INVESTIGATING THE HEALTH-ECONOMIC IMPACT OF BIOMARKER-DRIVEN IMMUNOSUPPRESSION (BIODRIM) FOLLOWING RENAL TRANSPLANTATION

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BACKGROUND AND OBJECTIVES

Immunosuppression (IS) following solid organ transplantation is indicated to avoid allograft rejection but puts a significant burden on patients due to • life-long dependency on medication and • exposure to potentially severe side-effects, as well as on health-care systems due to • medication costs and • costly treatments of side-effects, e.g., malignancies, cardiovascular events, post transplant diabetes.

Organ-tolerance with low IS medication or no IS at all has been observed1, triggering less side-effects and downstream costs. It has been shown that tolerance might be forecasted with the help of appropriate biomarkers. BioDrIM will evaluate the clinical and health-economic performance and utility of appropriate pre- and post-transplant biomarkers, able to predict the risk of rejection and thereby indicating patients eligible for a reduced IS medication plan.

Our objective is to present the study design incorporated in the CELLIMIN trial of BioDrIM, to investigate the health-economic profile of a biomarker-guided reduced IS medication regime and to determine whether biomarker-guided reduced IS following renal transplantation is associated with less costs and better clinical outcomes compared to a status-quo IS regime.

METHODS

CELLIMIN is a prospective randomized controlled clinical trial that will randomize 301 patients, eligible for reduced IS, on a 1:1 ratio to a “high-IS” (arm A, standard of care) and a “low-IS” regime (arm B). Comparisons will be made between these arms and assumed full IS regimes using health-economic modelling.

QALY Assessment

Health-related Quality of Life (QoL) will be assessed using standard generic and disease-specific questionnaires, see table 1. Timing of QoL assessments has been set according to expected changes in QoL considerations into clinical trials is crucial for establishing a solid individualized IS regimes and have been addressed in the study design of CELLIMIN. However, early integration of health-economic considerations into clinical trials is crucial for establishing a solid evidence base for future decisions by authorities as well as clinicians and treatment developers.

CONCLUSIONS

Several health-economic challenges arise in the context of evaluating individualized IS regimes and have been addressed in the study design of CELLIMIN. However, early integration of health-economic considerations into clinical trials is crucial for establishing a solid evidence base for future decisions by authorities as well as clinicians and treatment developers.

Table 1: Quality of Life Instruments to be applied in CELLIMIN Trial

<table>
<thead>
<tr>
<th>Questionnaire</th>
<th>Type</th>
<th>Dimensions</th>
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<tbody>
<tr>
<td>EQ-5D-5L</td>
<td>generic</td>
<td>Mobility, Self-Care, Usual Activities, Pain / Discomfort, Anxiety / Depression</td>
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<tr>
<td>SF-36v2</td>
<td>generic</td>
<td>Vitality, Physical Functioning, Bodily Pain, General Health Perceptions, Physical Role Functioning, Emotional Role Functioning, Social Role, Functioning, Mental health</td>
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<tr>
<td>KTQ-25</td>
<td>disease-specific</td>
<td>Symptoms related to kidney transplantation and subsequent Immunosuppression</td>
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</table>

Table 2: expected outpatient-visit frequencies for CNI blood level concentration measurements

<table>
<thead>
<tr>
<th>month post transplantation</th>
<th>W1</th>
<th>W2</th>
<th>W3</th>
<th>W4</th>
<th>W5</th>
<th>W6</th>
<th>W7</th>
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<tbody>
<tr>
<td>day post transplantation</td>
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<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
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<td>x</td>
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<tr>
<td>recommended clinic frequency</td>
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<td>1</td>
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Figure 1a: Flowchart illustrating patient allocation in CELLIMIN trial

Figure 1b: Flowchart illustrating health-economic evaluation principles

Cost Assessment

The cost-assessment alongside the CELLIMIN trial is separated into two major blocks:

• Micro-costing procedure to determine appropriate costs for the biomarker-stratification procedure in specialized laboratories
• Assessment of patient-specific resource consumption, employment status and medical leave periods by using situation-dependent and study-specific questionnaires for patients and study personnel at regular study visits (M3, M6, M12, M18, M24) and in cases of repeated hospitalizations.

The Micro-Costing procedure will be performed in a central study-lab used for analyzing individual pre-transplant biomarker results. The assessment of patient-specific resource consumption will be conducted using questionnaires to be answered by patients and trial staff reviewing inpatient records. Three versions of the questionnaire have been designed to suit various situations in the study context:

• Details of initial hospitalization
• Details of repeated hospitalization
• Details of regular study visits

Assessed resource-use items include but are not limited to: Inpatient length of stay, Time spent in each hospital ward, Major diagnostic assessments (e.g. CT, MRI, etc.), Major therapeutic procedures (e.g. Revision surgery, chemo-therapy, etc.), Treatment of complications (e.g. rejection episodes), Post-transplantation diseases (e.g. stroke, myocardial infarction, etc.), Re-transplantation, Dialysis, Outpatient visits incl. reason for visit and applied services, Employment status, Medical leave periods, Dependency on care-giving.

DISCUSSION

Costs for IS medication are likely to decrease in case of reduced IS. A reduction in adverse events attributable to IS might further reduce costs. Additional costs for the stratification process drive costs in the opposite direction.

Metabolization of IS shows great variability among patients requiring monitoring visits to adjust dosages and effectively reach target levels of IS medication. At least four additional outpatient visits to precisely control blood trough concentration levels of IS medication are expected in case of the reduced IS regime according to clinical practice guidelines2 and the CELLIMIN study protocol (see table 2).

Table 2: expected outpatient-visit frequencies for CNI blood level concentration measurements

<table>
<thead>
<tr>
<th>month post transplantation</th>
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<td>Recommended clinic frequency</td>
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References


Disclosures

Celogic GmbH (S. Weber and Dr. Pietzsch) provide consulting services for BioDrIM to conduct health-economic analyses.