Monitoring within a Healthcare System

The Sanford PLEDGE Study

Kurt J. Griffin PhD, MD
Director of Clinical Trials
Sanford Health
Sioux Falls, South Dakota

In Partnership with

6th Childhood Diabetes Prevention Symposium
Barbara Davis Center
9 November 2023
PLEDGE Overview
Enrolling at every primary care clinic across Sanford footprint

0 – 6 y OR once 9 -16 y.
Genetic Risk Score
GRS2 Once at study entry
(blood spot; can be with Newborn Screening)

T1D AutoAb
Celiac Testing

Consent
(MyChart)

Completed Consent
Self-eligibility

Routine Care
Lab Collection

Lab Results
Epic / MyChart

Existing Infrastructure
– Collection
– Processing
– Shipping (PNRI)
– Results

Research Staff will:
– Contact Family & Explain
– Retest
– Persistent Positives → Monitoring

Goals: Prevent DKA at diagnosis!
Offer early interventions/trials
Referral to clinical care at appropriate time
PLEDGE Monitoring

• Centralized management in Sioux Falls, SD
  • 1 program manager
  • 1 clinical coordinator

• Decentralized Procedures
  • 157 clinics screening
  • Monitoring visits performed in local clinics
    • Use in-clinic labs for OGTT
    • Local staff start CGM
PLEDGE Monitoring

- Separate Protocol and Consent after confirmation of persistent antibody.
- Tailor extent and frequency to expected risk

Single Islet antibodies:
- Periodic reassessment of antibodies, Hemoglobin A1c
- Home ketone testing PRN symptoms or illness
PLEDGE Monitoring

- Separate Protocol and Consent after confirmation of persistent antibody.
- Tailor extent and frequency to expected risk

- Single Islet antibodies:
  - Periodic reassessment of antibodies, Hemoglobin A1c
  - Home ketone testing PRN symptoms or illness

- Stage 1: Multiple Islet Antibodies with Normal Glucose Regulation
  - Metabolic monitoring: Add OGTT, Hemoglobin A1c, Proinsulin:C-peptide ratio
  - Home testing: Ketones and Blood Glucose PRN Symptoms or illness

- Stage 2: Multiple Islet Antibodies with Impaired Glucose Regulation
  - Monitoring visits at least q 6 months.
  - Home testing:
    - Blood glucose 2 points monthly
    - Ketones and Blood Glucose PRN Symptoms or illness

---

**Positive Antibody Screen**

- Repeat Antibody Test

  - No Persistent Ab?
    - Exit
      - Rescreen PRN Sw/Concern or per local schedule
  - Single Positive
    - Periodic Autoantibody Reassessment
      - Yes
        - > 1 T1D Autoantibody?
          - Metabolic Monitoring
            - Lab
            - Home
          - Impaired Stage 2 (Increase Frequency)
          - Glycemic Status
            - Normal Stage 1a
            - Diagnostic
          - Offer Participation in appropriate Trials
      - No
        - Stable Single IA+ over time
          - Offer Participation in appropriate Trials
  - ≥ 2 Positive OR Single High Affinity
    - Persistent Ab?
      - Exit
        - Rescreen PRN Sw/Concern or per local schedule
      - Single Positive
        - Periodic Autoantibody Reassessment
          - Yes
            - > 1 T1D Autoantibody?
              - Metabolic Monitoring
                - Lab
                - Home
              - Impaired Stage 2 (Increase Frequency)
              - Glycemic Status
                - Normal Stage 1a
                - Diagnostic
              - Offer Participation in appropriate Trials
          - No
            - Stable Single IA+ over time
              - Offer Participation in appropriate Trials
**Education**

- **Ongoing education at every contact with families**
  - Signs/Symptoms of clinical T1D
  - Whom to contact for questions

- **Additional teaching & materials at specific events**
  - First Antibodies
  - Entry to stage 1
  - Entry to stage 2
  - Stage 3 & transition to clinical care
Alert for Clinicians

- How help providers recognize a child at risk for T1D when they present with relevant symptoms?

- “Patient Chart Advisory”
  - Appears on opening chart
  - Reminder to consider T1D
  - Provides guidance
  - Does not slow work
  - Less intrusive than BPA
Transition to Clinical Care

- When meet standard ADA diagnostic criteria
- Close communication with pediatric endocrine clinic
- Assessment of urgency may be aided by CGM data
- Goal: start insulin when necessary to keep within treatment targets
  - Start with mealtime rapid insulin if there are postprandial spikes
  - Basal insulin if fasting blood glucose is elevated

PLEDGE Monitoring Participants with Diagnostic (Stage 3) T1D labs

Positive urine ketones? T1D (Bloody)

- YES
  - Urgent clinical referral for initiation of insulin (Admission if appropriate)

- NO
  - Study team will educate family regarding S/Sx hyperglycemia
  - Home BG testing 8/9 (excl. postprandial)
  - Home Ketone testing PRR high 8G or 8x
  - Discuss with Peds Endo on call so that clinic team is aware of possible transition
  - Discuss timing of clinic appointment

- NO
  - Home BG >100 ± Moderate Ketones
    - YES
      - Family to call peds endo on call for clinical direction (Admission if appropriate)
    - NO
      - Consistent BG >200; Time in Range < 80%; HgbA1c > 5.9%
        - YES
          - Non-urgent initiation of Insulin (Admission if appropriate)
        - NO
          - Consider prandial coverage if having excursions after meals
            - ≥5 days CGM data may be helpful

- NO
  - Continue home monitoring
    - Periodic review of BG patterns

*Child may have linked CGM in place after PLEDGE monitoring visit

CGM may be downloaded at any interval

Hemoglobin A1c is a lagging indicator and BG may be well above target before A1c becomes abnormal
A work in Progress

• Multiple refinements already implemented based on new information
  – “high affinity” antibodies
  – Frequency of monitoring
  – Educational materials
  – Timing of reminders

• Feedback has been very helpful
  – External advisors and collaborators
  – Participating providers and staff
  – Laboratory staff and leadership
  – Participating families
Thank you!

The Sanford Project Team
Ann Mays
Magdalena Skon
Lana Baerenwald
Vanessa Williams
Mary Berg
Connie Hoffman
Staci Schwingler

Parent Representatives
Kristin Little
Holly McMahon

Clinical Providers
Luis Casas
Stephanie Hanson
John Shelso
Rashmi Jain
Benjamin Hoag
Jennifer Richstmeier

Sanford Health Plan
Emily Griese

www.sanfordhealth.org/PLEGE
Kurt.Griffin@sanfordhealth.org
Faculty Positions Available