysis were used to determine agreement and correlation between both analysers. *Results and Discussion:* The Bland-Altman plot showed dispersion of data within the 95% limit of agreement with positive mean bias of 0.2779%, which is lower than the allowable bias of 4.7%. The linear regression showed r = 0.99 indicating there is a strong correlation between the analysers. The slope (m) exceeded about 0.0647, indicating a 6.47% higher HbA1c result with Variant II Turbo. The intercept (c) was -0.3083 indicating that the absolute difference is 0.3083 lower with Variant II Turbo. *Conclusion:* The strong correlation and good clinical agreement of HbA1c values between both analysers indicate that these analysers can be used interchangeably.

CP11: Value assignment of mean, SD and quality control ranges for technopath Multichem QC on Beckman Coulter DxC700 AU Platform

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Introduction: Laboratory quality control is an essential part of ensuring the accuracy and reliability of results released for patient management. The study purpose is to establish mean and standard deviation (SD) for seven analytes in Technopath Multichem QC products. *Materials & Methods*: The study was done from 1-8 August 2022 at Pathology Department, Hospital Sultan Ismail Petra. Technopath Multichem QC materials were analysed on Beckman Coulter (BC) DxC700 AU analyser for 7 analytes (HDL, UIBC, Ammonia, Total Bilirubin, Direct Bilirubin, CSF Glucose and CSF Total Protein) in duplicates, over 10 separate runs over 10 days. A minimum of 20 data points for each control level was generated and recorded in IAMQC Infinity Data Management software. Data generated was reviewed to ensure coefficient variation (CV) is lower than performance goals. Mean and SD values for each analyte were calculated. Outliers whereby data points exceed 3SD, were removed from statistical calculation. *Results*: CV for HDL range 1.38-1.92% (goal <2.85%), UIBC range 1.37-4.13% (<20.0%), Ammonia range 1.03-5.77% (<20.0%), Total Bilirubin 0.96% (<10.0%), Direct Bilirubin 2.39% (<18.4%), CSF Glucose range 5.39-5.40% (<10.0%) and CSF Total Protein range 1.85-2.05% (<17.75). Mean and SD values for each analyte are tabulated. *Discussion*: The Multichem QC materials on BC DxC system gives acceptable analytical performance across all tests evaluated and the values were within analytical performance specification. These values will be used as a guideline by all laboratories that using the same Multichem QC products with same lot numbers to perform method evaluation and establish their own mean and SD.