QUESTIONS FOR CAC ON THE USE OF MOLECULAR DIAGNOSTIC TESTING TO IDENTIFY ACUTE REJECTION IN HEART OR LUNG TRANSPLANT RECIPIENTS

Heart Transplant Recipients

Test(s): AlloMap, AlloSure, Prospera, Viracor TRAC

1. Is there sufficient evidence to identify the patient population that the molecular diagnostic test could be used? (e.g., risk level, ethnic/cultural demographics, repeat transplant recipients, etc.)

2. Is there sufficient evidence on the clinical context (i.e., for-cause vs. surveillance) in which the molecular diagnostic test could be used?

3. In the existing evidence, what is the level of confidence (or certainty) regarding test performance data reported without any confidence intervals?

4. Is there sufficient evidence to support the utility of surveillance (not for-cause) testing in heart transplant recipients?

    4b. If yes, what is the appropriate testing schedule based on the published evidence?

5. Is there sufficient evidence on the ability of the molecular diagnostic test (or combination of tests) to discriminate rejection (acute T-cell-mediated or antibody-mediated) from quiescence?

6. Is there sufficient evidence to standardize thresholds/cutoffs in heart transplant recipients?

    6a. Are currently published thresholds/cutoffs affected by the time post-transplant?

    6b. If "yes" for any of the tests (AlloMap, AlloSure, Prospera, and Viracor TRAC) please comment on how the thresholds/cutoffs are affected by the time post-transplant.

    6c. Based on the evidence, for heart transplant recipients, what should the appropriate thresholds/cutoffs be for AlloMap, AlloSure, Prospera, and Viracor TRAC?

7. Is there sufficient evidence to indicate that in patients **without signs and symptoms** of rejection, use of the molecular diagnostic test (or combination of tests) would preclude the need for endomyocardial biopsy?

8. Is there sufficient evidence to indicate that in patients **with signs and symptoms** of rejection, use of the molecular diagnostic test (or combination of tests) would preclude the need for endomyocardial biopsy?

9. Is there sufficient evidence on the ability of the molecular diagnostic test (or combination of tests) to guide clinical management without endomyocardial biopsy?

    8b. If yes, what aspect of your clinical management would be influenced by the test result?

10. Would you perform an endomyocardial biopsy if the molecular diagnostic test indicates rejection, but the patient exhibits no signs and symptoms of rejection?

11. How confident are you in the evidence that, for AlloMap, an elevation in the AlloMap score, indicates rejection?

12. How confident are you in the evidence that, for AlloSure, Prospera, and Viracor TRAC, an elevation in donor-derived cell-free DNA indicates rejection?

Lung Transplant Recipients

Test(s): AlloSure, Prospera and Viracor TRAC

1. Is there sufficient evidence to identify the patient population that the molecular diagnostic test could be used? (e.g., risk level, ethnic/cultural demographics, repeat transplant recipients, etc.)

2. Is there sufficient evidence on the clinical context (i.e., for-cause vs. surveillance) in which the molecular diagnostic test could be used?

3. In the existing evidence, what is the level of confidence (or certainty) regarding test performance data reported without any confidence intervals?

4. Is there sufficient evidence to support the utility of surveillance testing in lung transplant recipients?

    4b. If yes, what is the appropriate testing schedule based on the published evidence?

5. Is there sufficient evidence on the ability of the molecular diagnostic test to discriminate rejection (acute cellular, antibody-mediated, chronic lung allograft dysfunction) from quiescence?

6. Is there sufficient evidence to standardize thresholds/cutoffs in lung transplant recipients?

    6a. Are currently published thresholds/cutoffs affected by the time post-transplant?

    6b. If “yes” for any of the tests (AlloSure, Prospera, Viracor TRAC) please comment on how the thresholds/cutoffs are affected by the time post-transplant.

    6c. Based on the evidence, for lung transplant recipients, what should the appropriate thresholds/cutoffs be for AlloSure, Prospera, and Viracor TRAC?

7. Is there sufficient evidence to indicate that in patients **without signs and symptoms** of rejection, use of the molecular diagnostic test would preclude the need for transbronchial biopsy?

8. Is there sufficient evidence to indicate that in patients **with signs and symptoms** of rejection, use of the molecular diagnostic test would preclude the need for transbronchial biopsy?

9. Is there sufficient evidence on the ability of the molecular diagnostic test to guide clinical management without transbronchial biopsy?

   8b. If yes, what aspect of your clinical management would be influenced by the test result?

10. Would you perform a transbronchial biopsy if the molecular diagnostic test indicates rejection, but the patient exhibits no signs and symptoms of rejection?

11. How confident are you in the evidence that, for AlloSure, Prospera and Viracor TRAC, an elevation in donor-derived cell-free DNA indicates rejection?