

Slides for projector

Immunosuppressive therapy for kidney transplantation in:

Adults (ID456; review of TA85)

Children and young people (ID346; review of TA99)

Multiple Technology Appraisals

4th Appraisal Committee meeting

26 July 2017

Background

- 2 MTAs on immunosuppressive therapy for kidney transplant
 - Adults (review of TA85, 2004)
 - Children and young people (review of TA99, 2009)
- FAD issued December 2015 – appeal hearing March 2016
- Post-appeal discussion March 2017 – key issues included:
 - Are 2nd/subsequent transplants and/or subsequent treatments during the life of a graft included in the scope?
 - Is there enough evidence to make a recommendation in these scenarios?
 - Any other evidence to consider, or value to the NHS of further work?
 - ACD released
- Fourth committee meeting: To consider consultation comments

ACD preliminary recommendations

Adults and children and adolescents

- Basiliximab, immediate-release tacrolimus and mycophenolate mofetil recommended as **initial** options to prevent organ rejection
- r-ATG, prolonged-release tacrolimus, mycophenolate sodium, sirolimus, everolimus and belatacept not recommended as **initial** treatments to prevent organ rejection
- Committee unable to make recommendations for people who are, or become, unable to have recommended technologies or standard triple therapy because of contraindications or intolerance, including:
 - People who need to switch to another therapy during the life of their graft
 - People having a 2nd/subsequent transplant, having previously found that 1 or more recommended treatments or standard treatments are unsuitable

r-ATG: rabbit anti-human thymocyte immunoglobulin

Immunosuppressive therapy for kidney transplantation in **adults** (review of TA85)

ACD consultation

ACD consultation

- Comments received from consultees:
 - Astellas
 - Novartis
 - Sanofi
 - British Kidney Patient Association (BKPA)
 - British Transplantation Society (BTS)
 - Efficacy and Safety of PRescribing In Transplantation (ESPRIT)
 - Clinical expert
 - Cheisi
 - Sandoz
 - Teva UK
- Web comments received from:
 - Consultant nephrologist/transplant physician

General comments

- Consultees support draft recommendations
- *Specific question: Would additional NICE technology appraisal guidance add value, or would other routes be more appropriate to eliminate any outstanding clinical or commissioning issues, e.g. other NICE programmes or NHS England commissioning policies?*
 - No need for further NICE technology appraisal work
 - NHS commissioning policy would be a suitable route for additional guidance to the NHS

Comments on the recommendations 1

- Recommendations don't provide explicit guidance for people who can't have immediate-release tacrolimus because of:
 - the gelatine capsule – *raised at previous ACD consultation*
 - *NICE response at previous ACD consultation: “NICE recommendations on interventions associated with animal-derived products do not pose an equality issue. When a topic is referred, the intervention is appraised for the population for which it is intended and the fact that some people may not be able accept the intervention cannot be addressed through any NICE recommendations.”*
 - *Gelatine-free formulations of immediate-release tacrolimus and ciclosporin are available*
 - *Issue also applies to some formulations of mycophenolate mofetil (others are gelatine-free) – azathioprine is gelatine-free*
 - allergies to different excipients – *covered in preliminary recommendations*

Recap: ACD preliminary recommendations

Committee unable to make recommendations for people who are, or become, unable to have recommended technologies or standard triple therapy including:

- *People who need to switch to another therapy during the life of their graft*
- *People having a 2nd/subsequent transplant, having previously found that 1 or more recommended treatments or standard treatments are unsuitable because of **contraindications or intolerance***

Comments on the recommendations 2

- Recommendations should state that the choice of treatment should be based on clinical judgement, accounting for the needs and preferences of the patient
- Include treatment failure as a situation in which the recommended treatments may be unsuitable

Recap: ACD preliminary recommendations

Committee unable to make recommendations for people who are, or become, unable to have recommended technologies or standard triple therapy including:

- *People who need to switch to another therapy during the life of their graft*
- *People having a 2nd/subsequent transplant, having previously found that 1 or more recommended treatments or standard treatments are unsuitable because of **contraindications or intolerance***

Comments on specific technologies

r-ATG

- Recommendations suggest r-ATG is not recommended for **treating** steroid-resistant acute rejection
 - The final recommendation should clarify that this use of r-ATG is outside the remit of the appraisal
- There is robust evidence to support a recommendation for r-ATG for grafts at high risk of acute rejection – *considered previously, not cost-effective*
- The economic analyses do not account for the lower incidence of antibody-treated acute rejection, and reduced costs, with r-ATG compared with basiliximab – *considered previously, no robust evidence to suggest significant difference between r-ATG and basiliximab for mortality, graft loss or graft function*

Recap: ACD preliminary recommendations

*r-ATG ... [is] not recommended as [an] **initial** treatment to prevent organ rejection*

Comments on specific technologies

Prolonged-release tacrolimus

- There is a clinical need for this option to achieve immunosuppression while mitigating the side effects associated with high peak levels of tacrolimus
- Guidance should highlight that prolonged-release tacrolimus would be an alternative to immediate-release tacrolimus if available at a similar cost – *discussed at appeal, costs not equivalent at time of appraisal*

Belatacept

- Belatacept is likely to be cost effective if the reduced incidence of myocardial infarction, cerebrovascular accidents, new-onset diabetes after transplant and resulting hospital visits are taken into account – *included in model*

Other comments

- Guidance doesn't account for the increased risk of graft loss due to non-adherence, and morbidity and increased mortality associated with a return to dialysis – *morbidity and increased mortality included in model*
- Guidance should highlight that:
 - a significant and recognisable group may need alternatives to calcineurin inhibitors
 - new evidence shows tacrolimus withdrawal should be avoided even in people with a low risk of rejection, as raised by the clinical expert
- 2 year review date would be more appropriate than 3 years given the changes to product availability and licences

Text clarifications within ACD

- Include Adoport in *'The committee concluded that its preferred analysis used eMIT prices when available and the prices agreed with the Commercial Medicines Unit for Modigraf and Advagraf.'*
 - *NICE response: agree*
- Include pack sizes available for immediate-release tacrolimus in line with the other technologies
 - *NICE response: agree*
- Change 'haemodialysis' to 'dialysis' because patients have the right to chose the therapy that suits them
 - *NICE response: agree*
- Conclusions should highlight the effects on quality of life and side effects as well as cost of dialysis if a transplant fails
 - *NICE response: agree*

Immunosuppressive therapy for kidney transplantation in **children and young people** (review of TA99)

ACD consultation

ACD consultation

- Comments received from consultees:
 - Astellas – *same comments as adult*
 - Novartis – *same comments as adult*
 - British Association for Paediatric Nephrology (BAPN) – *new comments*
 - British Kidney Patient Association (BKPA) – *same comments as adult*
 - Efficacy and Safety of PRescribing In Transplantation (ESPRIT) – *same comments as adult*
- Several comments received about the adult ACD also apply to the children and young people ACD
 - Chiesi, Sanofi, Sandoz, Teva, British Transplantation Society (BTS), clinical expert, consultant nephrologist/transplant physician

Comments on the recommendations: Children and young people-specific

- Ciclosporin is not standard therapy in UK paediatric transplant units. Amend description of standard therapy in recommendations to '**tacrolimus**, azathioprine and a corticosteroid'
- Clarify that standard therapy is acceptable in the context of the recommendations. There is no evidence to support improved outcomes with basiliximab and mycophenolate mofetil over tacrolimus, azathioprine and a corticosteroid in children
- Clarify the use of immunosuppression in people (highly) sensitised for reasons other than a previous transplant

Recap: ACD preliminary recommendations

*Committee unable to make recommendations for children and young people who are, or become, unable to have recommended technologies or standard triple therapy (**ciclosporin**, azathioprine and a corticosteroid) including:*

- *People who need to switch to another therapy during the life of their graft*
- *People having a 2nd/subsequent transplant, having previously found that 1 or more recommended treatments or standard treatments are unsuitable because of contraindications or intolerance*

Key issues for consideration: Adults

- Is there robust evidence to support a recommendation for r-ATG for grafts at high risk of acute rejection?
- Should the recommendations provide explicit guidance if immediate-release tacrolimus is not suitable because of religious or cultural reasons?
 - Comments would also apply to the children and young people ACD
- Are there any other issues that the committee needs to discuss as a result of the consultation?

Key issues for consideration

Children and young people-specific

- Should the guidance:
 - clarify the use of immunosuppression in people (highly) sensitised for reasons other than a previous transplant?
 - state that standard therapy in UK paediatric transplant units is '*tacrolimus*, azathioprine and a corticosteroid'
 - clarify that standard therapy is acceptable in the context of the recommendations?
- Are there any other issues that the committee needs to discuss as a result of the consultation?