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TRANSPLANTAČNO-NEFROLOGICKÉ ODDELENIE
TRANSPLANT-NEPHROLOGY DEPARTMENT

STUDY TITLE

Daratumumab for Late Antibody-Mediated Rejection in Kidney Transplant Recipients with De Novo Donor-Specific Antibodies: A Case-Control Study

(DARTABMR)

NCT number:

In Martin, Slovakia 8th JULY 2025

Study Title:

Transplantačno – Nefrologické oddelenie Univerzitná nemocnica Martin

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Acronym: DARTABMR

1. Study Design:

- Case-Control Study

2. Research Question:

- Is daratumumab superior to standard therapies (IVIG, plasmapheresis, rituximab) in improving outcomes in kidney transplant recipients with late antibody-mediated rejection (ABMR) and de novo donor-specific antibodies (DSA)?

3. Hypothesis:

- Kidney transplant recipients with late ABMR and de novo DSA treated with daratumumab will have a higher rate of treatment success (defined as improvement or stabilization of kidney function, reduction in DSA levels, and improvement in biopsy features) compared to those treated with standard therapies.

4. Groups:

- **Cases (Daratumumab Group):** Kidney transplant recipients with late ABMR and de novo DSA treated with daratumumab (1800mg subcutaneous, weekly x 4, then monthly x 6).
- **Controls (Standard Therapy Group):** Kidney transplant recipients with late ABMR and de novo DSA treated with standard therapies (IVIG, plasmapheresis, rituximab, etc.) *prior* to the start of the daratumumab study.

5. Inclusion Criteria:

- Kidney transplant recipient (first or subsequent transplant)
- Diagnosis of late ABMR (diagnosed >12 months post-transplant)
- Biopsy-proven ABMR
- Presence of de novo DSA

6. Exclusion Criteria:

- Active infection
- Other significant comorbidities that could affect outcomes or treatment safety
- Contraindications to daratumumab
- Prior treatment with daratumumab
- Specific types of DSA (consider specifying, e.g., unacceptable antigens)
- Non-adherence to standardized immunosuppression protocol (tacrolimus, MMF, steroids)

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- iFTA 2 or 3 on baseline biopsy

7. Matching Criteria (for Cases and Controls):

- Time of ABMR diagnosis (within a specified window)
- Baseline kidney function (eGFR at the time of ABMR diagnosis)
- Type and strength of DSA (anti-HLA Class I vs. Class II, MFI values)
- Number of previous transplants (if applicable)
- Age (within a specified range)
- Ethnicity

8. Standardized Immunosuppression Protocol:

- All participants (both cases and controls) should be on a standardized immunosuppression regimen consisting of tacrolimus, MMF, and steroids.
- Specify target tacrolimus levels, MMF dose, and steroid tapering schedule.
- Document any deviations from the protocol.

9. Data Collection:

- **Cases (Daratumumab Group):**
    - **Baseline:** Demographics, clinical history, immunosuppression regimen, kidney function (creatinine, eGFR), DSA levels (Luminex), kidney biopsy (Banff scoring, molecular analysis), cfDNA levels, flow cytometry for lymphocyte subsets, infection screening (CMV, EBV, BKV).
    - **During Treatment:** Monitor for infections regularly, tacrolimus levels, adverse events.
    - **Post-Treatment (After last daratumumab dose):** Kidney function (creatinine, eGFR), DSA levels (Luminex), kidney biopsy (Banff scoring, molecular analysis), cfDNA levels, flow cytometry for lymphocyte subsets, infection screening (CMV, EBV, BKV).
- **Controls (Standard Therapy Group):**
    - **Retrospective Data Collection:**
        - Treatment regimen (IVIG dose, plasmapheresis sessions, rituximab dose, etc.)
        - Kidney function (creatinine, eGFR) at baseline (time of ABMR diagnosis), after treatment, and during follow-up.
        - DSA levels (if available) at similar time points as the daratumumab group.

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- Biopsy findings (if available) at similar time points (challenging to obtain).
- Infections and adverse events during and after standard treatment.

10. Definition of Treatment Success:

- Improvement or stabilization of kidney function (e.g., increase or no significant decline in eGFR). Define "significant decline."
- Reduction in DSA levels (define a clinically meaningful reduction, e.g., >50% reduction in MFI).
- Improvement in biopsy features (e.g., reduction in Banff scores for glomerulitis, peritubular capillaritis). *This may be difficult to assess in the control group if repeat biopsies were not performed.*
- Absence of graft loss during a specified follow-up period.

11. Sample Size:

- Perform a power analysis to determine the appropriate sample size for both the case and control groups. This will depend on the expected effect size of daratumumab compared to standard therapies for the primary outcome (treatment success).

12. Statistical Analysis:

- Compare the proportion of patients who achieve treatment success in the daratumumab group versus the control group (using a chi-square test or Fisher's exact test).
- Compare changes in kidney function, DSA levels, and biopsy scores (if available) between the two groups (using t-tests, ANOVA, or non-parametric equivalents, as appropriate).
- Perform regression analysis to adjust for any remaining confounding variables that were not perfectly matched.
- Assess the incidence of infections and adverse events in both groups.

13. Ethical Considerations:

- Obtain informed consent from all participants.
- Ensure the study is approved by the Institutional Review Board (IRB).

14. Potential Biases:

- Selection bias (address through careful selection of controls).
- Information bias (address through thorough data collection and validation).
- Confounding bias (address through matching and regression analysis).

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