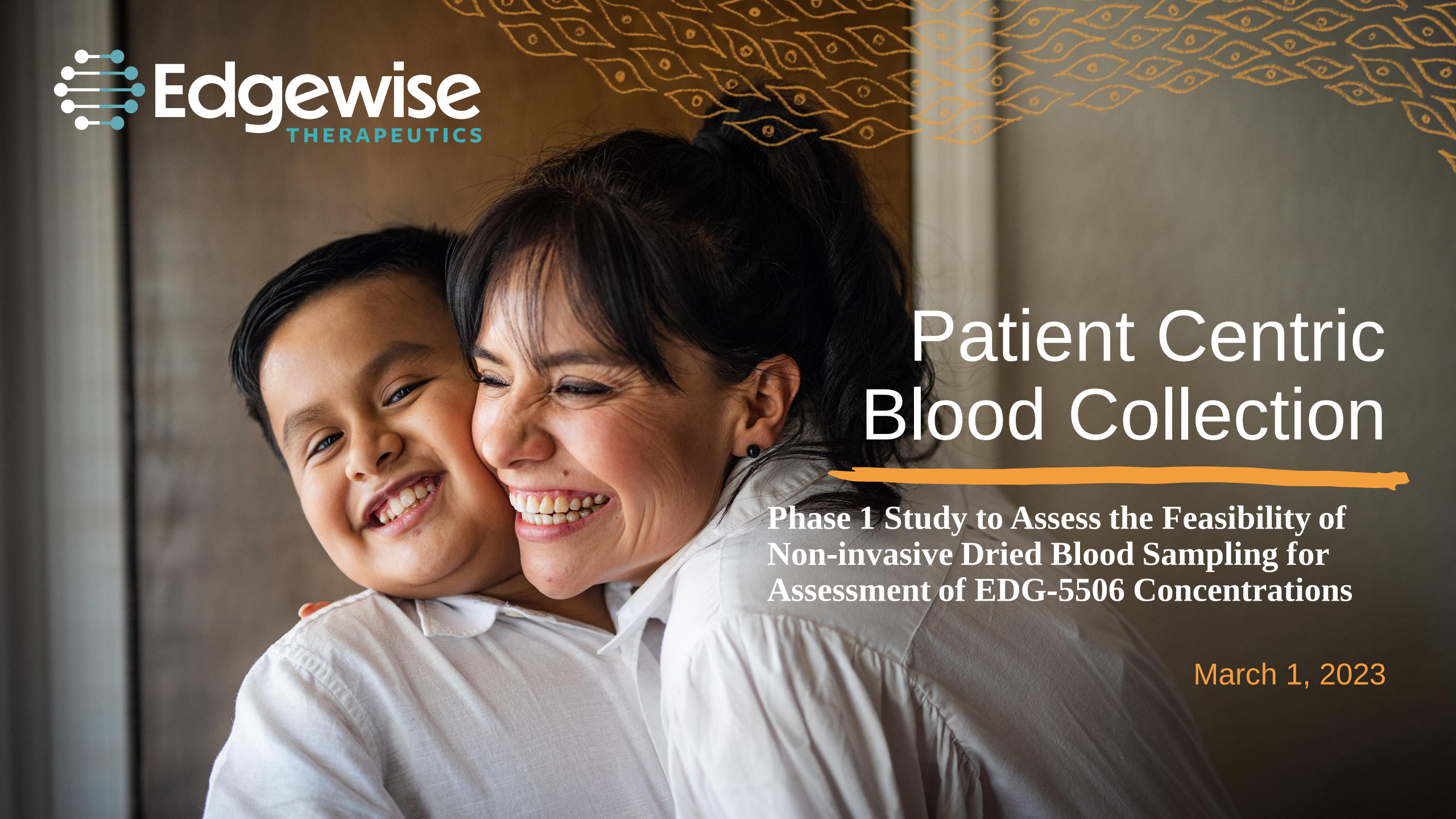


Edgewise THERAPEUTICS

Patient Centric Blood Collection

Phase 1 Study to Assess the Feasibility of Non-invasive Dried Blood Sampling for Assessment of EDG-5506 Concentrations

March 1, 2023

Primary Objective

- To assess the pharmacokinetics (PK) of EDG-5506 derived from a capillary blood self-sampling device in comparison to traditional venous blood sampling in healthy adult subjects
  - The motivation for this work was to facilitate collection of PK samples without requiring patients to come to the clinics and to reduce the number of traditional blood draws in a very sensitive patient population
  - What I am going to focus on today is a study in adult volunteers to investigate the feasibility of using an interesting collection device that may allow sample collection in non-traditional settings

EDG-5506

EDG-5506 is a novel, orally bioavailable, small molecule designed to selectively modulate type II fast skeletal myosin with the goal to protect dystrophic muscle from contraction-induced damage. By protecting fast muscle fibers, EDG-5506 may limit muscle breakdown and disease progression in DMD.

EDG-5506 is being developed for patients with muscular dystrophies. Initial focus is on DMD and BMD. It is currently in Phase 2 studies.

Study and Rationale Design

Overall Design

- Open label, 1 period, single dose, study comparing EDG 5506 concentrations measured in plasma, whole blood and capillary blood (collected using a Tasso M20 device)
- Adult healthy volunteers

Rationale

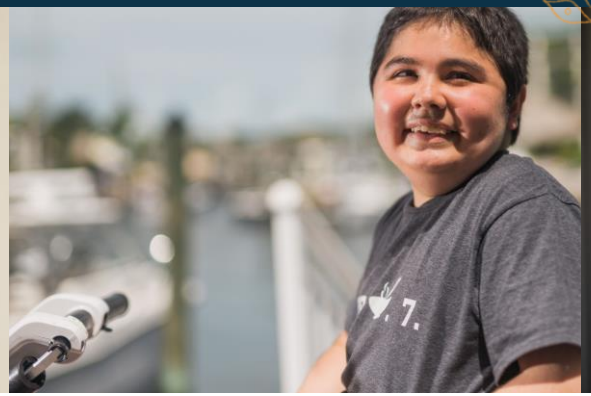
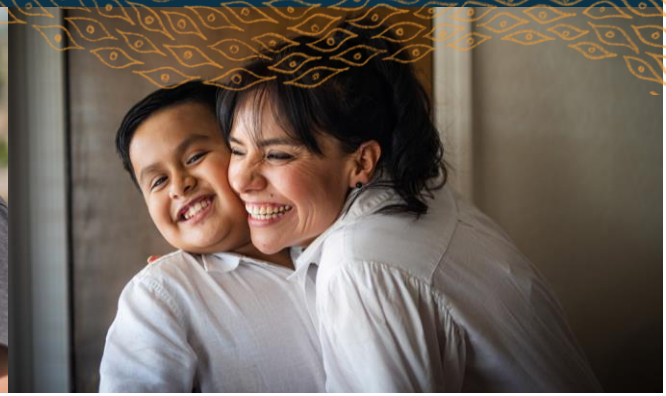
- Allow for collection of samples at home
  - reduces travel burden on patient and caregivers
- Reduces pain and stress to overcome fear of needles in pediatric subjects
- Facilitate collection of samples throughout studies
- Facilitate collection of samples throughout the day
- Efficiency versus home phlebotomist collection

Tasso M20 Device

- Sample collection device that enables microsampling outside of traditional clinics and hospitals
- Provides accurate and precise collection of a fixed volume of whole dried blood from a capillary needle
- Activated by push of a button to accurately and painlessly collect approximately 150 µL blood (4 samples of 17.5µL)

Images from Tasso.com, Dec,2022



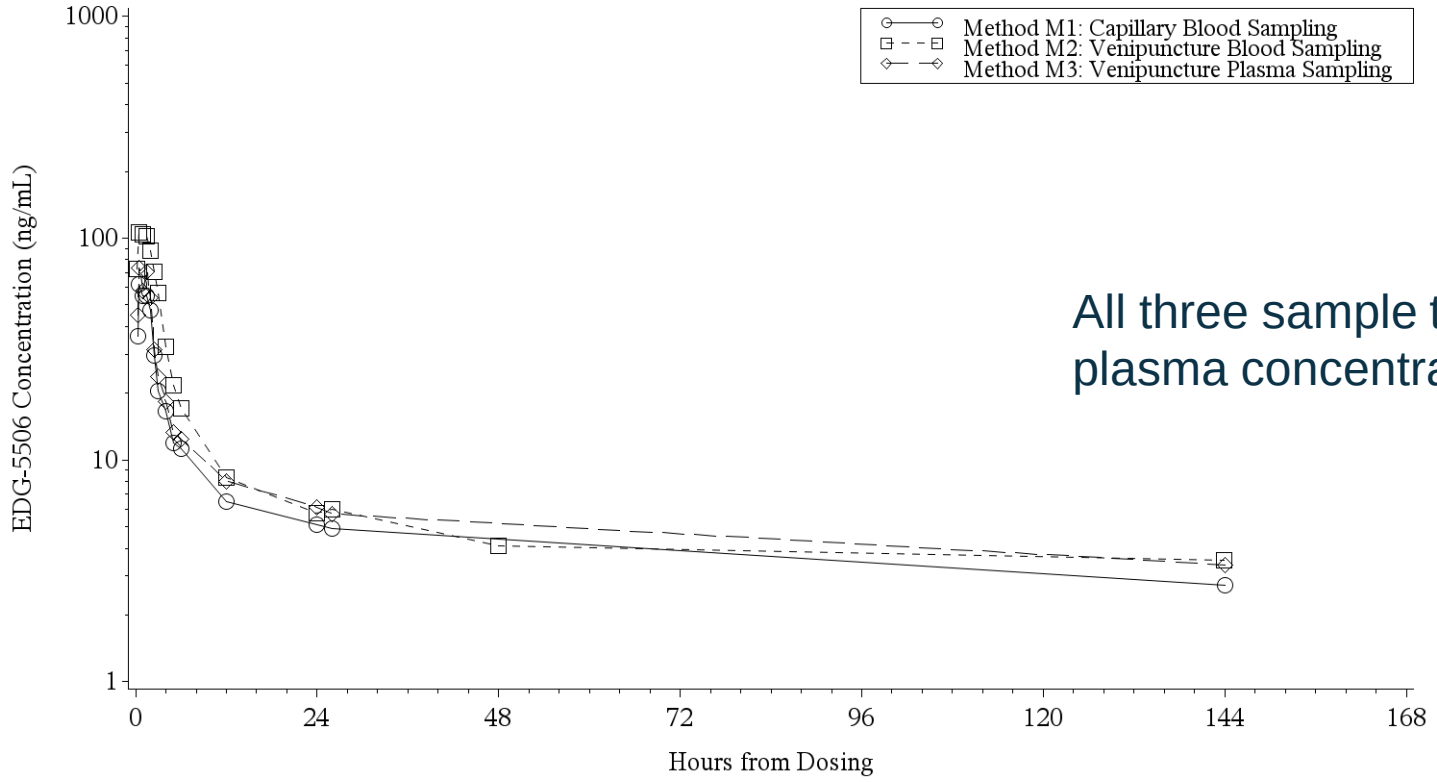



Primary Focus on M1 vs M3

Plasma vs Capillary Blood (Tasso)

We compared three different sample types: M1 traditional plasma samples; M2 whole blood collected by venipuncture; and M3 capillary blood collected using the Tasso M2 device

Arithmetic Mean EDG-5506 Concentration Versus Time Profiles Using Capillary Blood Sampling (M1), Venipuncture Blood Sampling (M2) and Venipuncture Plasma Sampling (M3) (Semi-Log Scale) (Pharmacokinetic Population)



All three sample types give similar plasma concentration-time profiles

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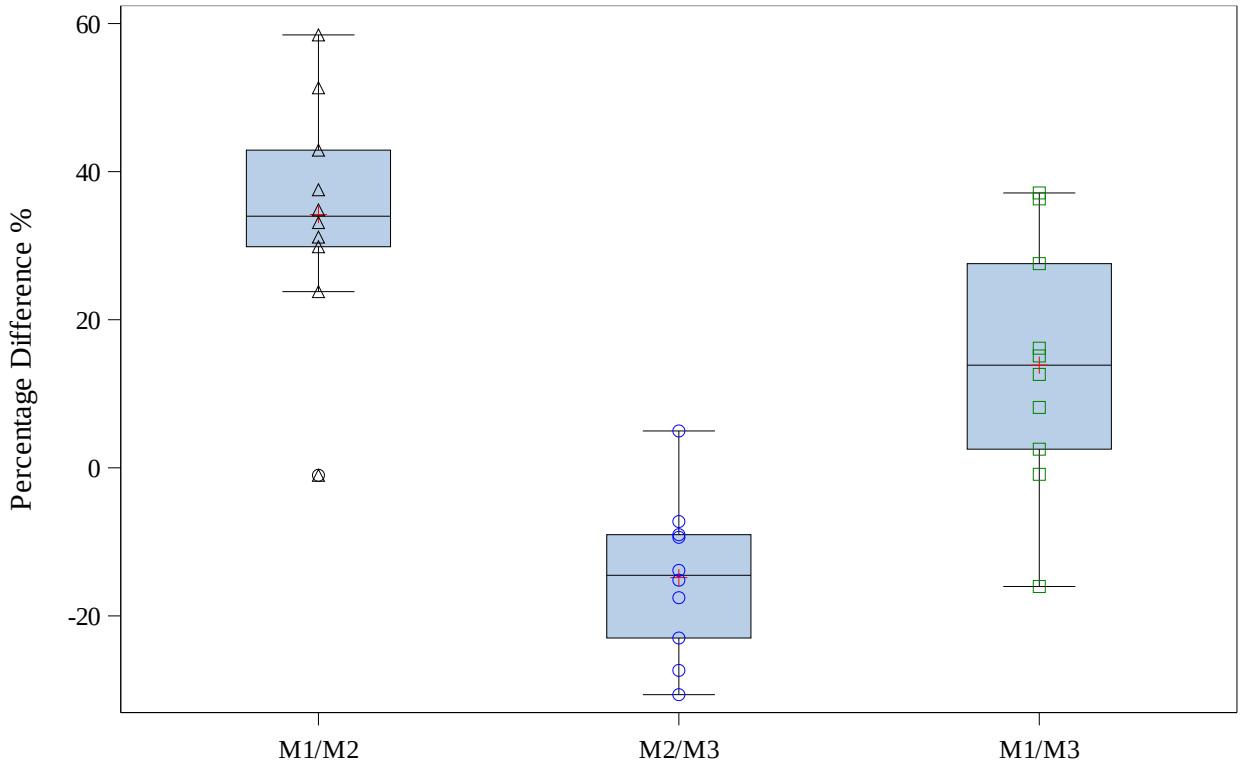
Percentage Difference of EDG-5506 AUC0-t: Capillary Blood Sampling (M1) Versus Venipuncture Blood Sampling (M2), Venipuncture Blood Sampling (M2) Versus Venipuncture Plasma Sampling (M3) and Capillary Blood Sampling (M1) Versus Venipuncture Plasma Sampling (M3)



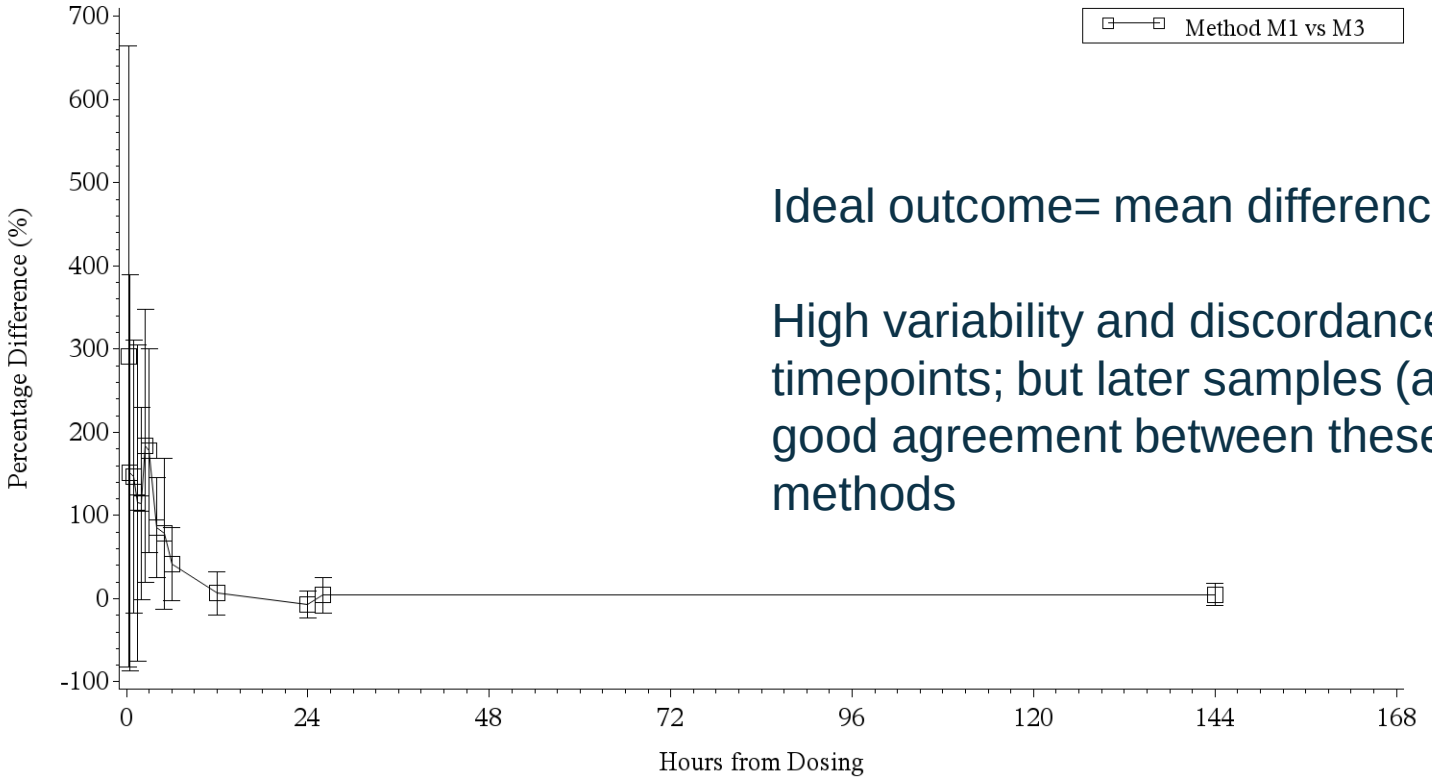
The upper and lower limits of the box represent the third and first quartiles, respectively, while the midline represents the median. The red '+' represents the mean.

The upper and lower whiskers of the boxplot represent the largest and smallest observed values within 1.5 x the interquartile range, respectively.

Program: /CA38181/sas_prg/pksas/adam_boxplot.sas 11NOV2022 12:29

High variability, particularly at the early timepoints (see subsequent slides) is driving the mean differences between the sample collection methods

Percentage Difference Arithmetic Mean (SD) of EDG-5506 Concentration Versus Time Profiles Using Capillary Blood Sampling (M1) Versus Venipuncture Plasma Sampling (M3) (Linear Scale) (Pharmacokinetic Population)



Percentage difference = ([concentration capillary/concentration venipuncture plasma]*100%)-100%
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Ideal outcome= mean difference is 0

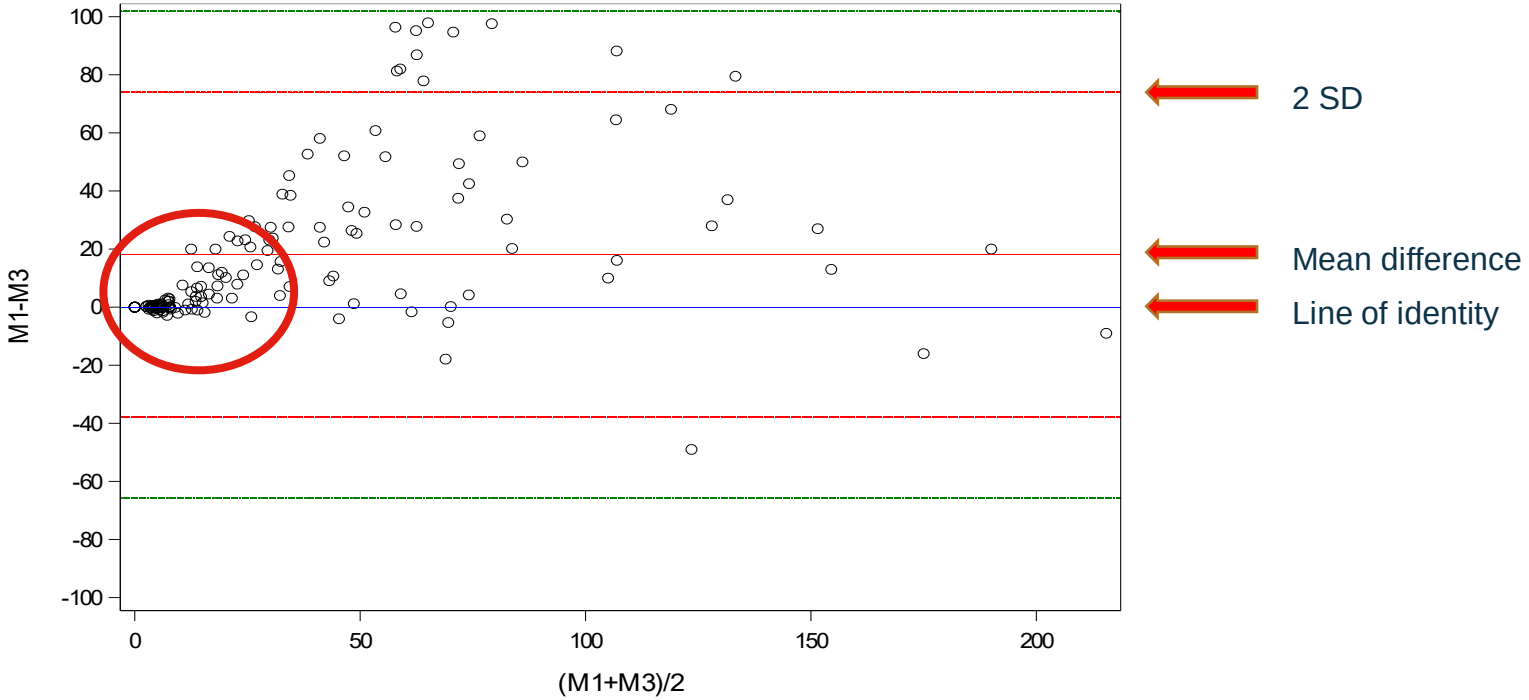
High variability and discordance at early timepoints; but later samples (after ~12 hrs) show good agreement between these two sampling methods

Bland-Altman Plot of EDG-5506 Concentration Using Capillary Blood Sampling (M1) Versus Venipuncture Plasma Sampling (M3) (Pharmacokinetic Population)

The Bland–Altman method calculates the mean difference between two methods of measurement (the 'bias'), and 95% limits of agreement as the mean difference (2 sd) (also known as Tukey mean –difference plot). Generally, if the differences within mean ± 1.96 SD are not clinically important, the two methods may be used interchangeably.

Ideal result= blue and red lines are very close or overlapping and 90% of datapoints are within 2SD

Red circle highlights later timepoints which show good agreement between the two sampling methods
The divergence at the higher concentrations (earlier timepoints) likely represents distribution phase kinetics



Red solid line: Mean M1-M3; Red Dashed line: ± 2 SD; Green Dotted line: ± 3 SD; Blue solid line: 0
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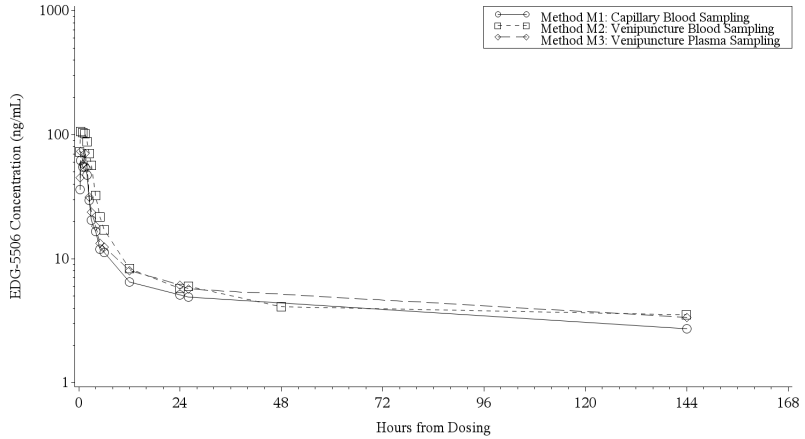
Summary and Conclusion (M1 vs M3)

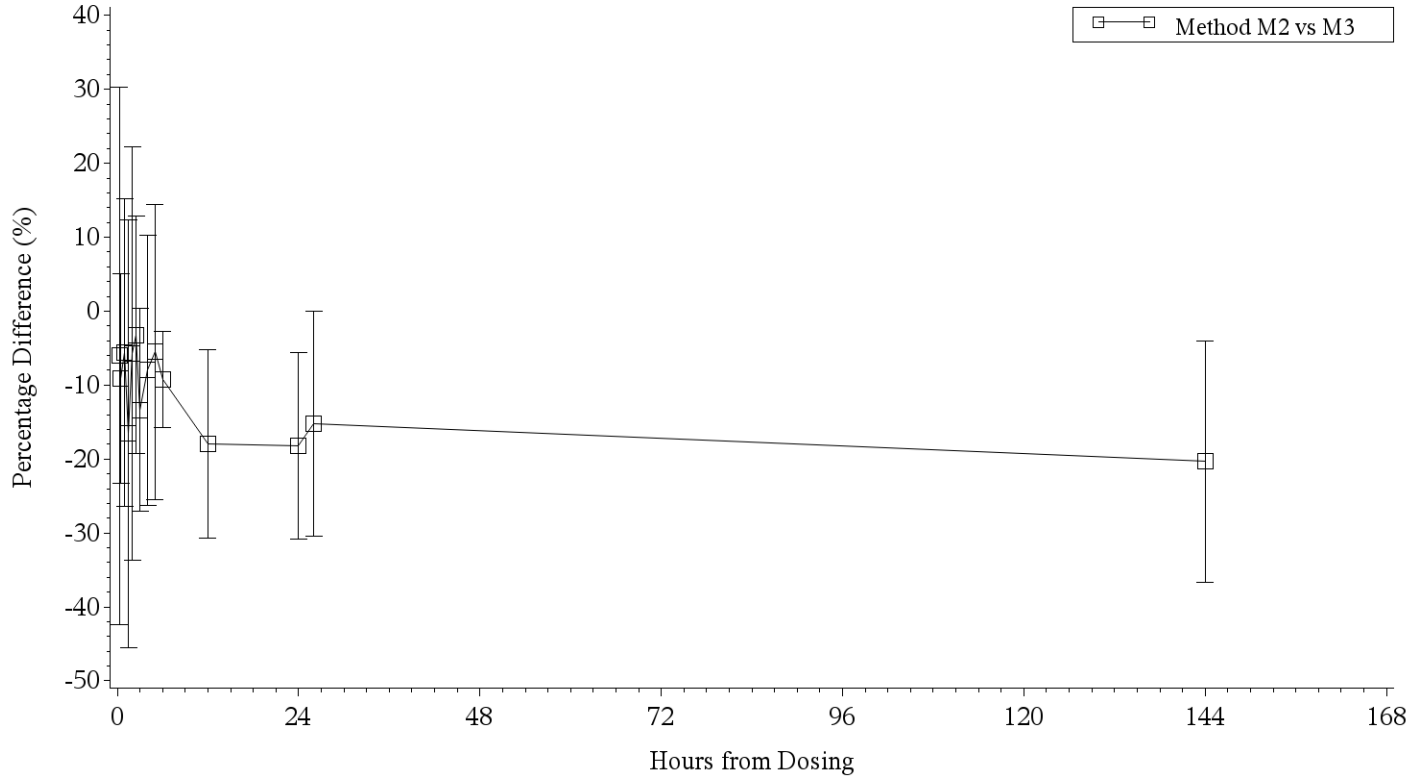
- Capillary blood (Tasso device) samples had similar 5506 concentrations as those obtained from traditional plasma sampling at later timepoints
- At early timepoints capillary blood sample concentrations were higher and more variable than plasma samples; this may represent distribution PK
- For the intended use, later timepoints after dosing at home, use of the Tasso device for sample collection is suitable and should result in similar drug concentrations as traditional venipuncture and plasma sampling



Additional comparison

- M2, venous blood, versus M3 venous plasma

Percentage Difference Arithmetic Mean (SD) of EDG-5506 Concentration Versus Time Profiles Using Venipuncture Blood Sampling (M2) Versus Venipuncture Plasma Sampling (M3)



Percentage difference = ([concentration venipuncture blood/concentration venipuncture plasma]*100%)-100%
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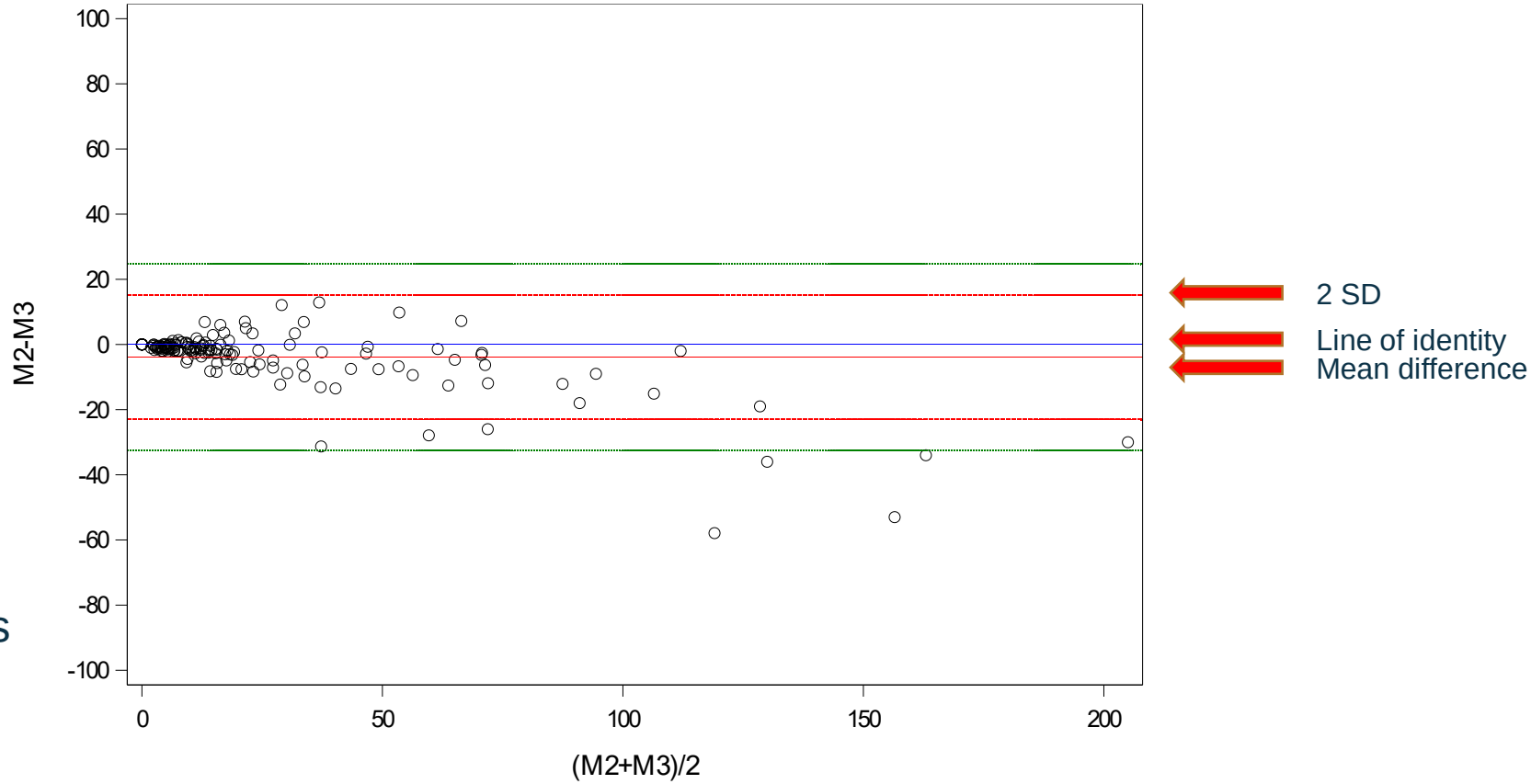
Bland-Altman Plot of EDG-5506 Concentration Using Venipuncture Blood Sampling (M2) Versus Venipuncture Plasma Sampling (M3)

Blue and red solid lines are close; most points within 2SD limits

Generally good agreement between these two sample types; the highest divergence is the high concentrations, which are the early timepoints

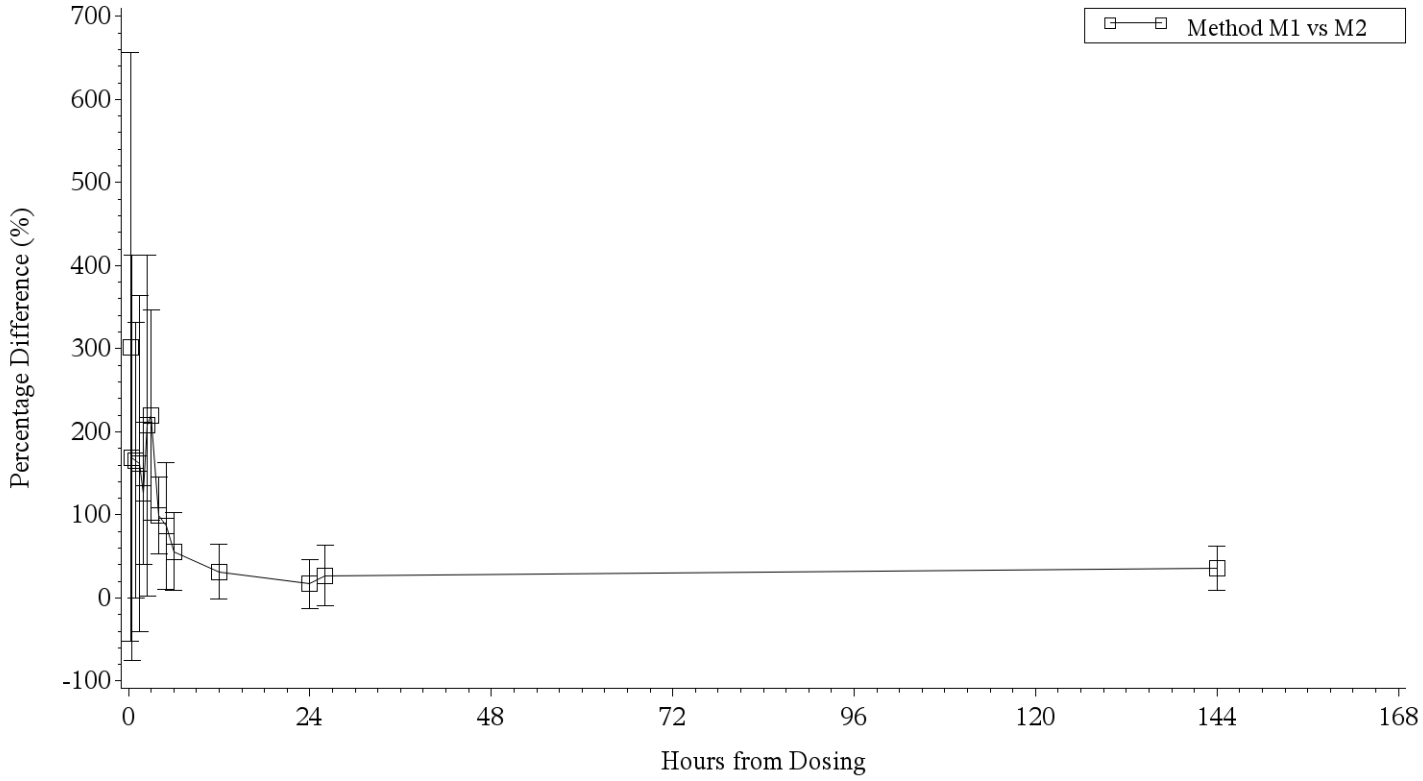


Red solid line: Mean M2-M3; Red Dashed line: ± 2 SD; Green Dotted line: ± 3 SD; Blue solid line: 0
Program: /CA38181/sas_prg/pksas/adam_bland_altman_conc.sas 11NOV2022 13:04

Additional comparison

- M1, capillary blood, versus M2 venous blood

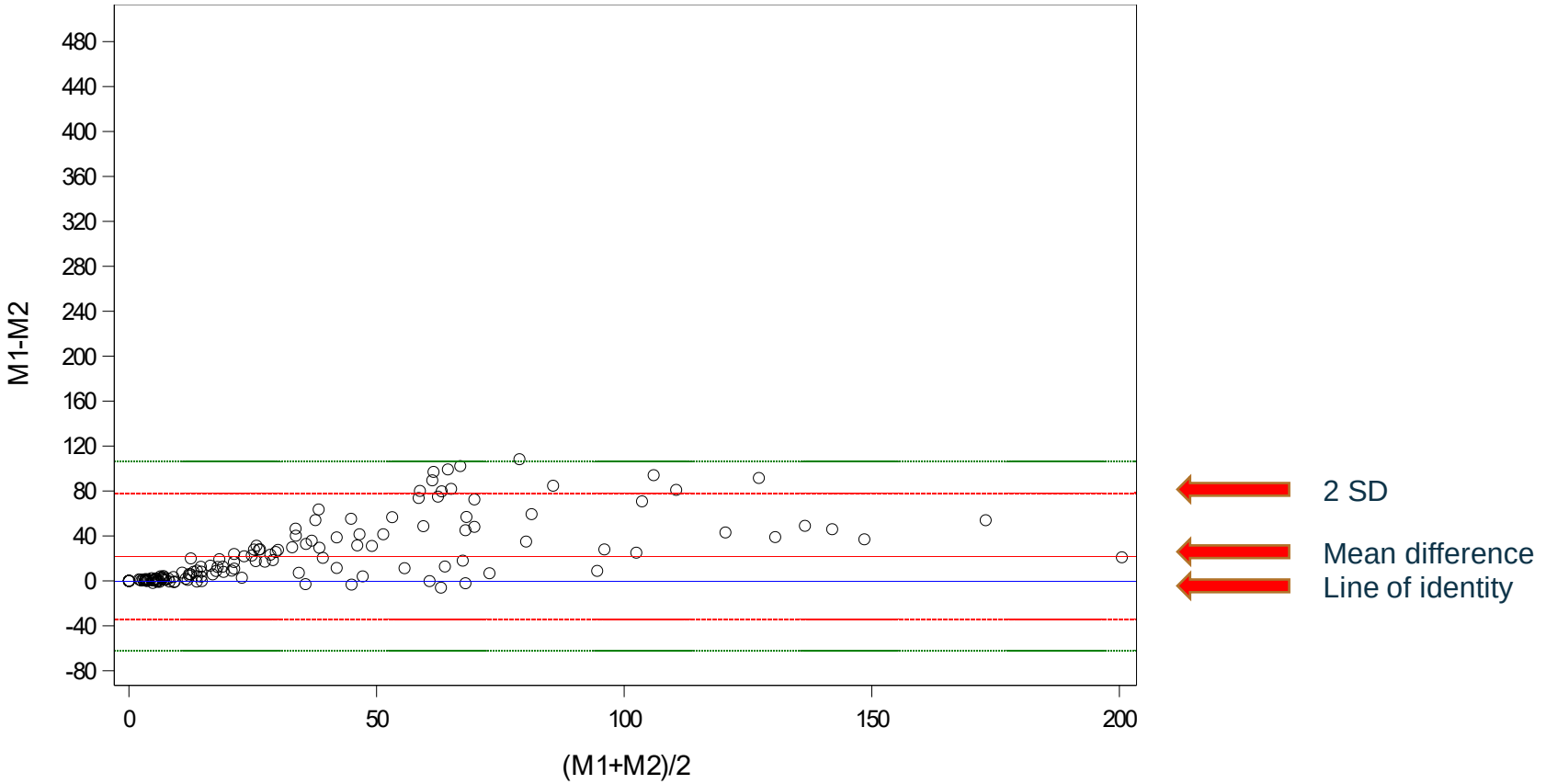
Percentage Difference Arithmetic Mean (SD) of EDG-5506 Concentration Versus Time Profiles Using Capillary Blood Sampling (M1) Versus Venipuncture Blood Sampling (M2)



Percentage difference = ([concentration capillary/concentration venipuncture blood]*100%)-100%
Source: ADaM.ADPC
Program: /CA38181/sas_prg/pksas/adam_meangraph_perc.sas 11NOV2022 12:29

Bland-Altman Plot of EDG-5506 Concentration Using Capillary Blood Sampling (M1) Versus Venipuncture Blood Sampling (M2)

Generally good agreement between these two sample types; the highest divergence is the high concentrations, which are the early timepoints and likely represents distribution phase kinetics



Red solid line: Mean M1-M2; Red Dashed line: ± 2 SD; Green Dotted line: ± 3 SD; Blue solid line: 0
Program: /CA38181/sas_prg/pksas/adam_bland_altman_conc.sas 11NOV2022 13:04

Summary- science perspective

- Drug levels from all three collection methods are generally consistent which facilitates flexible sample collection in patient trials
  - At early timepoints capillary blood sample concentrations were higher and more variable than plasma samples; this may represent distribution PK
- Use of the Tasso M20 device may help with sample collection on days when clinic visits are not scheduled or possible.
- It also may help with sample collection in patients who are resistant to traditional venipuncture
- Currently Edgewise is exploring use of this sample collection methodology for both PK and PD samples

Preliminary Trial Experience- caregiver/patient perspective

- Families said the Tasso is a “cool device” and “easy”
- Appreciate not having to travel, take off work, or skip school for additional onsite blood draws
- Like that samples are shipped at room temp via USPS (can drop in their mailbox vs waiting for a courier or going to UPS/FedEx)
- First few draws went smoothly
  - However, a few pts struggled getting enough blood from the 2nd draw (pts were using different arms for each draw & the 2nd one would only fill 1-2 spots)
  - We provided some suggestions to help (stay hydrated, draw early in the morning, use the heat packs prior to collection, if it doesn’t work use their back-up device and try again the next day)

Edgewise THERAPEUTICS

THANK YOU!