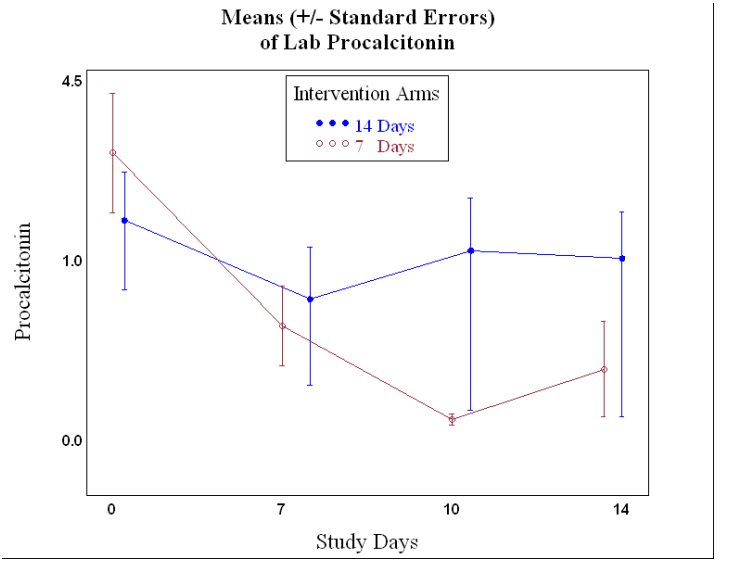
Procalcitonin and Endothelial Biomarkers Sub-Study

The BALANCE Trial is randomizing patients to fixed shorter (7 days) versus fixed longer (14 days) treatment for bacteremia, rather than assessing an individualized biomarker-guided antibiotic stopping rule.

However, in this sub-study we will assess the time profile of PCT and other markers among a subset of patients enrolled at BALANCE study sites. Blood samples will be drawn on the randomization day and at days 7, 10 and 14 from the index blood culture collection. Around 3 ml of whole blood will be drawn from those participants who have signed the optional additional informed consent for blood collection. Samples will be stored in a freezer at -25 ± 6°C at each participating site, and then batched and forwarded to the central study site for processing at the end of the study period. The results will not be made available to the treating team, because this could unduly influence clinical practice and protocol adherence, and is ethical because none of the

participating sites are currently using PCT as part of routine clinical practice.

The sub-study will compare the performance characteristics of circulating endothelial and inflammatory biomarkers to PCT for these outcomes. The panel of analytes include mediators of endothelial activity (Ang-1, Ang-2, Tie1, Tie2, sFlt-1, and Slit2/ROBO4) and markers of systemic inflammation (IL-6, sTNFR1, sTNFR2, sTREM-1, CHI3L1), and are described in greater detail below. With the exception of Ang-1, we hypothesize that circulating concentrations of these analytes will be higher on Day7 among those patients who fail short-courses of antibiotic therapy. As Ang-1 is a marker of endothelial stability, we hypothesize that relatively decreased circulating concentration will be associated with treatment failure.


Means (+/- Standard Errors)
of Lab Procalcitonin
Intervention Arms
14 Days
7 Days
Procalcitonin
4.5
1.0
0.0
0
7
10
14
Study Days