Viral Pneumonia and Bacterial Infections in the Age of Novel Viruses

The ALINTY i B·R·A·H·M·S PCT [1] and ARCHITECT B·R·A·H·M·S PCT [2] assays are chemiluminescent microparticle immunoassays (CMIA) for the quantitative determination of procalcitonin (PCT) in human serum and plasma (lithium heparin and K2EDTA) on the Alinity i and ARCHITECT analyzers. Used in conjunction with other laboratory findings and clinical assessments the assays are intended for use as an:

- Aid in the risk assessment of critically ill patients on their first day of intensive care unit (ICU) admission for progression to severe sepsis and septic shock.
- Aid in assessing the cumulative 28-day risk of all-cause mortality for patients diagnosed with severe sepsis or septic shock in the ICU or when obtained in the emergency department or other medical wards prior to ICU admission, using a change in PCT level over time.
- Aid in decision making on antibiotic therapy for patients with suspected or confirmed lower respiratory tract infections (LRTI) - defined as community-acquired pneumonia (CAP), acute bronchitis, and acute exacerbation of chronic obstructive pulmonary disease (AECOPD) - in an inpatient setting or an emergency department.
- Aid in decision making on antibiotic discontinuation for patients with suspected or confirmed sepsis.

See Page 2 for additional Safety Information

PCT testing is important when evaluating patients with any community acquired pneumonia as its use helps distinguish patients presenting with viral pneumonia from those that have bacterial infections that predispose to development of severe bacterial sepsis.[1,2] Patients with bacterial infections benefit from initiation of antibiotic therapy. [1,2] PCT testing may also help identify patients initially presenting with viral infection who subsequently develop secondary bacterial infections, as the patients who develop bacterial infections may benefit from initiation of antibiotics.[1,2,3,4]

PCT testing is important during viral pandemics such as the current COVID-19 pandemic, as some patients may still present with bacterial infections and other critically ill patients may develop secondary bacterial infections. [3-4,10] Identifying those patients with bacterial infections that may benefit from antibiotics and monitoring the antibiotic treatment is always important.[1,2]

During this crisis the data is rapidly changing. Some recent studies reporting information gathered during this pandemic have suggested there may be additional benefit to PCT testing when evaluating and treating patients infected with the SARS-CoV-2.[5-9] The IFCC recommends certain tests, including PCT, as helpful in assessing severe infection.[10]

For In Vitro Diagnostic Use
Rx Only: For use by or on the order of a physician only

WARNINGS AND PRECAUTIONS – TEST INTERPRETATION

• The Alinity i B·R·A·H·M·S PCT and ARCHITECT B·R·A·H·M·S PCT assays are not indicated to be used as a stand-alone diagnostic assay and should be used in conjunction with clinical signs and symptoms of infection and other diagnostic evidence.

• **Decisions regarding antibiotic therapy should NOT be based solely on PCT concentrations.**

• PCT results should always be interpreted in the context of the clinical status of the patient and other laboratory results. Changes in PCT levels for the prediction of mortality, and overall mortality, are strongly dependent on many factors, including preexisting patient risk factors and clinical course.

• The need to continue ICU care at Day 4 and other covariates (e.g., age and Sequential Organ Failure Assessment [SOFA] score) are also significant predictors of 28-day cumulative mortality risk.

• Certain patient characteristics, such as severity of renal failure or insufficiency, may influence PCT values and should be considered as potentially confounding clinical factors when interpreting PCT values.

• PCT levels may not be elevated in patients infected by certain atypical pathogens, such as Chlamydophila pneumoniae and Mycoplasma pneumoniae.

• **Low PCT levels do not always indicate absence of bacterial infection.** Falsely low PCT levels in the presence of bacterial infection may occur during the early course of infections, in localized infections, and in subacute infectious endocarditis.

• **Increased PCT levels may not always be related to systemic bacterial infection.** There are a few situations where PCT levels may be elevated by non-bacterial causes. These include, but are not limited to, the following:

- Neonates at < 48 hours of life (physiological elevation)
- Severe illness such as polytrauma, burns, major surgery, and prolonged or cardiogenic shock
- Treatment with OKT3 (muromonab-CD3) antibodies and other drugs stimulating the release of pro-inflammatory Cytokines
- Patients with invasive fungal infections
- Patients with acute attacks of Plasmodium falciparum malaria
- Patients receiving peritoneal dialysis or hemodialysis treatment
- Patients with biliary pancreatitis, chemical pneumonitis, or heat stroke
- Patients with small cell lung cancer, severe liver cirrhosis and acute or chronic viral hepatitis, or medullary C-cell carcinoma of the thyroid

• The safety and performance of PCT-guided therapy for individuals younger than age 18 years, pregnant women, immunocompromised individuals, or those on immunomodulatory agents was not formally analyzed in the supportive clinical trials.

• Alinity i B·R·A·H·M·S PCT and ARCHITECT B·R·A·H·M·S PCT results should not be used interchangeably with other methods for PCT determinations for monitoring patients.

References

1. Alinity B·R·A·H·M·S PCT [package insert]. 2018; G99806R01
2. ARCHITECT B·R·A·H·M·S PCT [package insert]. 2017; G1-0601/ R01

3. van der Sluijs et al. Bench-to-Bedside review: Bacterial pneumonia with influenza - pathogenesis and clinical implications. *Critical Care* 2010, 14:219
4. D. Morens, et al. Predominant Role of Bacterial Pneumonia as a Cause of Death in Pandemic Influenza: Implications for Pandemic Influenza Preparedness. *J Infect Dis*. 2008 October 1; 198(7): 962–970. doi:10.1086/591708
5. M. Singer, C.S. Deutschman, C.W. Seymour, M. Shankar-Hari, D. Annane, M. Bauer, et al., The third international consensus definition for sepsis and septic shock (Sepsis-3). JAMA 2016; 315: 801-810.
6. W-J. Guan, Z-Y Ni, Y-H. Hu, W-H. Liang, C-Q. Ou, J-X. He, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020; DOI: 10.1056/NEJMoa2002032
7. G. Lippi, M. Plebani. Procalcitonin in patients with severe coronavirus disease 2019 (COVID-19): A meta-analysis. Clin Chim Acta 2020;
8. F. Zhou, T. Yu, R. Du, G. Fan, Y. Liu, Z. Liu, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020; https://doi.org/10.1016/S0140-6736(20)30566-3
9. Istituto Superiore di Sanità (Italian NIH). [Report on the characteristics of patients died with COVID-19 disease in Italy] March 20th, 2020.
10. https://www.ifcc.org/ifcc-news/2020-03-26-ifcc-information-guide-on-covid-19/