Effective Health Care

Monitoring of Maintenance Immunosuppressants in Solid Organ Transplantation Nomination Summary Document

Results of Topic Selection Process & Next Steps

- Monitoring of maintenance immunosuppressants in solid organ transplantation will go forward for refinement as a systematic review. The scope of this topic, including populations, interventions, comparators, and outcomes, will be further developed in the refinement phase.

- When key questions have been drafted, they will be posted on the AHRQ Web site and open for public comment. To sign up for notification when this and other Effective Health Care (EHC) Program topics are posted for public comment, please go to http://effectivehealthcare.ahrq.gov/index.cfm/join-the-email-list1/.

Topic Description

Nominator: Health care professional organization

Nomination Summary: The nominator questions the utility of diagnostic methods to monitor immunosuppressant drug therapy during the maintenance stage following solid organ transplantation. This nomination is focused on the optimization and monitoring of the calcineurin inhibitors (cyclosporine and tacrolimus) and mTOR inhibitors (sirolimus and everolimus).

Staff-Generated PICO
Population(s): Heart, lung, liver, and kidney transplant patients
Intervention(s): Calcineurin and/or mTOR inhibitors for maintenance therapy regimens, therapeutic drug monitoring, timing of therapeutic drug monitoring (e.g., trough, AUC, 2 hours post dose), monitoring frequency (e.g., 24, 48, twice weekly), and diagnostic methods to monitor immunosuppressant drug therapy (e.g., liquid chromatography or mass spectrometry)
Comparator(s): Comparison between different calcineurin and/or mTOR inhibitor treatment regimens, fixed dose immunosuppressant therapy, comparison of therapeutic drug monitoring methods including timing, frequency, and diagnostic method
Outcome(s): Fewer rejection episodes, patient and graft survival, cost savings, adverse effects

Key Questions from Nominator:

1. Is the concept of a core/maintenance drug regimen specific to a particular transplanted organ feasible, given the variety of factors involved (i.e., individual differences in pharmacokinetics, combination therapy, clinical state, and time post

transplant)?

2. If an organ specific regimen is possible, should there be a subset treatment guideline for each organ that is customized for particular cohorts of patients, for example pediatric, the elderly, patients with specific disease conditions, or by race?
3. What initiatives should be undertaken to provide more standardized laboratory drug levels given the different methodologies and standardization material and sample timing?
4. Can optimum therapeutic goals be established for each regimen and its subsets, particularly given differences in methodology and sampling times?
5. Is there evidence that better utilization of core/maintenance immunosuppressants will result in fewer rejection episodes, better graft survival, and/or cost savings?

Considerations

- The topic meets all EHC Program selection criteria. (For more information, see http://effectivehealthcare.ahrq.gov/index.cfm/submit-a-suggestion-for-research/how-are-research-topics-chosen/.)

- Maintenance immunosuppressive therapy occurs after the transplant, usually for the life of the transplanted organ. The goals of immunosuppression in solid organ transplant are to prevent allograft (organ transplant from another individual) rejection, optimize the organ function, and prolong and improve patient survival. However, due to the adverse effects of many of these immunosuppressive agents, the focus of care has more recently shifted to finding a balance between acceptable rates of rejection with tolerable adverse effects. There is no universal protocol for immunosuppressive treatment across all solid organ transplants. The choice of treatment remains specific to the organ in question and must also include consideration of patient factors and acceptable levels of adverse effects. Therapeutic drug monitoring (TDM) comprises the measurement and interpretation of drug exposure, and aims to assist physicians in choosing the drug dose for an individual patient. TDM is mandatory for most immunosuppressants and has become an integral part of immunosuppressive drug therapy; however, there is still considerable uncertainty as to optimal monitoring strategy for different transplanted organs.