density (QID) was CPS minus TPS. TPS, CPS, and QID ability to predict ORR (ROC analysis) and overall survival (OS) hazard ratio (HR) (pembrolizumab vs chemotherapy) were evaluated.

Results: With pembrolizumab, area under ROC curve (95% CI) was 0.69 (0.58–0.80) for CPS, 0.67 (0.56–0.77) for QID, and 0.55 (0.46–0.64) for TPS. At each cutoff, QID had lower sensitivity and Youden Index and larger OS HR than CPS. QID appeared to be orthogonal to TPS.

Conclusions: Trends suggest tumour cell expression is an important component of PD-L1 as a predictive biomarker of pembrolizumab in mTNBC. When immune cells alone were used, a meaningful number of responders was missed, and OS benefit trended toward higher HR estimates.

PAN-TUMOUR ANALYSIS OF THE ASSOCIATION BETWEEN PD-L1 COMBINED POSITIVE SCORE (CPS) AND RESPONSE TO PEMBROLIZUMAB MONOTHERAPY

Lingkang Huang, Jared Lunceford, Junshui Ma,
Kenneth Emancipator
Merck & Co Inc, Kenilworth, NJ, USA

PD-L1 is expressed on tumour and immune cells; PD-L1 CPS captures tumour and immune cell expression in one aggregate score. We performed a retrospective, exploratory analysis of CPS as an enrichment biomarker of pembrolizumab monotherapy across multiple tumour types. PD-L1 expression was assessed using PD-L1 IHC 22C3 pharmDx and measured using CPS (number of PD-L1-staining cells [tumour cells, lymphocytes, macrophages] divided by total number of tumour cells, multiplied by 100). Data were pooled from 11 studies across tumour types for pembrolizumab and for standard-of-care (in controlled studies). Estimates of ORR, prevalence, and receiver operating characteristics (ROC) analysis was performed over various CPS cut-points. CPS distribution by response, tumour type, and line of therapy were also assessed. 3769 patients had available PD-L1 CPS (pembrolizumab, $n=2678$; standard-of-care, $n=1091$). Area under the ROC curve for ORR was 0.63 (95% CI, 0.61–0.66; pembrolizumab) versus 0.48 (95% CI, 0.43–0.53; standard-of-care); cut-points of 1, 10, 20, and 50 were also examined. This pan-tumour analysis demonstrates that CPS is an effective method for scoring PD-L1 expression and can be used as a predictive biomarker to identify patients likely to respond to pembrolizumab monotherapy. CPS demonstrated enrichment of response to pembrolizumab monotherapy across most tumour types.

INTERNAL AUDIT OF TWO ANTINEURONAL IMMUNOBLOTS AND THE ROLE OF INDIRECT IMMUNOFLUORESCENCE IN SAMPLE SCREENING

L. S. Gardner^{1,2}, S. Culican¹, D. Campbell¹, M. Dela Cruz¹,
D. McDonald¹, D. A. Brown^{1,3}, M. W. Lin^{1,3}

¹Immunopathology Department, ICPMR, Westmead Hospital, Sydney, NSW, Australia; ²Faculty of Medicine, University of Queensland, Qld, Australia; and ³Faculty of Medicine, University of Sydney, NSW, Australia

Anti-neuronal antibodies are associated with a range of clinical phenotypes that are often preceded by malignancy. Most of these antibodies can be identified by indirect immunofluorescence

(IIF) using commercial primate neural tissue slides. The EUROImmun 12 and upgraded RAVO 14 antigen line immunoblots were directly compared to replace a 9 antigen RAVO immunoblot. Initial assessment was with samples with known positive specificities by IIF. The second phase involved parallel testing of routine pooled negative IIF samples as per institutional standard antineuronal testing algorithm. IIF results and clinical correlation were used to arbitrate on discordant immunoblot results. Correlation in known positives was 80%. The EURO-Immun immunoblot did not identify disease causing SOX1 and Recoverin antibodies. Routine pooled analysis did not identify discrepancy between the platforms. Assessment of 318 patient samples did not reveal any cases where a diagnosis was correctly identified by line immunoblot and not IIF. A single sample with positive Yo antibodies was identified by both platforms without clinical or IIF correlation, making this a likely false positive. Subsequent to this audit, Westmead ICPMR has migrated to the 14 antigen RAVO line blot for confirmation of positive IIF or for patients with equivocal results only.

CHALLENGES OF PRODUCING A NEW EXTERNAL QUALITY ASSURANCE PROGRAM – A PROCESS IMPROVEMENT PROJECT

Grace Moyo, Loriza Khan
Royal College of Pathologists of Australasia Quality Assurance Programs (RCPAQAP), St Leonards, Sydney, Australia

A requirement for validation and accreditation of a new test in many laboratories is the availability of an accredited external quality assurance (EQA) program. RCPAQAP conducted a process improvement project to reduce the turnaround time to introduce a new accredited EQA program. A voice of customer (VoC) survey was distributed to identify customer requirements for EQA availability at the time of test verification. Data was collected for 13 serology and immunology EQA programs dating from 2006. Total cycle time for introducing a new program was captured in days. 73% of customers required a new EQA program to be available in 6 months or less of a test becoming available. The median number of days to achieve accreditation was 1427 days. Three areas of improvement were identified. These were (1) time taken to select a program to pilot, (2) time taken to source clinically appropriate samples, and (3) the time taken to gather program-specific information regarding the new test. The process improvement project has allowed RCPAQAP to understand customer needs and the complexities of planning a new EQA program better and develop processes to deliver superior EQA programs to advance outcomes in patient care and promote excellence in laboratory output.

ARTHROGRAPHIS KALRAE PROSTHETIC JOINT INFECTION: CASE REPORT AND REVIEW OF THE LITERATURE

Lucy C. Crawford^{1,2}, Sarah E. Kidd^{2,3}, Tom Savvoulidis⁴,
Renjy Nelson^{2,5}

¹Microbiology and Infectious Diseases Directorate, SA Pathology, Adelaide, SA, Australia; ²Faculty of Health Sciences, University of Adelaide, SA, Australia; ³National Mycology Reference Centre, SA Pathology, Adelaide, SA, Australia; ⁴Medacta International, Australia; and ⁵Infectious

Diseases Unit, Central Adelaide Local Health Network, Adelaide, SA, Australia

Arthrographis kalrae is a saprophytic fungus with initially yeast-like colonies, eventually developing hyphae and distinctive cylindrical arthroconidia. *A. kalrae* is rarely associated with human infection. This study reports the first case of prosthetic joint infection.

A 75-year-old male with a background of type 2 diabetes, obesity and total knee replacement underwent debridement and polyliner exchange for chronic methicillin-resistant *Staphylococcus aureus* (MRSA) prosthetic joint infection. He was treated with vancomycin for 6 weeks and oral trimethoprim/sulfamethoxazole (SXT) for 18 months. Although the wound remained intact, knee inflammation progressed after cessation of SXT. First stage revision revealed loose femoral and tibial components, tibial and patellar bone defects, and turbid synovial fluid. Histology demonstrated chronic inflammation and small branching hyphae but no neutrophils. MRSA was not isolated however cultures from multiple specimens grew a fungus. The isolate was referred to the National Mycology Reference Centre (NMRC) for confirmation and susceptibility testing, where morphological features were consistent with *Arthrographis* spp. *A. kalrae* was confirmed using the Bruker Biotyper MALDI-ToF MS (Score 2.28).

Liposomal amphotericin for 2 weeks followed by voriconazole and terbinafine were given in conjunction with repeated debridement and voriconazole-infused cement. A review of the literature and the implications of prosthetic joint associated fungal infection will be discussed.

COMPARATIVE EVALUATION AND LONGEVITY OF NEUTRALISING AND BINDING ANTIBODIES FOR SARS-COV-2

Natalie Davidson¹, Jenny Evans², Jenny Robson¹

¹Department of Microbiology, Sullivan and Nicolaides Pathology, Brisbane, Qld, Australia; and ²Department of Immunology/Serology, Sullivan and Nicolaides Pathology, Brisbane, Qld, Australia

There are many unanswered questions regarding serological testing for SARS-CoV-2 including the longevity of the neutralising antibody response and correlation with binding antibodies and subsequent protection. This study evaluated the durability of neutralising antibody response over a 12-month period using the cPass™ SARS-CoV-2 sVNT and correlation with binding antibodies using both the LIAISON® SARS-CoV-2 S1/S2 IgG and Abbott Architect SARS-CoV-2 IgG. 214 samples were evaluated from 81 SARS-CoV-2 NAAT confirmed positive patients collected from March 2020-March 2021 at various time intervals post symptom onset. 120 samples from a reference non-infected population were used for specificity analysis. The cPass™ SARS-CoV-2 sVNT had the highest overall sensitivity 90.3% [CI 84.9, 93.1]. Specificity was comparable to both binding antibody assays, 98.33 [CI 95.4, 99.96]. Sensitivity peaked at 3-6 months post symptom onset at 100% [CI 91.4, 100.0] and persisted up to 9-12 months post infection with sensitivity of 78.8% [CI 62.3, 89.3]. S1/S2 binding antibodies demonstrated satisfactory correlation with RBD neutralising antibodies (Spearman coefficient 0.8937 [CI 0.86, 0.92]); nucleocapsid antibodies, however, waned markedly 6 months following

infection. There was an association with clinical severity and degree of neutralising antibody response ($p=0.0025$). No association between age or gender was demonstrated in this study. These results support both the use of the cPass™ SARS-CoV-2 sVNT to assess neutralising antibodies and the possible use S1/S2 binding antibodies as a surrogate for neutralising antibodies in diagnostic laboratories; as well as provides information on durability of neutralising antibody response and kinetics over time as the COVID-19 pandemic unfolds.

LABORATORY SAFETY: HANDLING *B. PSEUDOMALLEI* ISOLATES WITHOUT A BIOSAFETY CABINET

Ian Gassiep^{1,2}, Michelle J. Bauer¹, Patrick N. A. Harris^{1,3}, Mark D. Chatfield¹, Robert Norton⁴

¹University of Queensland Centre for Clinical Research, Royal Brisbane and Women's Hospital, Herston, Qld, Australia;

²Department of Infectious Diseases, Mater Hospital Brisbane, South Brisbane, Qld, Australia; ³Pathology Queensland, Royal Brisbane & Women's Hospital, Herston, Qld, Australia; and

⁴Pathology Queensland, Townsville University Hospital, Townsville, Qld, Australia

Background: *B. pseudomallei* is a tier 1 select agent that is associated with laboratory-acquired melioidosis, with international guidelines recommending isolate handling within a class II biosafety cabinet (BSC) in a Biosafety Level (BSL) 3 facility. In low-resource settings this may not be practical, and therefore the authors aimed to assess the risk of laboratory-acquired melioidosis during routine work.

Methods: A questionnaire combined with two serological assays were conducted to determine prior exposure to the organism. Additionally, we performed controlled environmental air sampling during 78 laboratory handling events including plate opening, oxidase testing, and McFarland suspension creation.

Results: Of 30 laboratory scientists to handle *B. pseudomallei* on 1,267 occasions outside a biosafety cabinet no infections were documented and all participants remained seronegative. None of the experiments demonstrated aerosolisation of the organism.

Conclusion: This study suggests the risk of laboratory-acquired melioidosis is likely to be low. However, individual laboratories will need to undertake a risk assessment including melioidosis endemicity, availability of resources for containment, the nature of routine handling to be undertaken, and the presence of predisposing risk factors for infection in the staff concerned. Further research is required to better understand on the risk of infection in the microbiology laboratory.

Contribution: IG conceived of the idea, obtained funding, obtained ethics approval, performed bioaerosol experiments and contributed to each section of the manuscript.

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NEONATAL CANDIDAEMIA; SIX-YEAR EXPERIENCE FROM A TERTIARY CARE CENTRE IN SRI LANKA

G. P. S. Gunaratna¹, M. G. T. D. Wijewardhane¹, A. Sutharson¹, U. A. G. H. Wickramasuriya¹, Y. C. Waniganayake¹, K. K. M. K. Premaratne¹, J. Galappaththi¹, D. Somasiri¹, S. M. P. Karunaratne¹,