Enrollment into Clinical Trials

HALI C. BRONCUCIA-RESEARCH INSTRUCTOR

ANDREA STECK, MD- PROFESSOR OF PEDIATRICS

Outline

- Background on TrialNet and BDC Prevention team
- Screening
- Metabolic Monitoring
- Clinical trial Enrollment
- Barriers to Enrollment

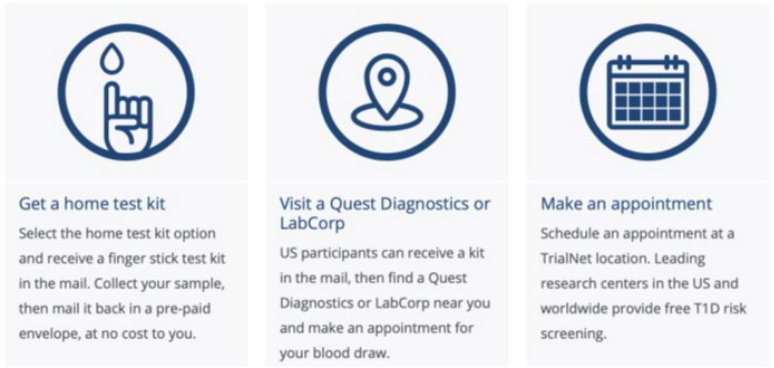
Introduction: Type 1 Diabetes TrialNet

TrialNet Offers

- Free screening for:
  - Family members of those with T1D:
    - 1st degree relatives between 2.5-45 years
    - 2nd/3rd degree relatives between 2.5-20 years
  - Anyone 2.5 to 45 years found AAb+ outside of TrialNet
- Monitoring for relatives with positive autoantibodies
- Offers participation in trials that may stop or slow the progression of T1D (both general population and relatives)

TrialNet Screening

- Sign up online from anywhere in the US
- Choice of venipuncture kit or capillary kit
- Partnered with Quest and LabCorp
- AAb+ participants receive follow up and monitoring at clinical sites



TrialNet Monitoring

- Single AAB+ participants
  - Annual monitoring for progression to Stage 1
- Multiple AAB+ participants
  - HbA1c and OGTT every 6-12 months depending on risk
- Access to prevention trials

TrialNet's Open Door Policy

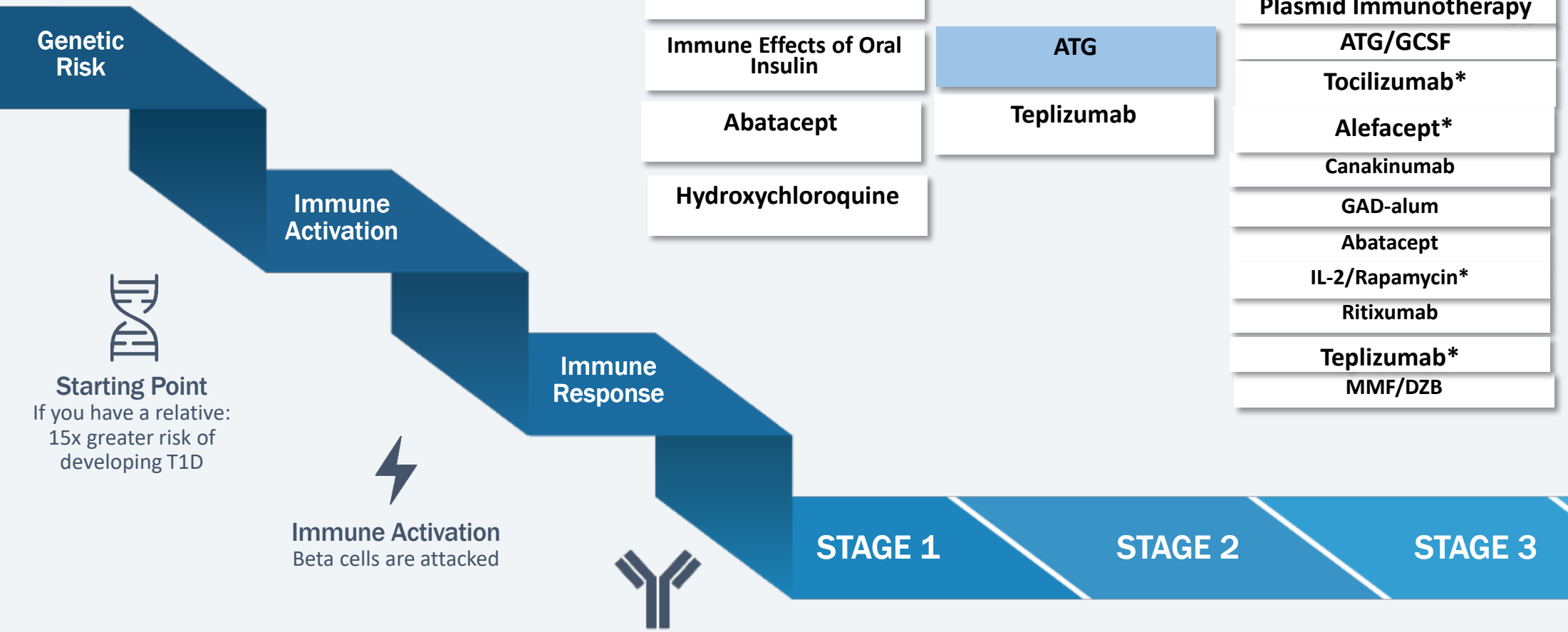
ANYONE who is identified as AAB+ can be part of TrialNet

AAB+ individuals do not need to be a relative to be part of a TrialNet Clinical Trial

Individuals identified as AAB+ outside of TrialNet interested in clinical trials will undergo TrialNet AAB confirmation testing and then other standard screening to determine trial eligibility

Pathway to Prevention

LIFT



* Immune Tolerance Network

TrialNet Overview 2/2023

TrialNet Research Currently Enrolling

TN01: Pathway to Prevention	TN28: ATG in Prevention (STOP-T1D)	TN25: Rituximab/ Abatacept (T1D RELAY)	TN31: JAK Inhibitors (JAKPOT T1D)	TN16: Long-Term Investigative Follow-up (LIFT)
RISK SCREENING & MONITORING: ENROLLING	STAGE 2: ENROLLING	STAGE 3: ENROLLING	STAGE 3: ENROLLING	STAGE 3 & 4: ENROLLING
First step to identify eligibility for clinical trial participation Annual Retesting for single aab+ Metabolic monitoring for 2+aab	Can ATG prevent or slow progression from Stage 2 to Stage 3?	Can rituximab followed by abatacept or rituximab alone preserve insulin production in new onset?	Can abrocitinib and ritlecitinib preserve insulin production in new onset?	Does starting insulin early improve blood glucose control and reduce long-term complications? Are there differences in diabetes control between the people who receive treatment and those who don't?

Teplizumab Delays T1D Diagnosis

TrialNet TN10 Prevention Trial

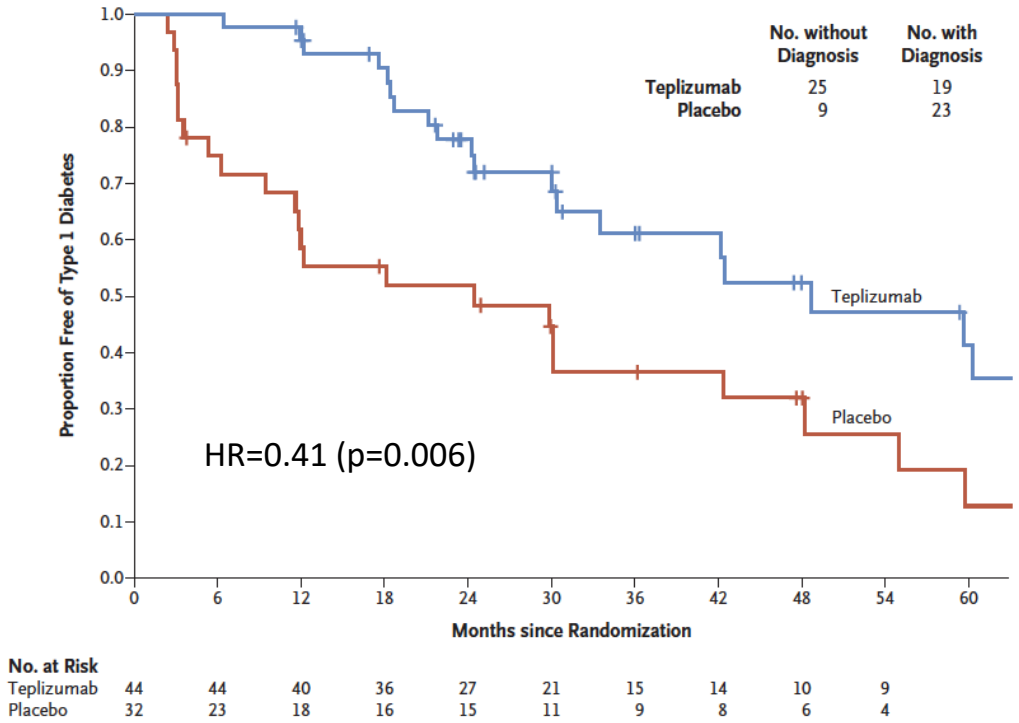
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 15, 2019 VOL. 381 NO. 7

An Anti-CD3 Antibody, Teplizumab, in Relatives at Risk for Type 1 Diabetes

Kevan C. Herold, M.D., Brian N. Bundy, Ph.D., S. Alice Long, Ph.D., Jeffrey A. Bluestone, Ph.D., Linda A. DiMeglio, M.D., Matthew J. Dufort, Ph.D., Stephen E. Gitelman, M.D., Peter A. Gottlieb, M.D., Jeffrey P. Krischer, Ph.D., Peter S. Linsley, Ph.D., Jennifer B. Marks, M.D., Wayne Moore, M.D., Ph.D., Antoinette Moran, M.D., Henry Rodriguez, M.D., William E. Russell, M.D., Desmond Schatz, M.D., Jay S. Skyler, M.D., Eva Tsalikian, M.D., Diane K. Wherrett, M.D., Anette-Gabriele Ziegler, M.D., and Carla J. Greenbaum, M.D., for the Type 1 Diabetes TrialNet Study Group*

2-year delay of clinical T1D (stage 3) onset in those at high risk for developing disease (relatives, 2+ T1D Ab+ and dysglycemia) with 1 course of teplizumab



Herold & al, NEJM 2019
Sims et al, Sci Transl Med. 2021

TrialNet at the Barbara Davis Center

The Prevention Team

- Mission
  - Inspiring hope for those impacted by type 1 diabetes through clinical research, community education, and personalized disease management.
- Focus
  - Type 1 diabetes prevention and intervention studies
- Investigators
  - Dr. Andrea Steck
  - Dr. Peter Gottlieb
  - Dr. Kimber Simmons
  - Dr. Taylor Triolo
  - Dr. Aaron Michels

BDC Research Participant Pathway

Screening

Monitoring

Clinical trial screening and enrollment

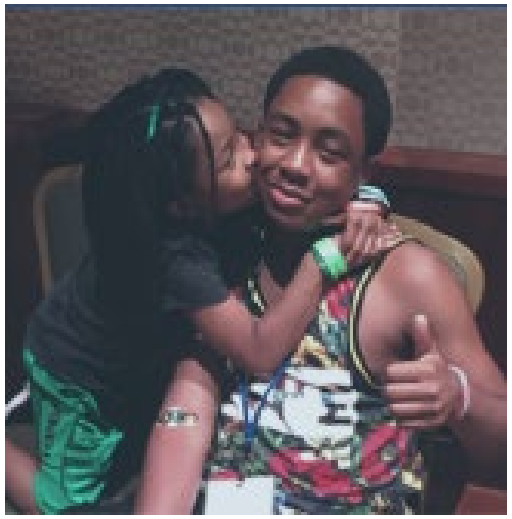
BDC Dual Screening

FDRs/2nd and 3rd degree relatives

- Identified during ASK screening
- TrialNet screening at confirmation visit

General Population

- TrialNet screening with clinical trial interest or once Stage 1 is reached.



Metabolic Monitoring

FDRs/Relatives

- Dual monitoring with TN/ASK
  - Combined visits/OGTTs
    - Participants who are not interested in completing OGTTs stay in ASK only monitoring
  - *Collaboration between ASK and Prevention teams ensures the best participant experience

GPs

- ASK monitoring
  - Not eligible for TN monitoring

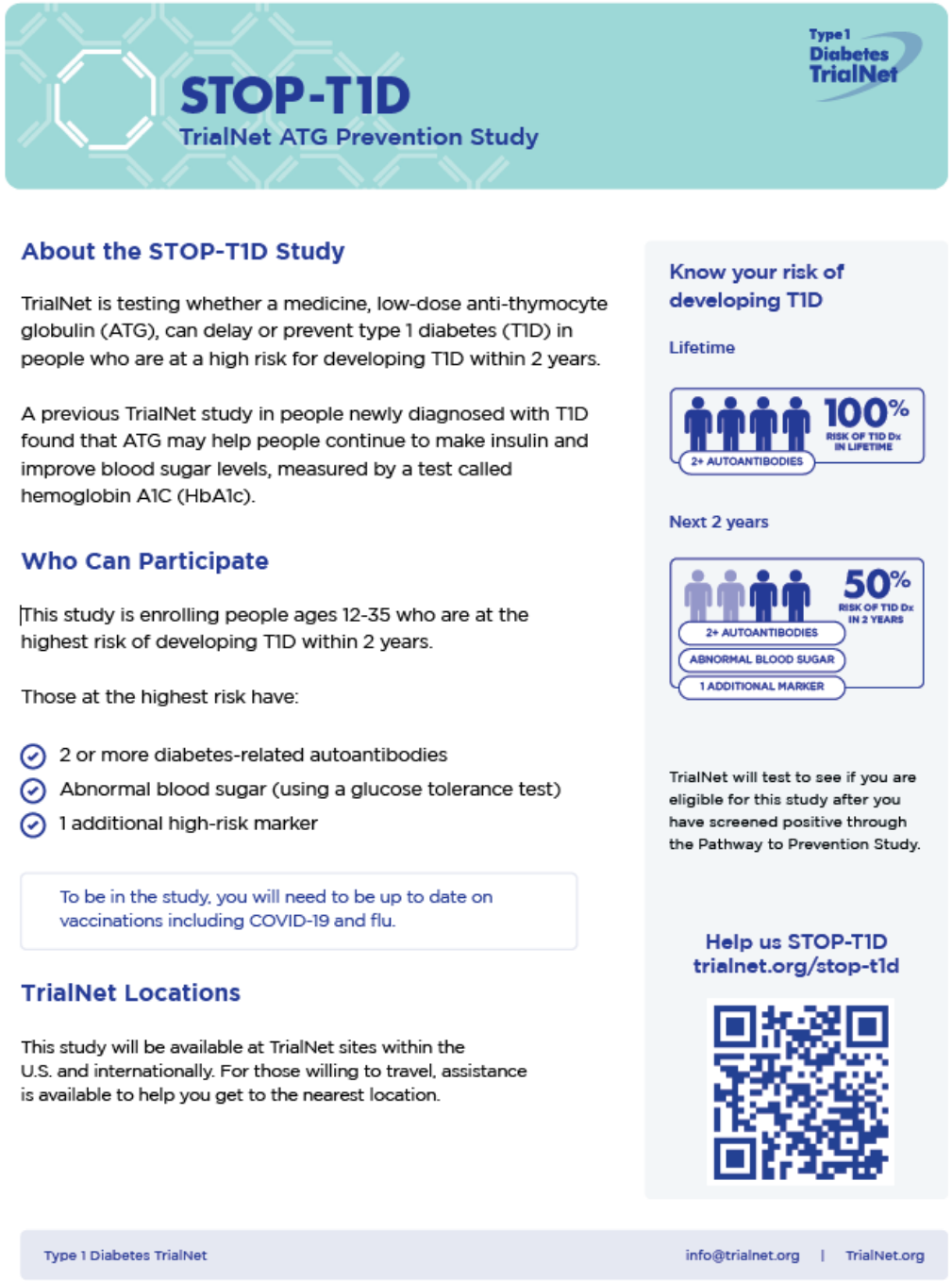
Clinical Trial Presentation

FDRs/Relatives

- Monitoring participants are notified of clinical trials at monitoring visits

GPs

- ASK team notifies Prevention Team of potentially eligible participants
  - Prevention Team visits family at next ASK visit to present trial and answer questions



STOP-T1D
TrialNet ATG Prevention Study

Type 1 Diabetes TrialNet

About the STOP-T1D Study

TrialNet is testing whether a medicine, low-dose anti-thymocyte globulin (ATG), can delay or prevent type 1 diabetes (T1D) in people who are at a high risk for developing T1D within 2 years.

A previous TrialNet study in people newly diagnosed with T1D found that ATG may help people continue to make insulin and improve blood sugar levels, measured by a test called hemoglobin A1C (HbA1c).

Who Can Participate

This study is enrolling people ages 12-35 who are at the highest risk of developing T1D within 2 years.

Those at the highest risk have:

- 2 or more diabetes-related autoantibodies
- Abnormal blood sugar (using a glucose tolerance test)
- 1 additional high-risk marker

To be in the study, you will need to be up to date on vaccinations including COVID-19 and flu.

TrialNet Locations

This study will be available at TrialNet sites within the U.S. and internationally. For those willing to travel, assistance is available to help you get to the nearest location.

Know your risk of developing T1D

Lifetime

100% RISK OF T1D Dx IN LIFETIME
2+ AUTOANTIBODIES

Next 2 years

50% RISK OF T1D Dx IN 2 YEARS
2+ AUTOANTIBODIES
ABNORMAL BLOOD SUGAR
1 ADDITIONAL MARKER

TrialNet will test to see if you are eligible for this study after you have screened positive through the Pathway to Prevention Study.

Help us STOP-T1D
trialnet.org/stop-t1d

Type 1 Diabetes TrialNet | info@trialnet.org | TrialNet.org

Clinical Trial Enrollment

FDRs/Relatives

- TrialNet data from recent (within 7 weeks) can be used as screening data
  - Eligible participants are enrolled and TN becomes primary study with ASK collecting samples at visits
  - Ineligible participants return to dual monitoring

GPs

- Complete full screening visit including TrialNet ABs and OGTT
  - Eligible participants are enrolled and TN becomes primary study with ASK collecting samples at visits
  - Ineligible participants return to ASK monitoring

Barriers to Enrollment

Type of therapy
- Oral vs IV/Injection

Type of proband
- Parent vs sibling/offspring or other

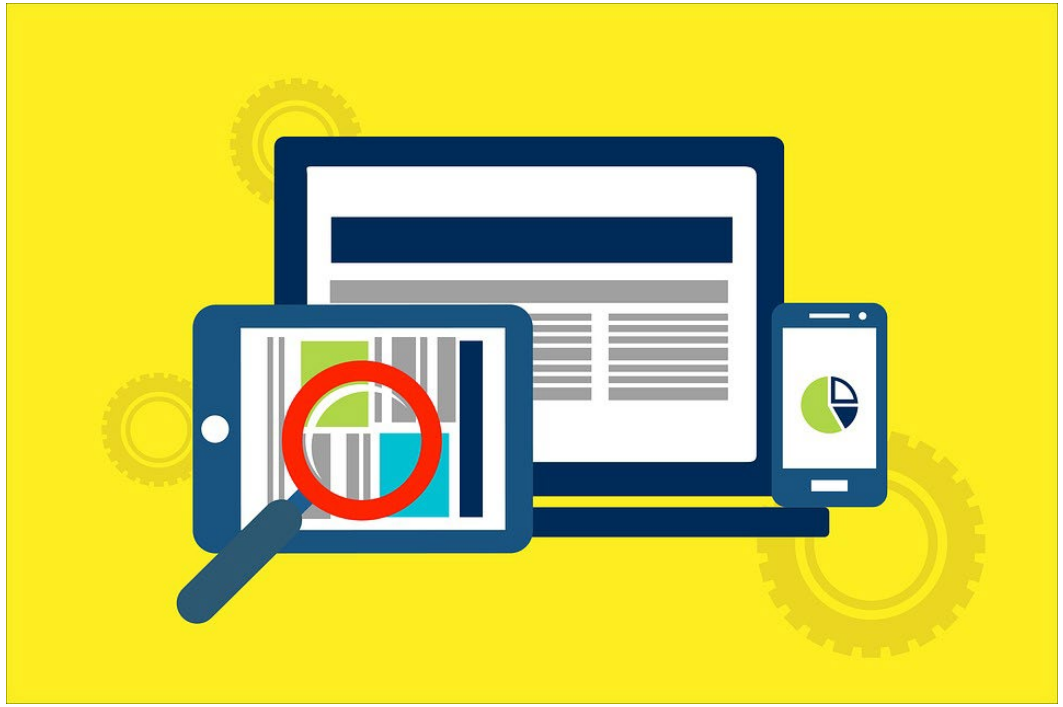
Age of subject
- Younger vs Older

Race/Ethnicity
- Non-Hispanic White vs Hispanic and Non-White

Kinney & al, Journal of the Endocrine Society, 2023

Links to Information on Screening and Trials

- Type 1 Diabetes TrialNet: https://www.trialnet.org
- Overall Clinical trials: https://clinicaltrials.gov
- TrialNet BDC team: https://www.trialnet.org/locations/barbara-davis-center
- BDC Prevention team: https://medschool.cuanschutz.edu/barbara-davis-center-for-diabetes/research/clinical-research/clinical-research-list



Thank you!