Unraveling Immune Therapy Efficacy Through Growth Kinetics Modeling

A Descriptive Analysis of Imaging Kinetic Biomarkers Using RECIST 1.1 Assessments

Immuno-Oncology 360°
Brooklyn, New York, USA | Feb. 28, 2024

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Applying AI and computer vision, we help conquer cancer and other life-threatening diseases by extracting powerful clinical insights from medical images.

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Our growth	Powered by proprietary AI, computer vision and signal processing technologies, strong KOL connections, and medical, scientific, technology partnerships.
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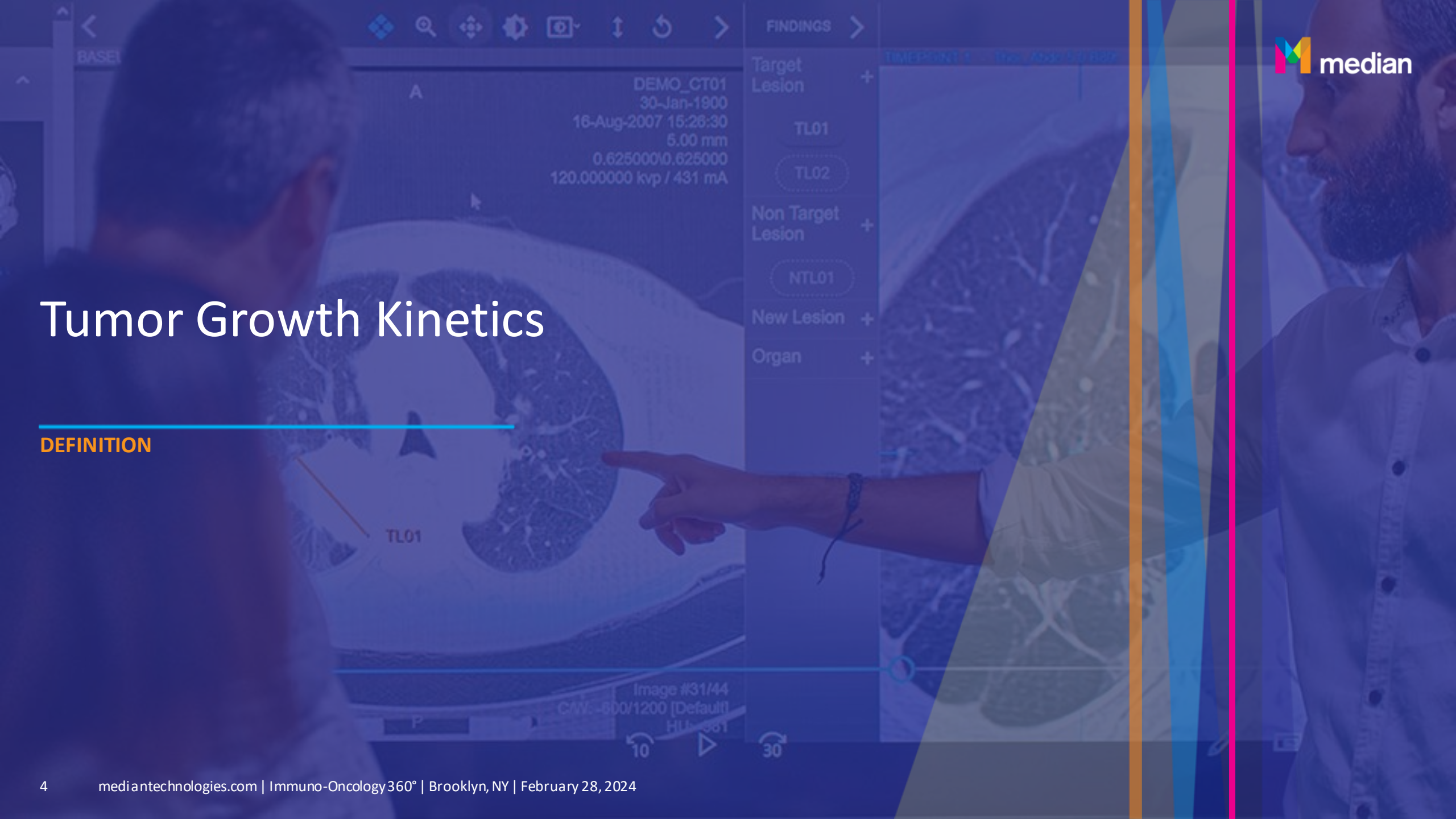
Agenda

- Tumor Growth Kinetics
- Mathematical Model
- Objective
- Material & Method
- Validation (Individual Data Fits)
- Descriptive Analysis
- Predictive Analysis
- Conclusion

Tumor Growth Kinetics

DEFINITION



Showing Promising Results for Over a Decade

Tumor Growth Metrics are readily available and clinically relevant

Cancer Therapy: Clinical

Clinical Cancer Research

2014

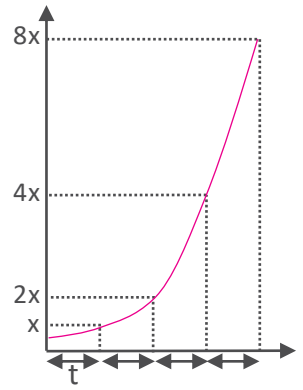
Tumor Growth Rate Is an Early Indicator of Antitumor Drug Activity in Phase I Clinical Trials

Charles Ferté[1,3,6,7], Marianna Fernandez[3], Antoine Hollebecque[1,3], Serge Koscielny[2,3], Antonin Levy[3,5], Christophe Massard[1,3,6], Rastislav Balheda[1,3], Brian Bot[7], Carlos Gomez-Roca[3], Clarisse Dromain[4], Samy Ammari[4], and Jean-Charles Soria[1,3,6]

> “**early** assessment of chemotherapy antitumor activity, independent **association with PFS** and reveals **drug-specific** profiles [...] guiding the further development of the investigational drugs”

Explainable

- **TGR** as a percent increase in tumor volume during one period
- **DOUBLING TIME**



Clinically Relevant across treatments periods

- Off-therapy (Prebaseline)
- On-therapy

Available

- RECIST 1.1 evaluations
- Spheric Equivalent Approximation Tumor volume

$$V = \frac{4}{3}\pi r^3$$

Mathematical Models

GOMPERTZ EQUATION

Gompertzian Equation (S-Shape Logistic Function)

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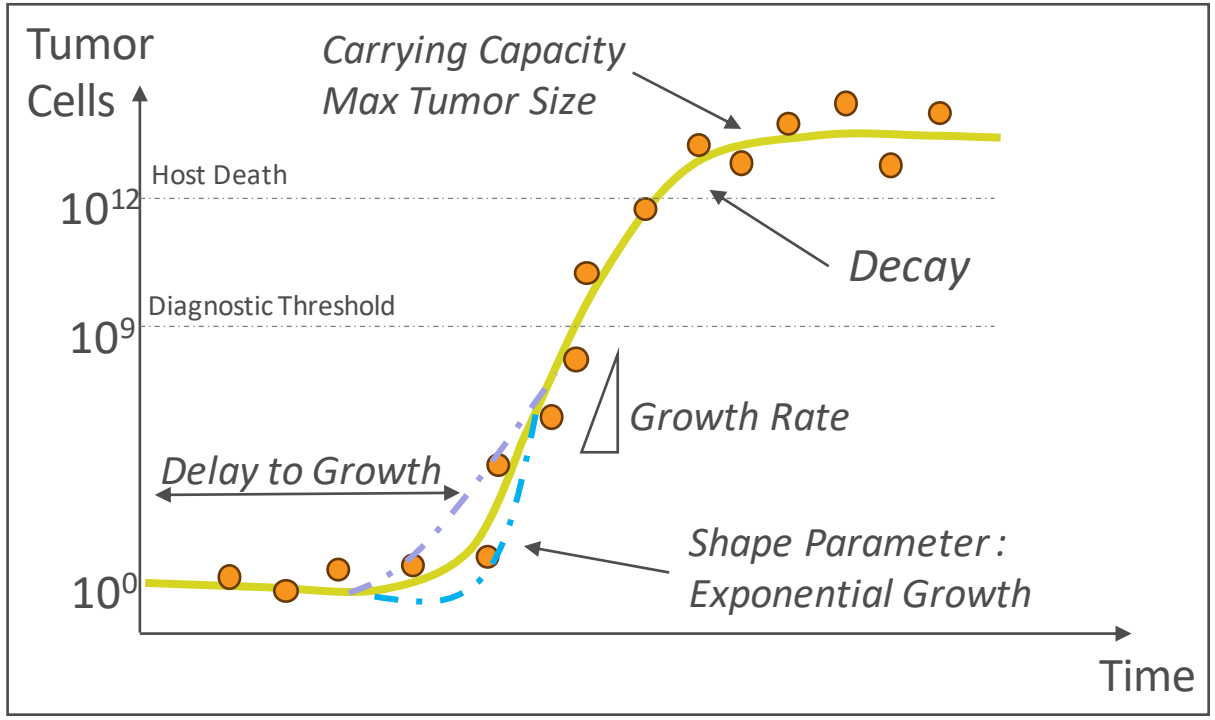
Clinically, mostly people die before the carrying capacity

Hypothetical Gomperztian Tumor Growth



$$V(t) = V_0 \cdot e^{Ae^{-Bt} + Mt}$$

V0: the initial tumor burden

A: Parameter that controls the rate of **growth**

B: Parameter that controls the rate of growth **deceleration (decay)**

M (Makeham Coefficient): represents external factors affecting the tumor growth e.g., treatment or environmental influences or aggressiveness of the tumor

Youtube @fauquierENT

Objectives for Tumor Growth Metrics in Oncology Clinical Research

1

Validate the model for immunotherapy efficacy data

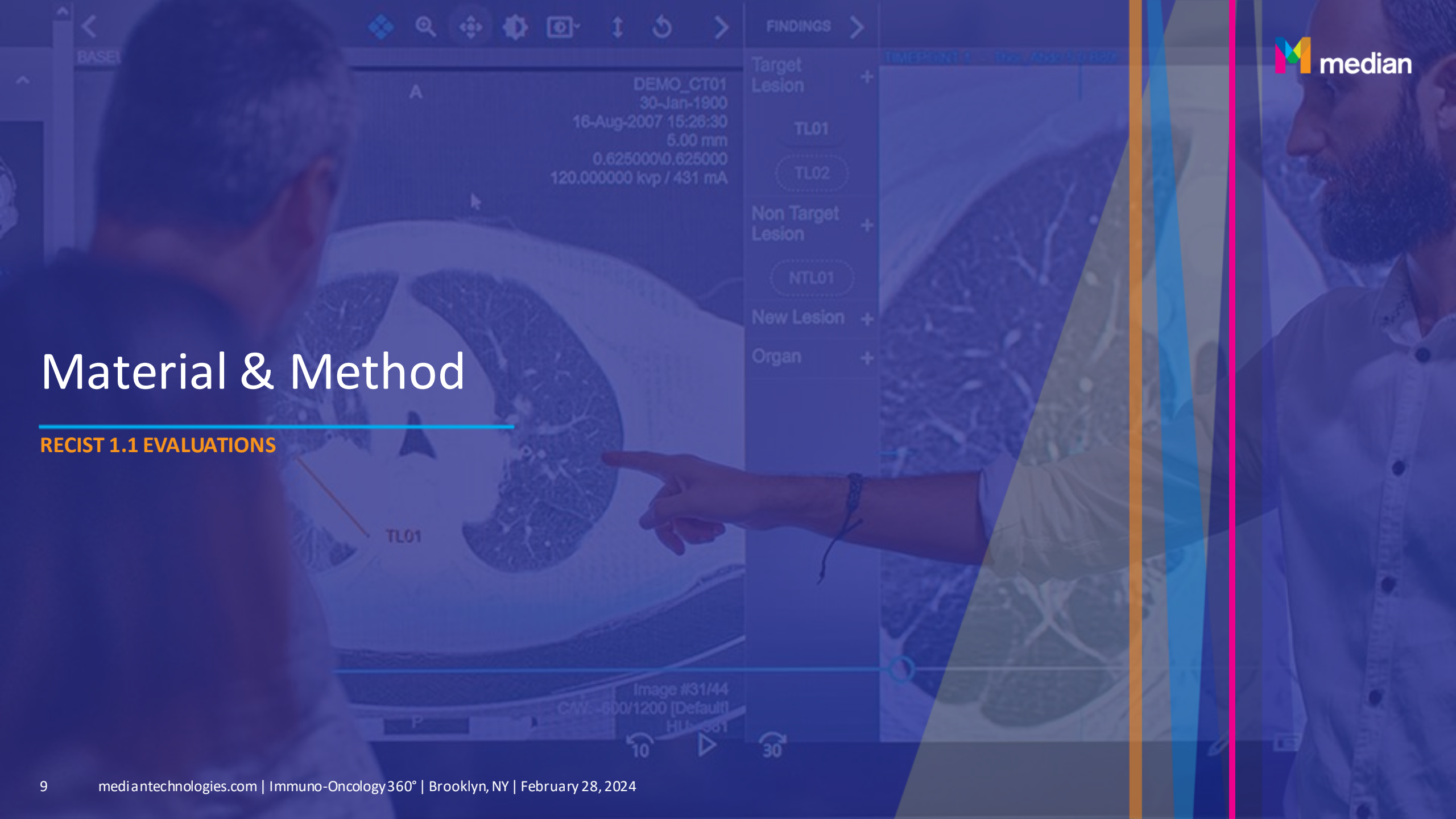
2

Demonstrate Early TGK are Predictive Biomarkers

- for Response
- for Atypical Patterns of Response/Progression

Material & Method

RECIST 1.1 EVALUATIONS



Study Specifications for Relevant TGK Trials

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Data descriptions

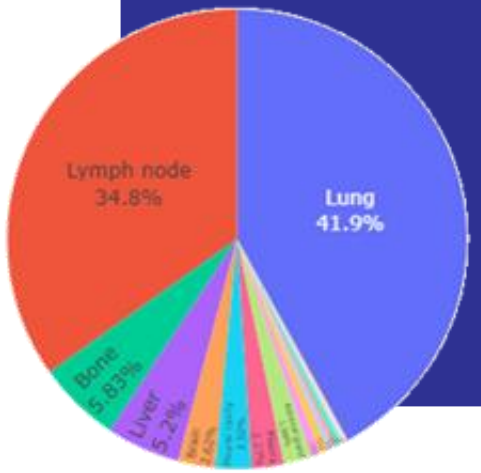
TRIALS SPECIFICATIONS

- **3 trials randomized**, double-blind, multicenter, phase III
- **NSCLC** patients stage IIIB and IV
- **Anti-PD1/PD-L1 Combination** (I+Chem)
- **RECIST 1.1 Evaluations** -8weeks-

* Intervention Blinded Data and No Overall Survival Data

POPULATION DESCRIPTION

- 1,175 Patients involved
- **861 Patients** with
  - At least 3 TP (to compute early TGK)
  - Measurable Disease



Mean baseline SOD 74.61 mm

Material: Efficacy RECIST 1.1

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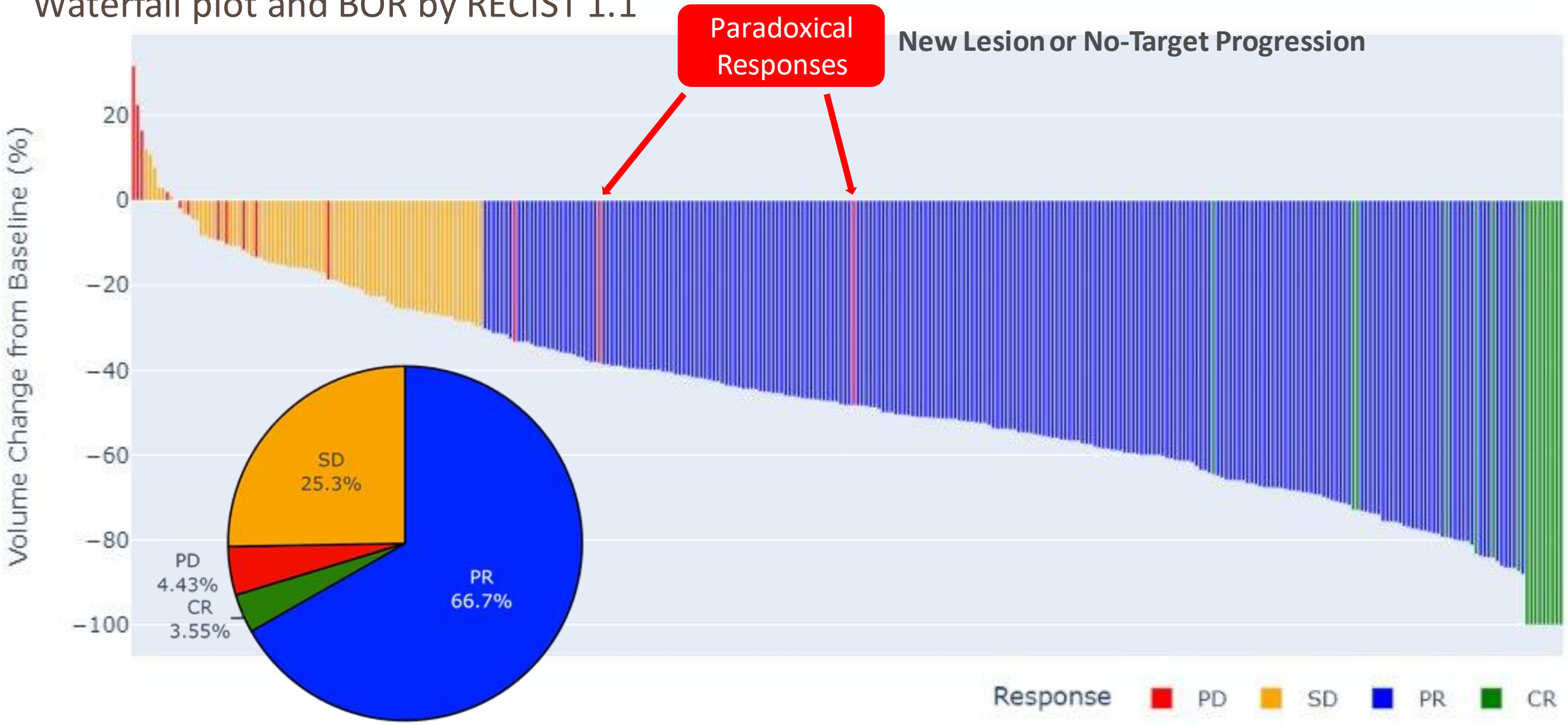
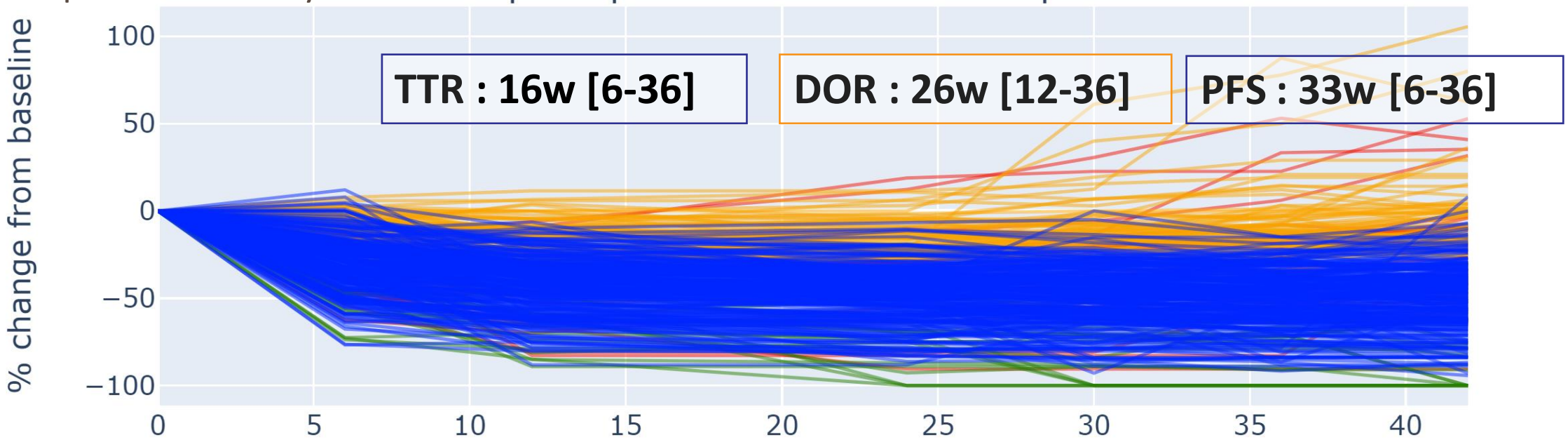
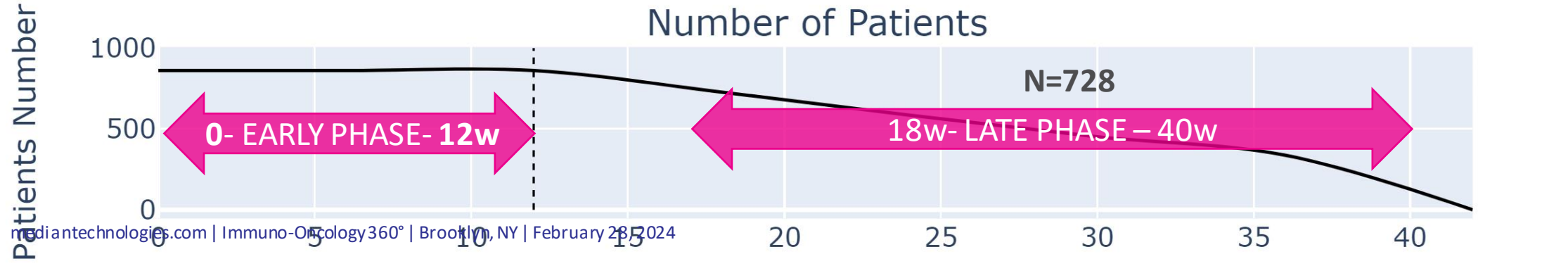
Waterfall plot and BOR by RECIST 1.1



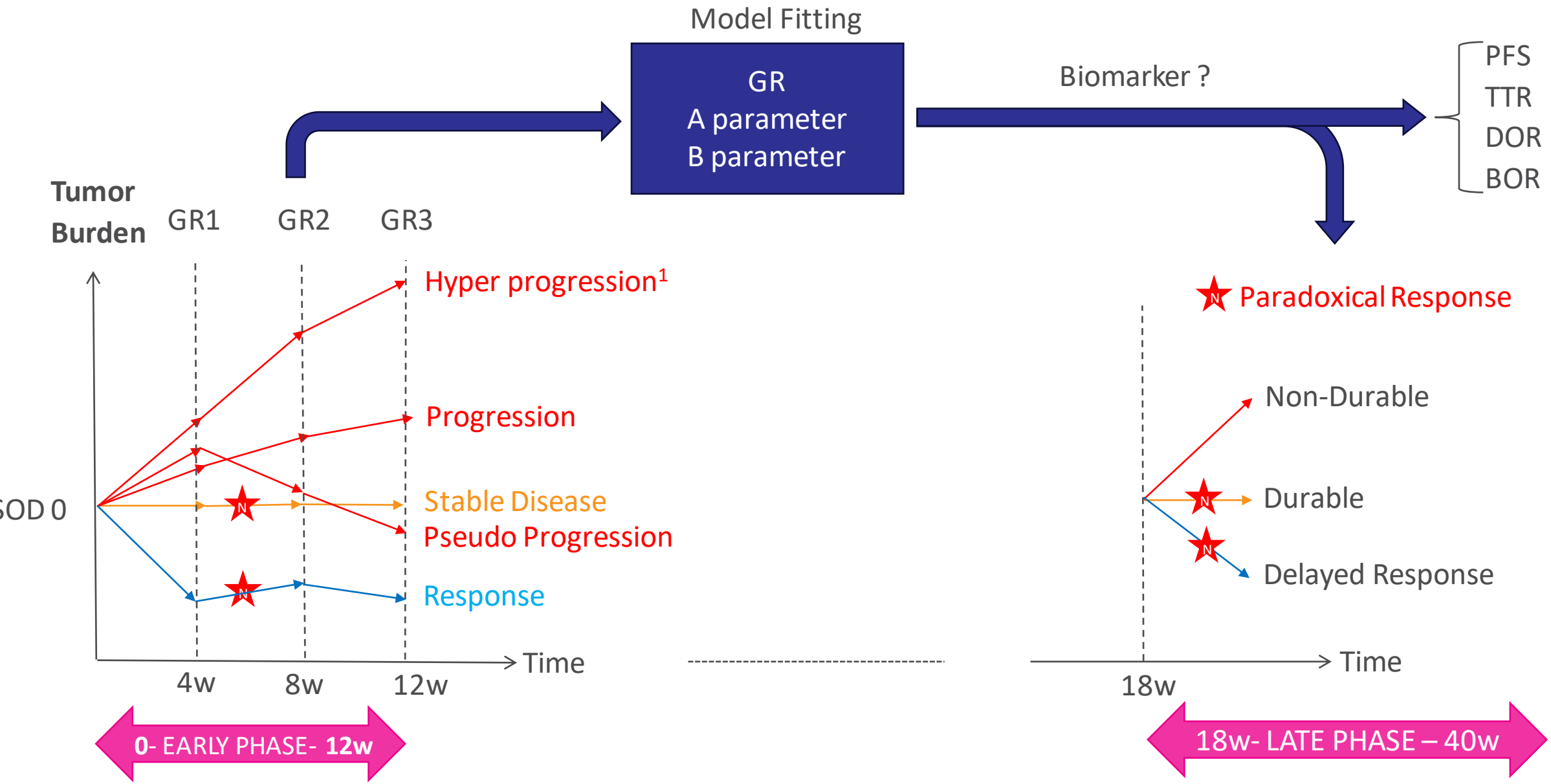
Method: Defining Period of Interest (early TGK)

Spider plot and BOR by RECIST 1.1

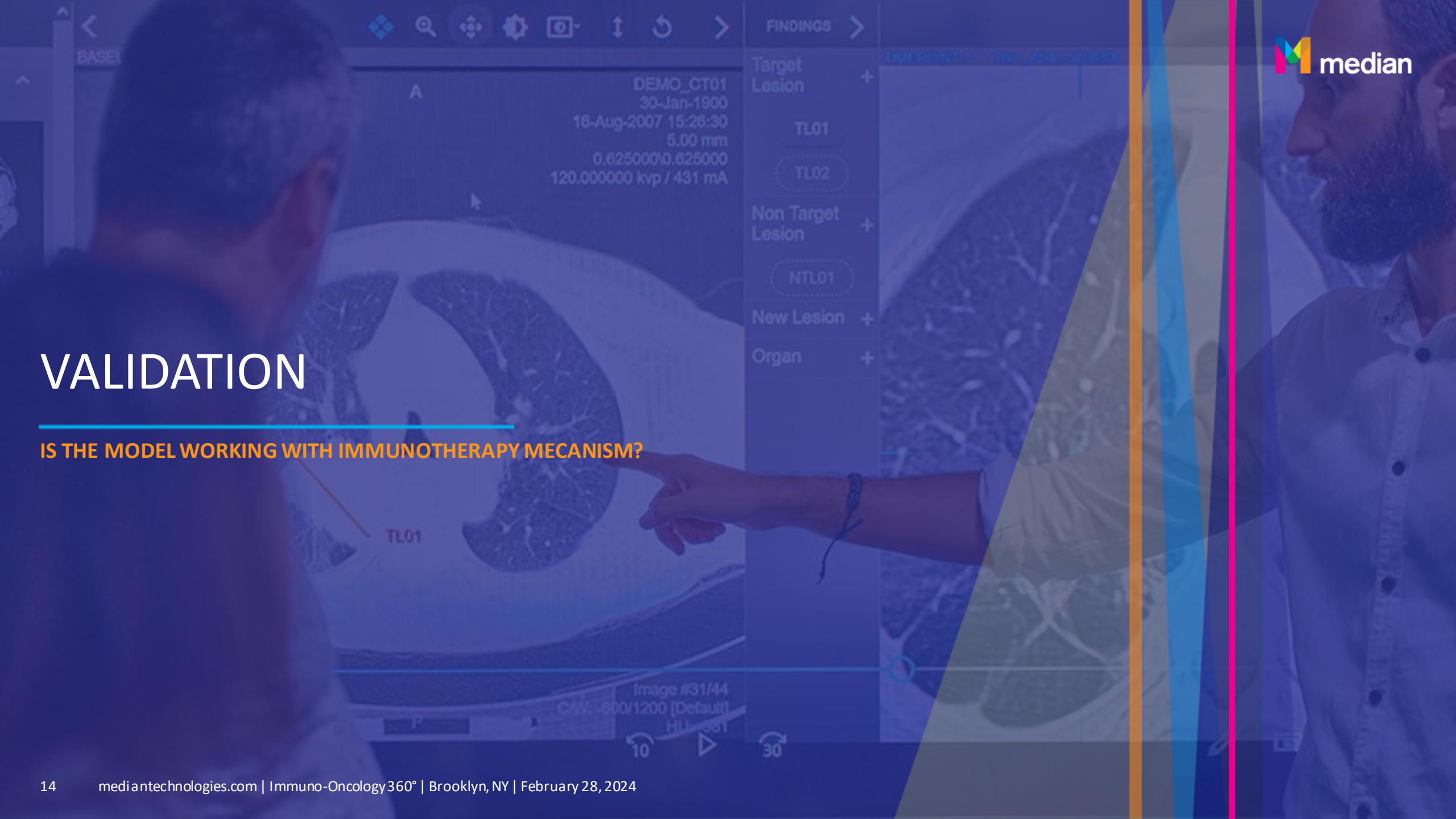




Method: Early Response Kinetics & Patterns



[1]Nota : definition based on median GR of progressor group

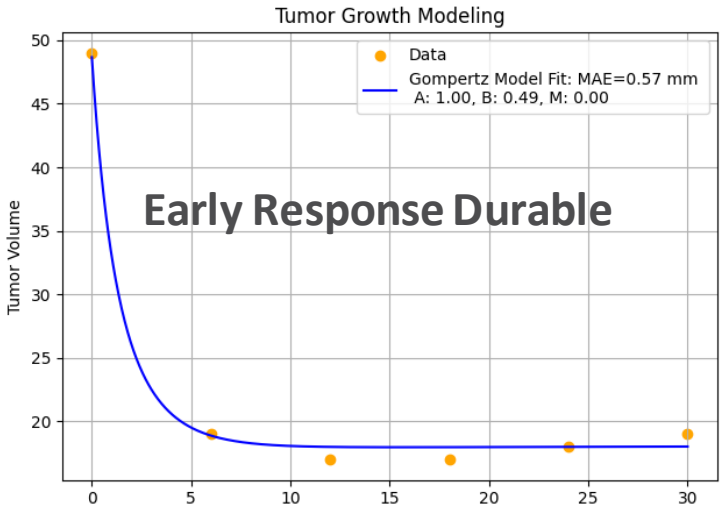


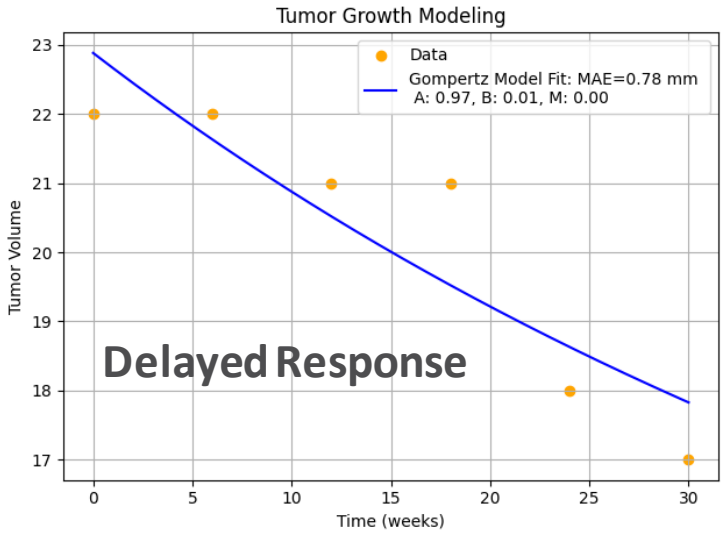
VALIDATION

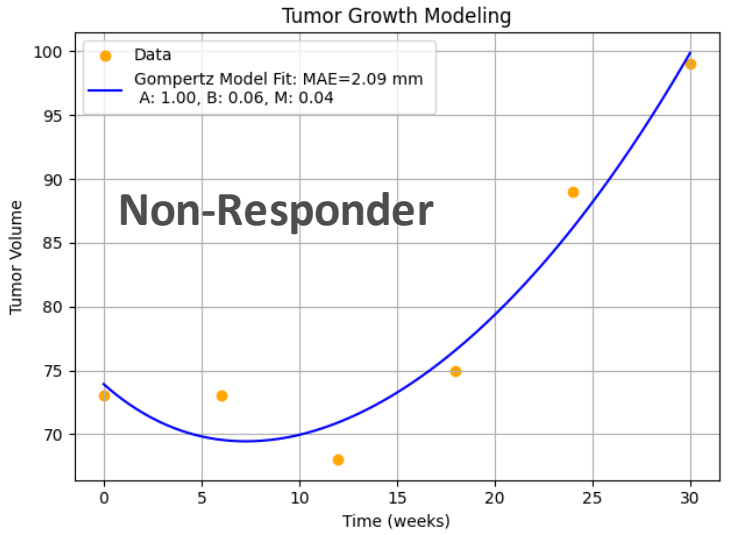
IS THE MODEL WORKING WITH IMMUNOTHERAPY MECANISM?

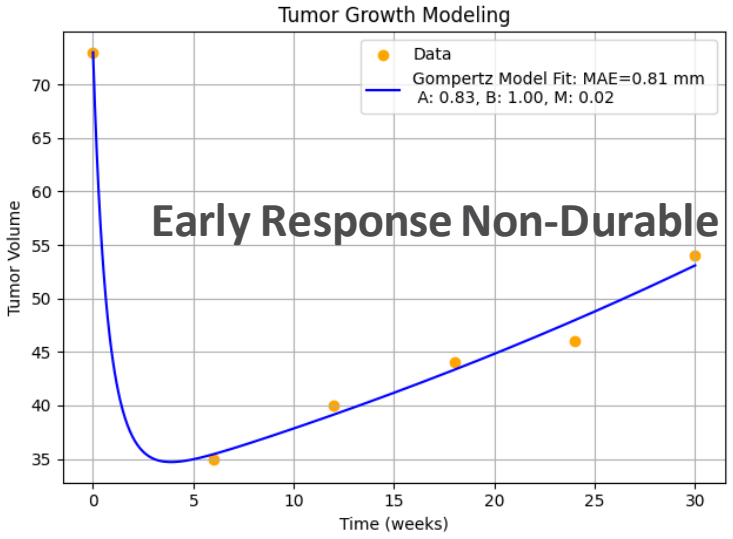
Data vs. Model (Individual Fits)

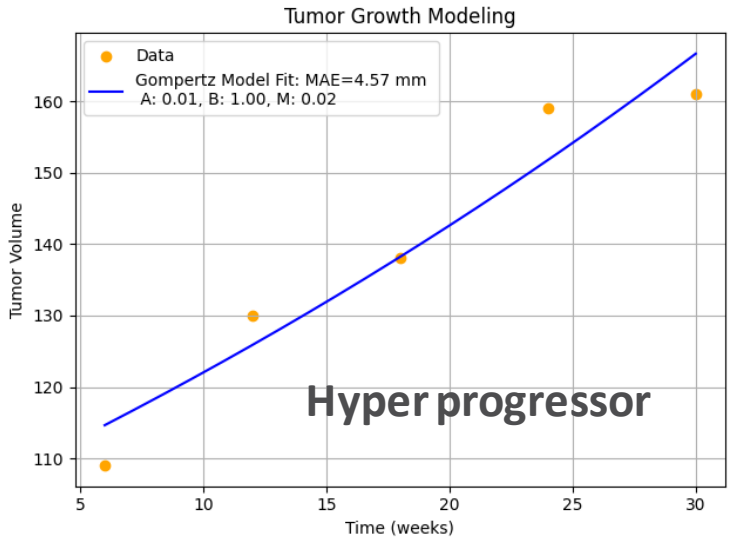
Mean Absolute Error

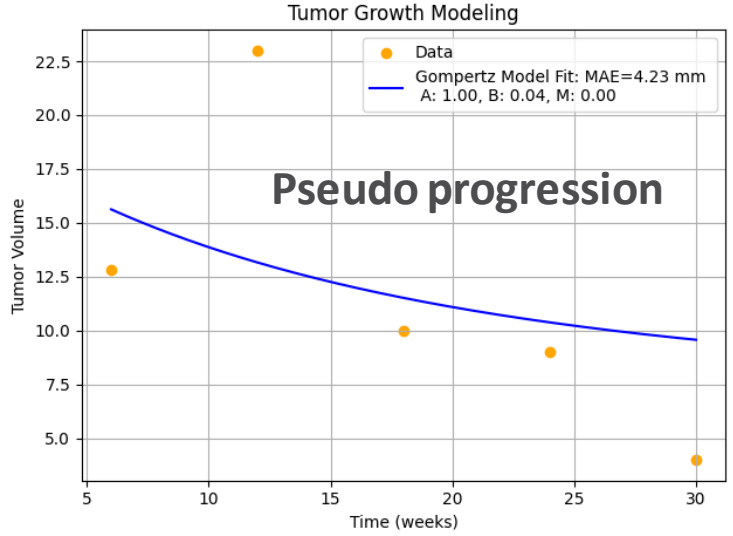


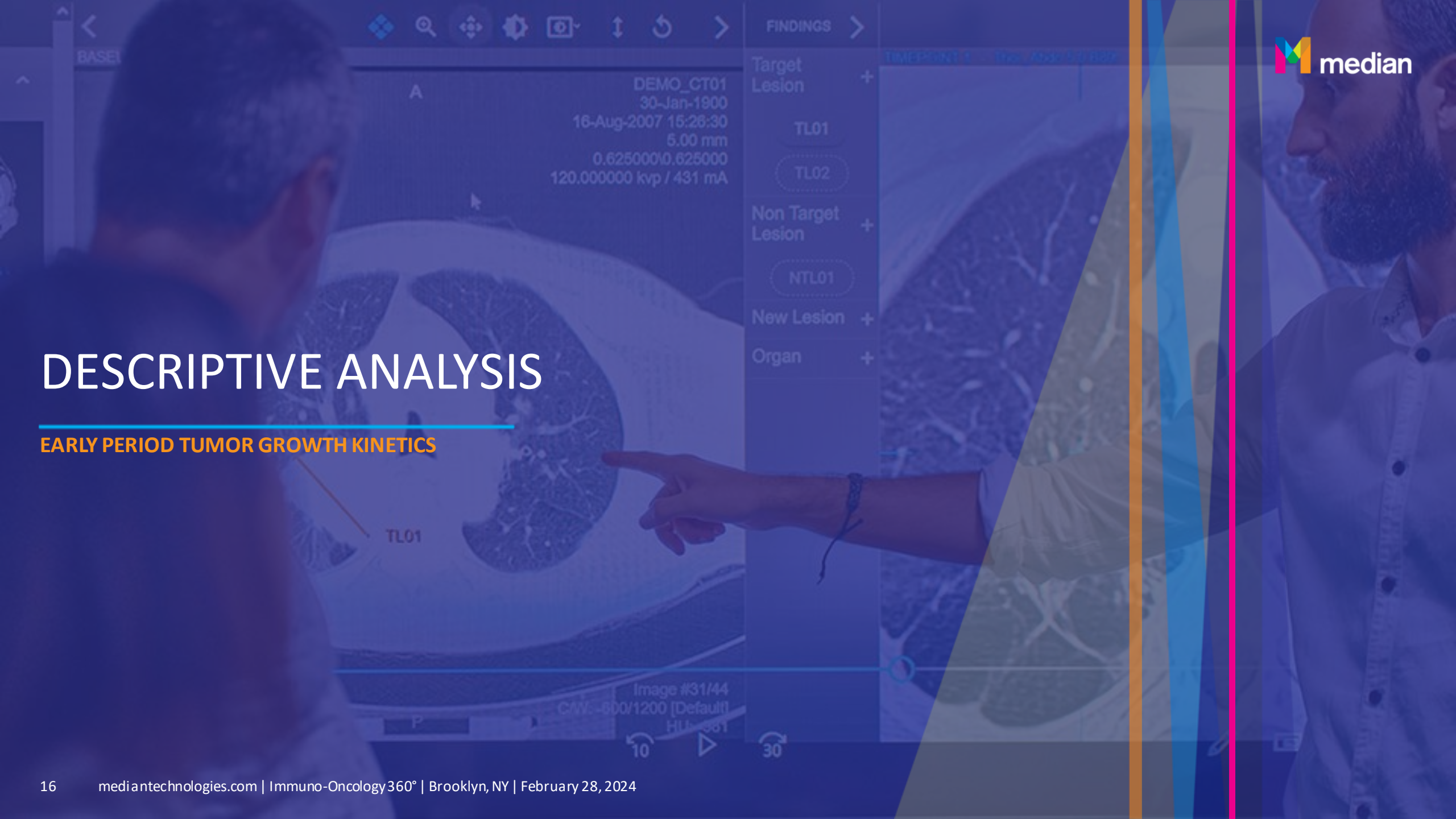












DESCRIPTIVE ANALYSIS

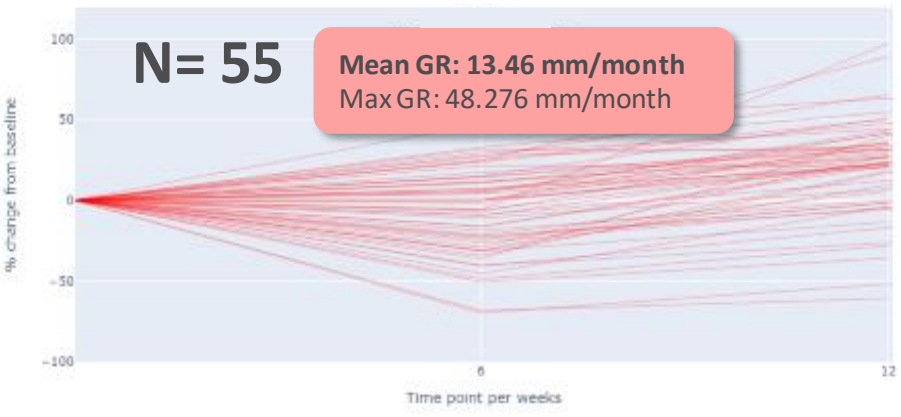
EARLY PERIOD TUMOR GROWTH KINETICS

Early Tumor Growth Kinetics

Progression

N= 55

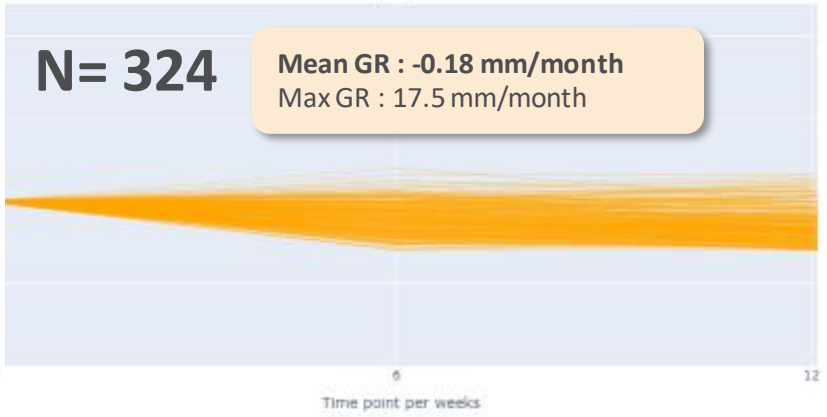
Mean GR: 13.46 mm/month
Max GR: 48.276 mm/month



Stable Disease

N= 324

Mean GR : -0.18 mm/month
Max GR : 17.5 mm/month



Response

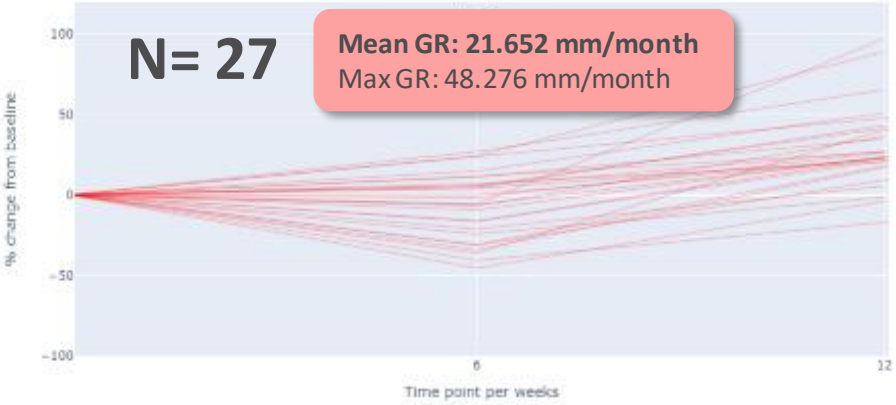
N= 473

Mean GR: -7.260 mm/month
Max GR: 21.292 mm/month

Hyper Progression

N= 27

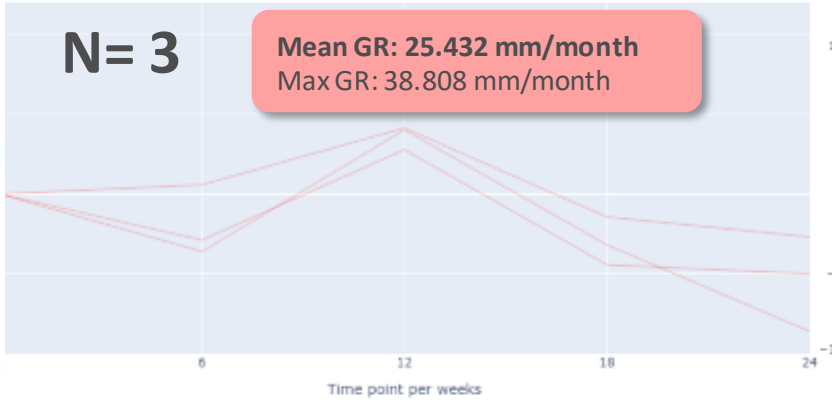
Mean GR: 21.652 mm/month
Max GR: 48.276 mm/month



Pseudo Progression

N= 3

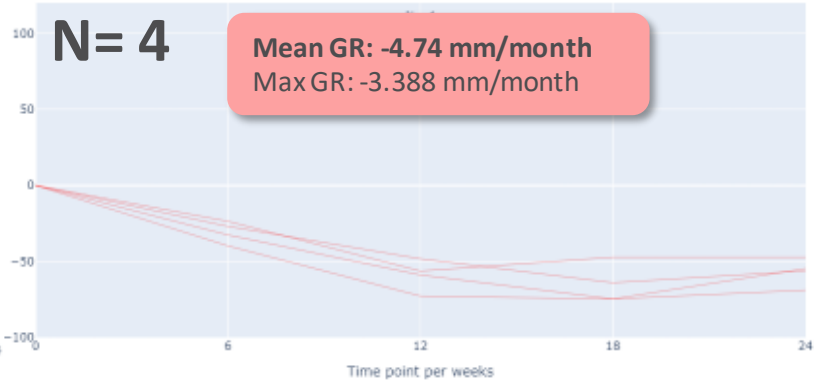
Mean GR: 25.432 mm/month
Max GR: 38.808 mm/month

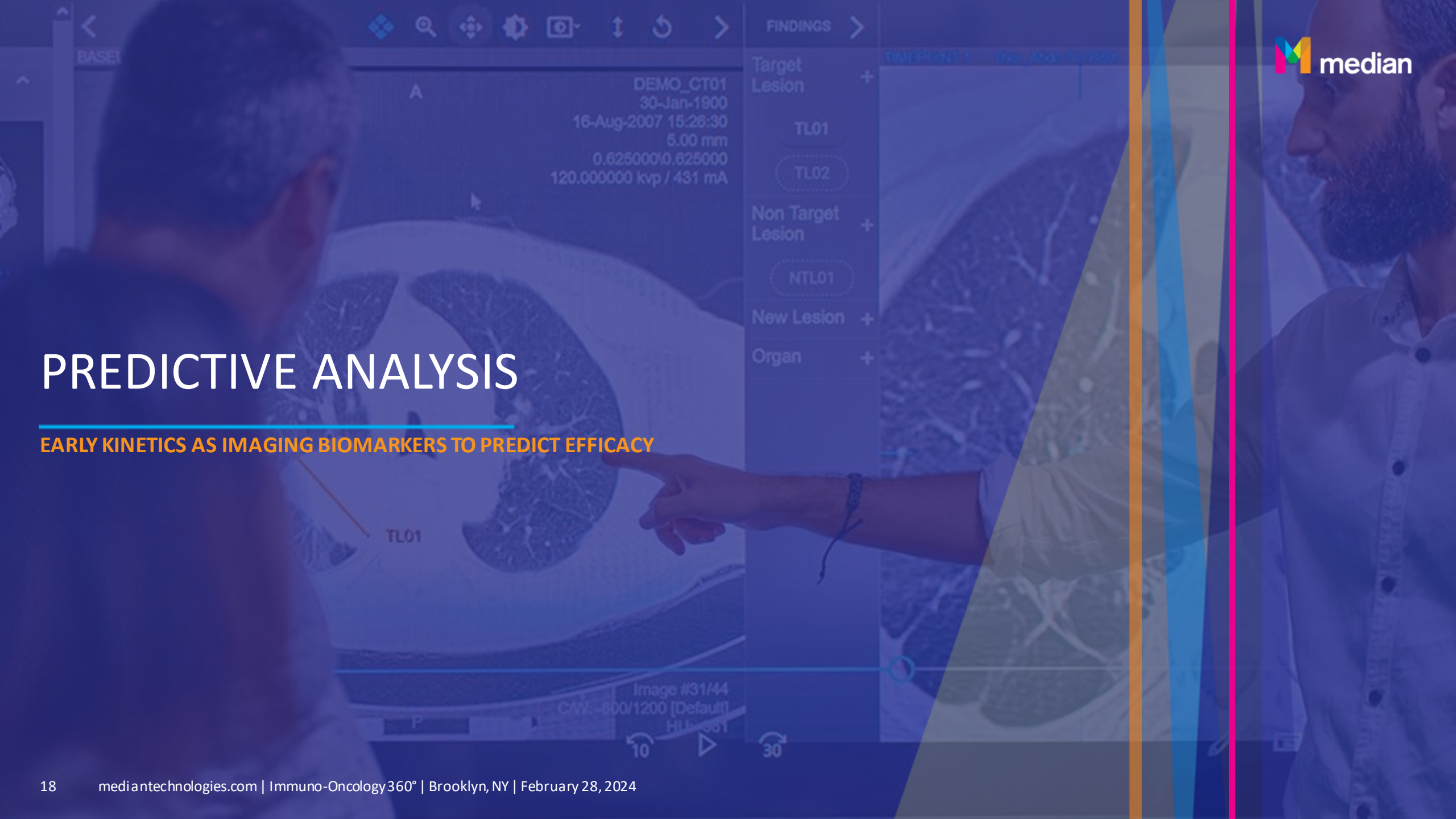


Paradox Response

N= 4

Mean GR: -4.74 mm/month
Max GR: -3.388 mm/month





PREDICTIVE ANALYSIS

EARLY KINETICS AS IMAGING BIOMARKERS TO PREDICT EFFICACY

RECIST 1.1 Early Kinetics are Biomarkers for First Response and the PFS

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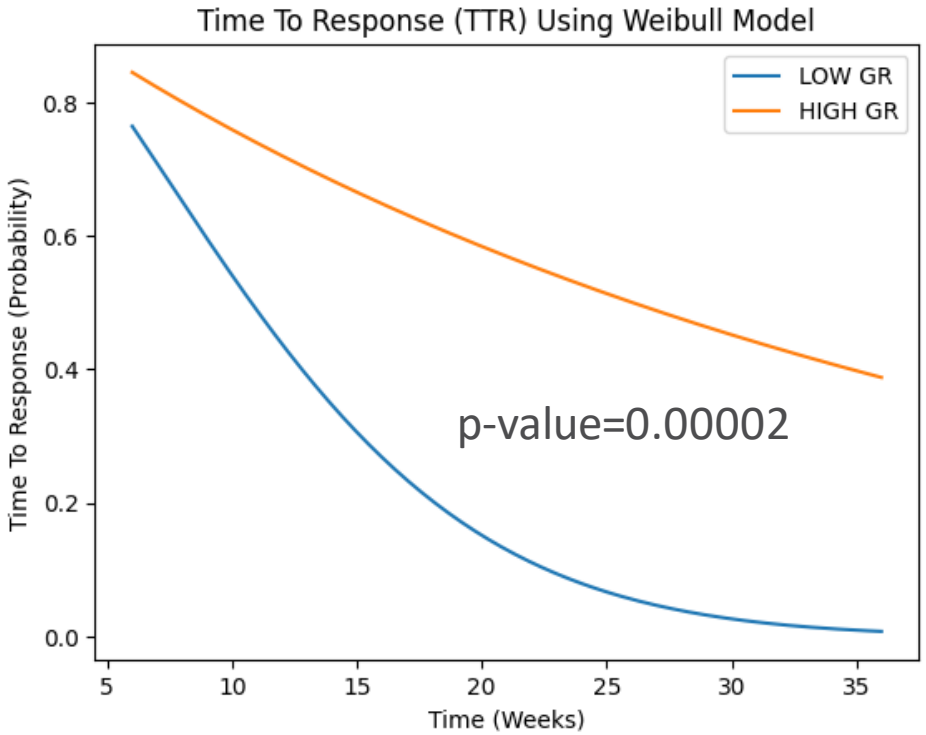
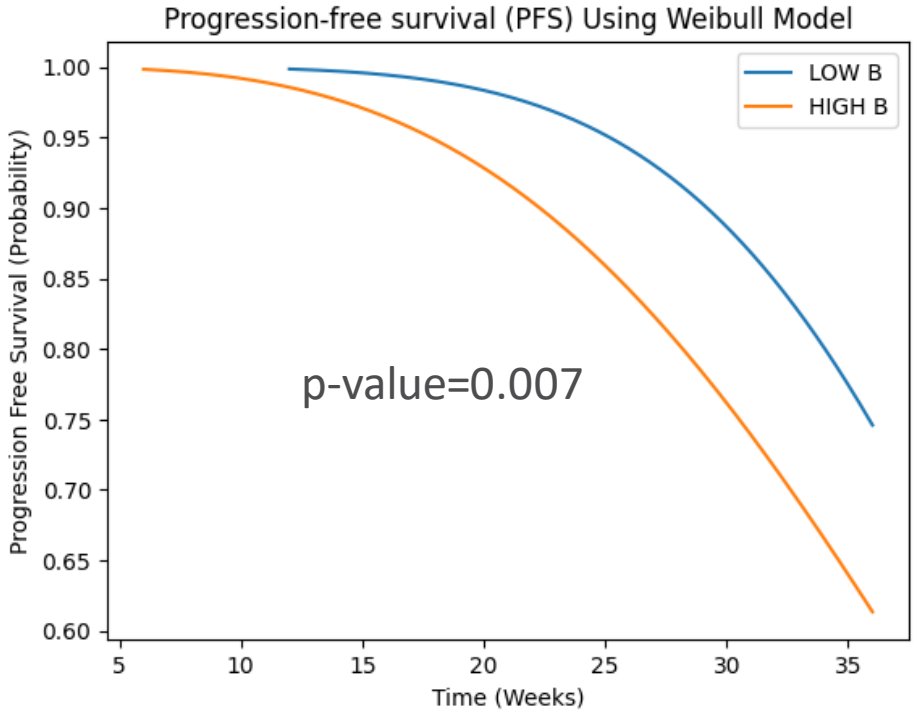
TTR : 16w [6-36]



"Patients with low early growth rate are having shorter TTR

PFS : 33w [6-36]

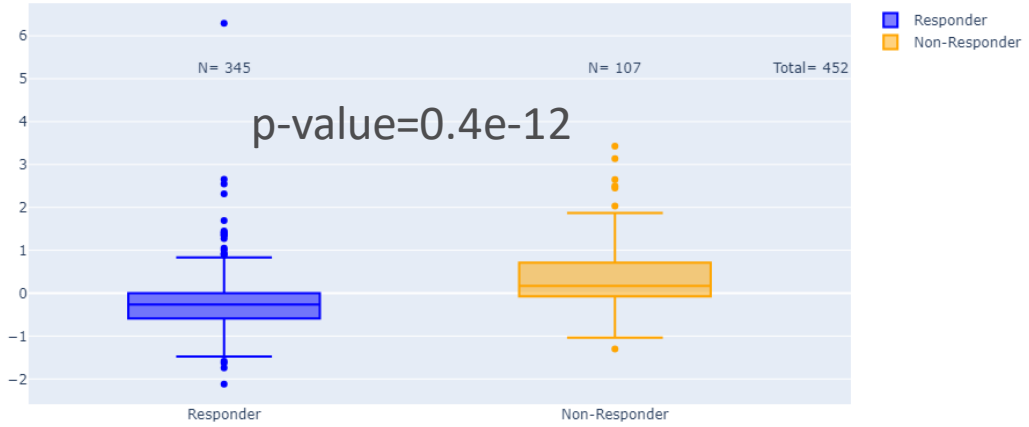


"Patients with low early growth decay parameter are having longer PFS

RECIST 1.1 Early Kinetics are Biomarkers for BOR and Correlate with Depth of Response

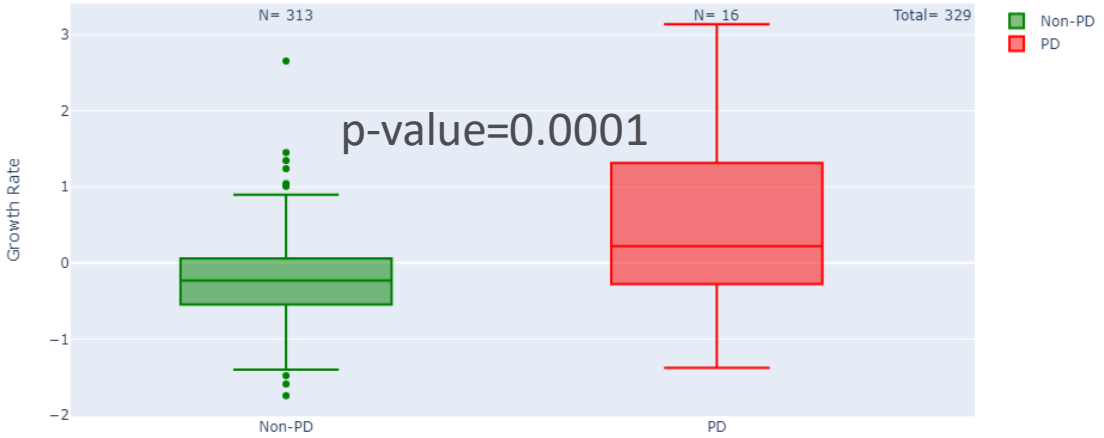
RESPONSE

GR Box plot



CLINICAL BENEFIT

GR Box plot



"Responders (CR/PR) have significantly lower early tumor grow rates than non-responders

TARGET LESION ONLY

RECIST 1.1 Early Kinetics are Biomarkers for Delayed Response

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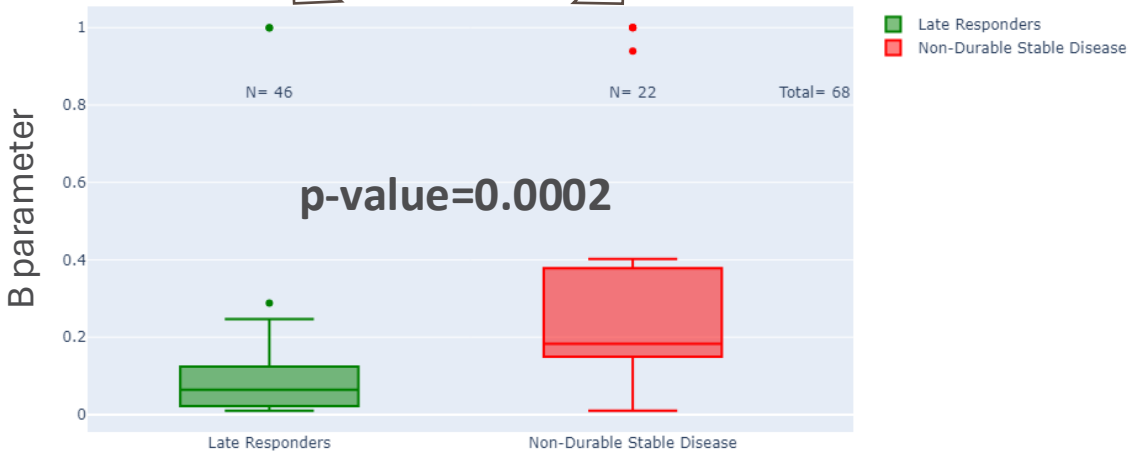
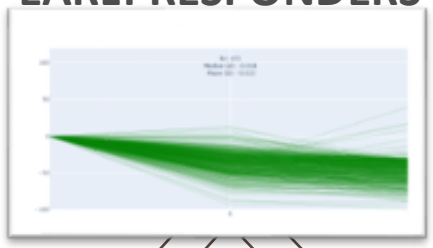
EARLY STABLES

Decay Box plot

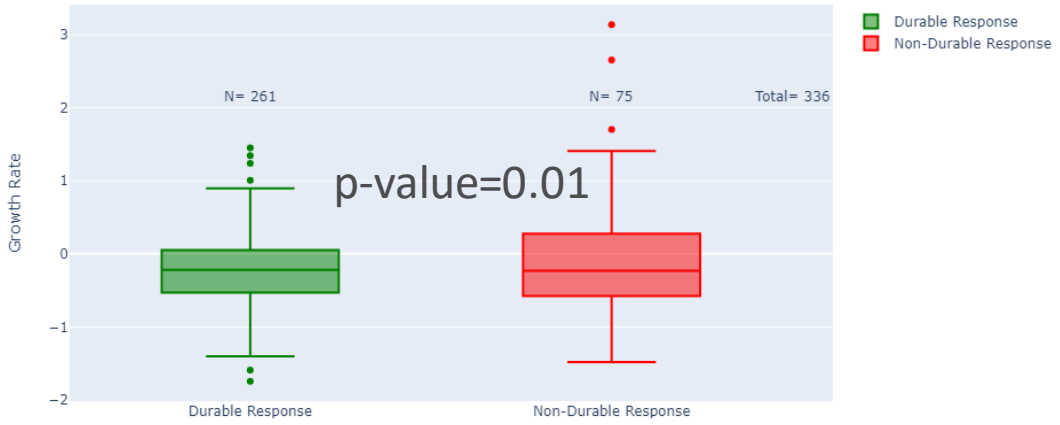


“ Patients stable with high decay parameter will more likely have an event of progression

EARLY RESPONDERS

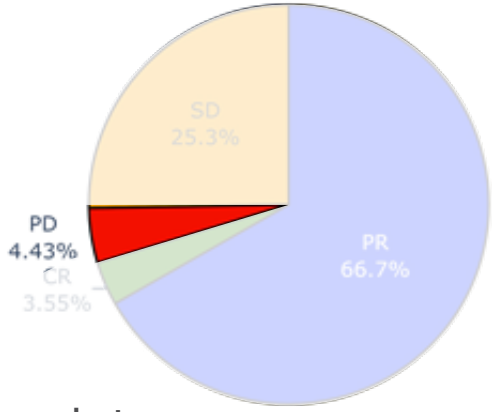


GR Box plot

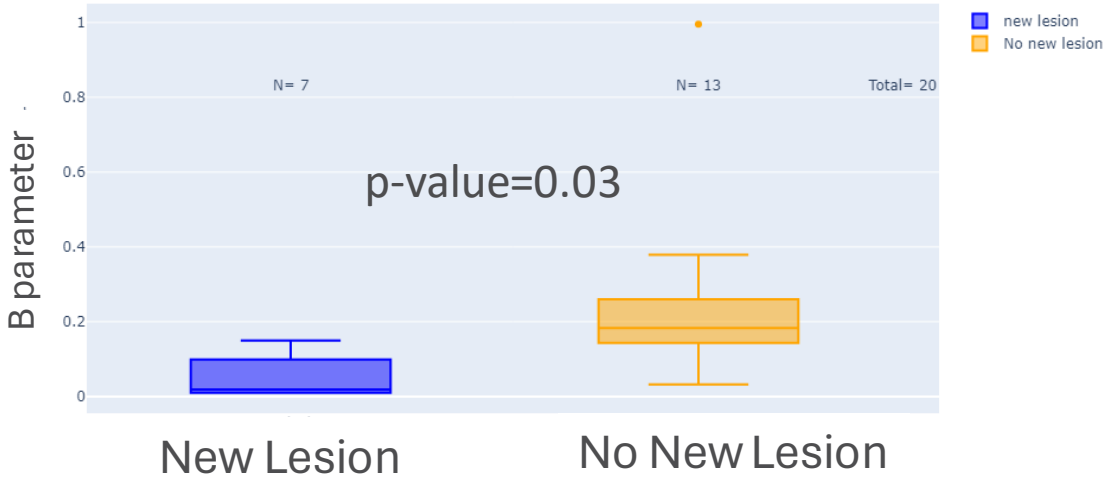


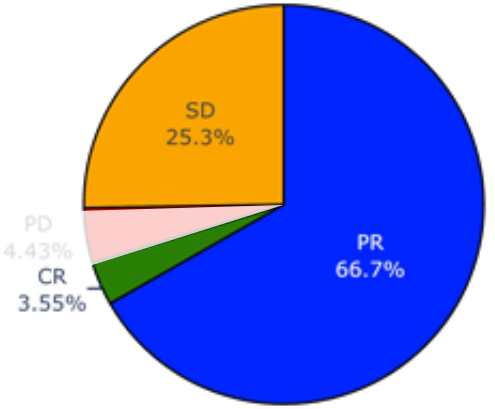
“ Early kinetics are not significantly different for durable or non-responders

Appearance of NL Can be Predicted, Paradoxical Responses Cannot

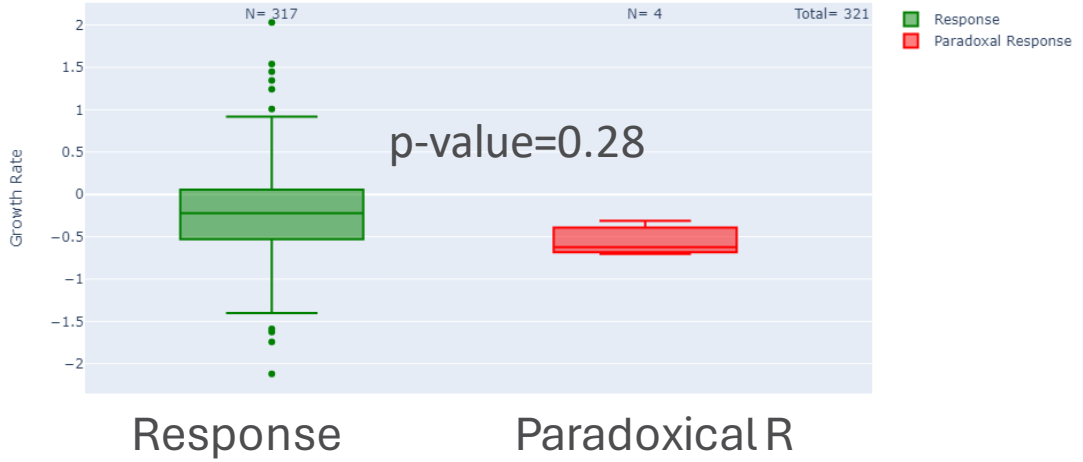


Decay Box plot

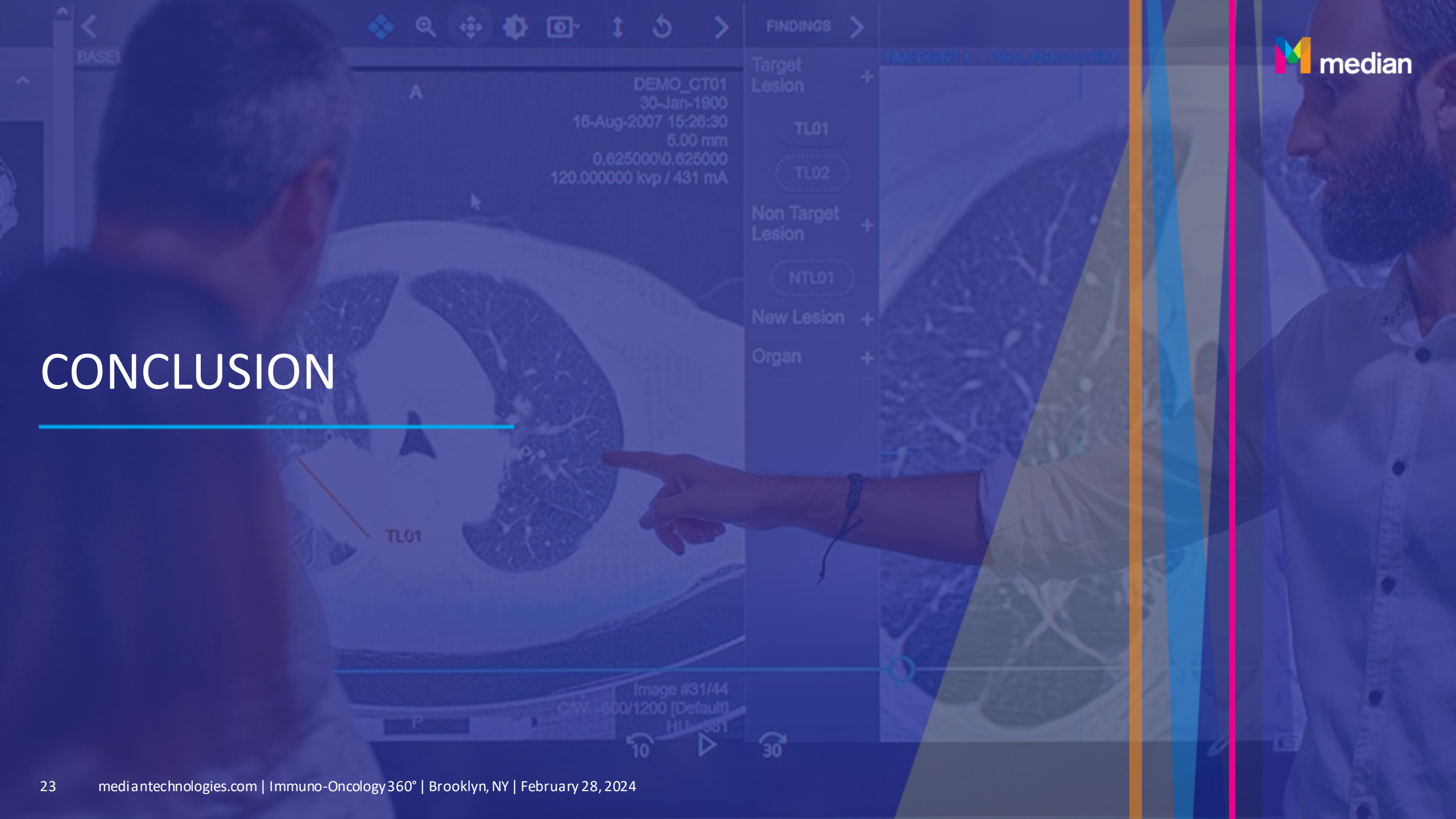




GR Box plot



CONCLUSION


FINDINGS
Target Lesion
TL01
TL02
Non Target Lesion
NTL01
New Lesion
Organ
DEMO_CT01
30-Jan-1900
16-Aug-2007 15:26:30
5.00 mm
120.000000 kvp / 431 mA
TL01
Image #31/44

Take Home Messages

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Tumor Growth Kinetics Modeling

1

Works with Combination Immunotherapy in NSLCC

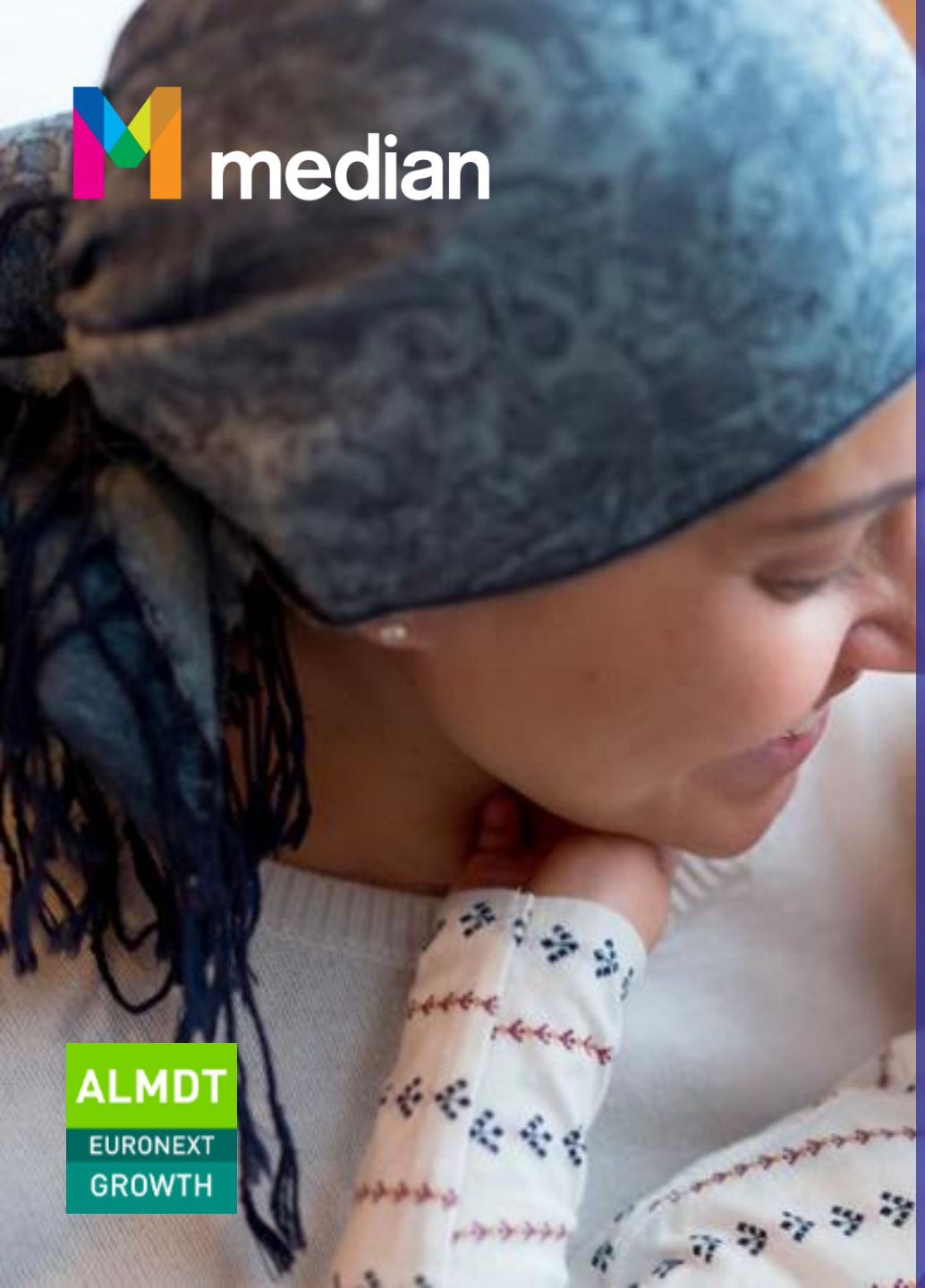
2

Early Available Biomarker from RECIST assessments

Propose additional TP during 2 first months and volume analysis

3

- **Differentiates 2 types of early stable disease**
- **Predicts Efficacy and Expected Clinical Trial Events**



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Committing to quality in all we do
Be dedicated to quality in everything we do. Quality begins with us and we are committed to it.

Supporting our customers in achieving their goals
Listen to the needs of our customers and help make their goals our goals through our innovation, imaging expertise, superior services, and quality solutions.

Putting the patient first
There is a person at the other end of the images we analyze who is counting on us to do everything we can to help make them healthier.

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