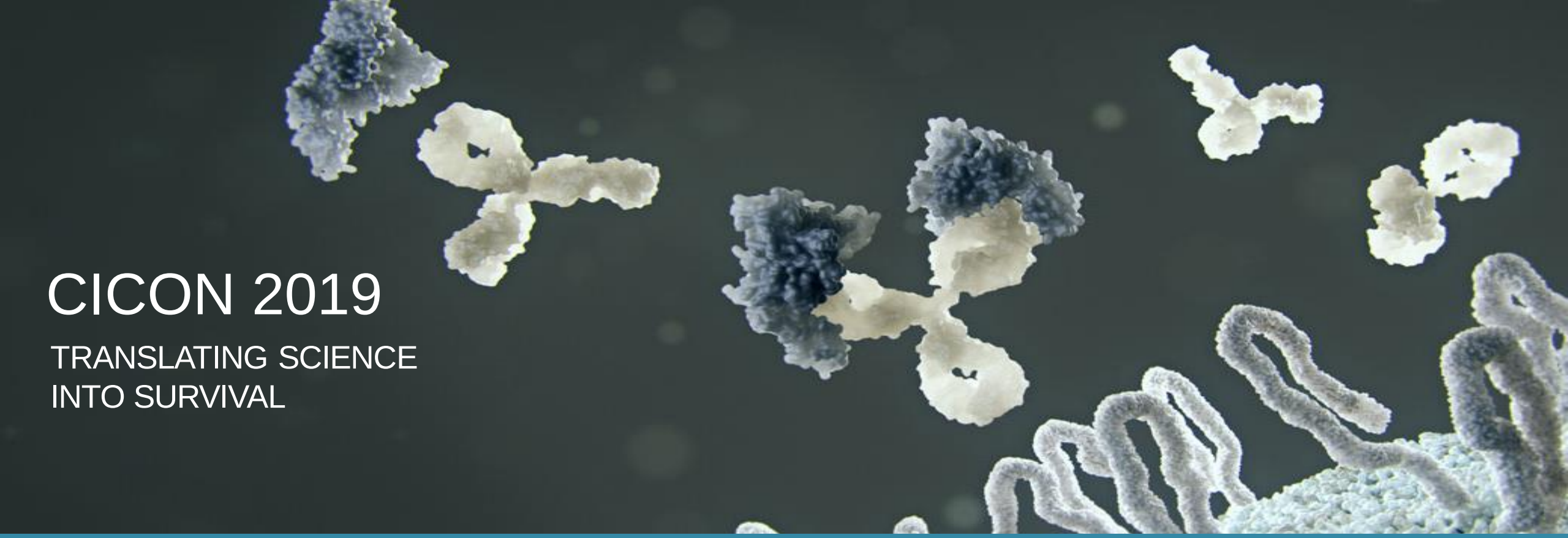

CICON 2019

TRANSLATING SCIENCE
INTO SURVIVAL

Interim results from CLASSICAL-Lung, a phase 1b/2 study of pepinemab in combination with avelumab in advanced NSCLC patients who progressed on prior anti-PDx therapy

Elizabeth Evans
Vice President, Discovery Research

VACCINEX

Disclosure Information

Fifth CRI-CIMT-EATI-AACR International Cancer Immunotherapy Conference: Translating Science into Survival, 2019

Elizabeth Evans

I have the following financial relationships to disclose:

Employee and share holder of: Vaccinex, Inc

- and -

I will discuss the following investigational use in my presentation: pepinemab and avelumab

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Forward Looking Statements

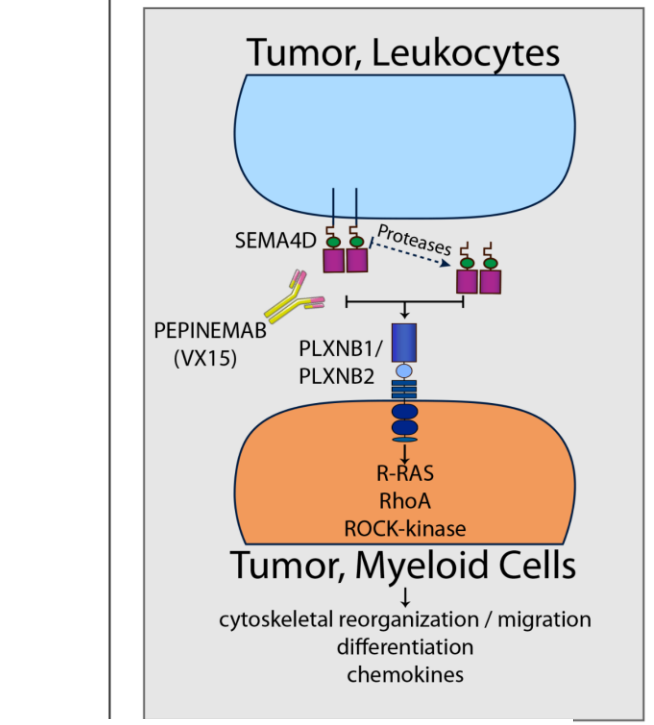
To the extent that statements contained in this press release are not descriptions of historical facts regarding Vaccinex, Inc. ("Vaccinex," "we," "us," or "our"), they are forward-looking statements reflecting management's current beliefs and expectations. Such statements include, but are not limited to, statements about our plans, expectations and objectives with respect to the CLASSICAL-Lung clinical trial, the combination of pepinemab and avelumab, and other statements identified by words such as "may," "will," "appears," "expect," "anticipate," "estimate," "intend," "hypothesis," "potential," "advance," and similar expressions or their negatives (as well as other words and expressions referencing future events, conditions, or circumstances). Forward-looking statements involve substantial risks and uncertainties that could cause our research and pre-clinical development programs, clinical development programs, future results, performance, or achievements to differ significantly from those expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, uncertainties inherent in the execution, cost and completion of preclinical and clinical trials, uncertainties related to regulatory approval, risks related to our dependence on our lead product candidate pepinemab (VX15/2503), and other matters that could affect our development plans or the commercial potential of our product candidates. Except as required by law, we assume no obligation to update these forward-looking statements. For a further discussion of these and other factors that could cause future results to differ materially from any forward-looking statement, see the section titled "Risk Factors" in our periodic reports filed with the Securities and Exchange Commission ("SEC") and the other risks and uncertainties described in our Form 10-K dated March 13, 2019 and subsequent filings with the SEC.

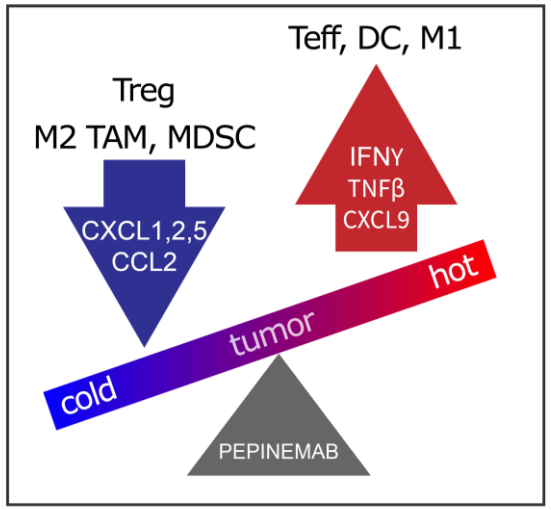
Pepinemab

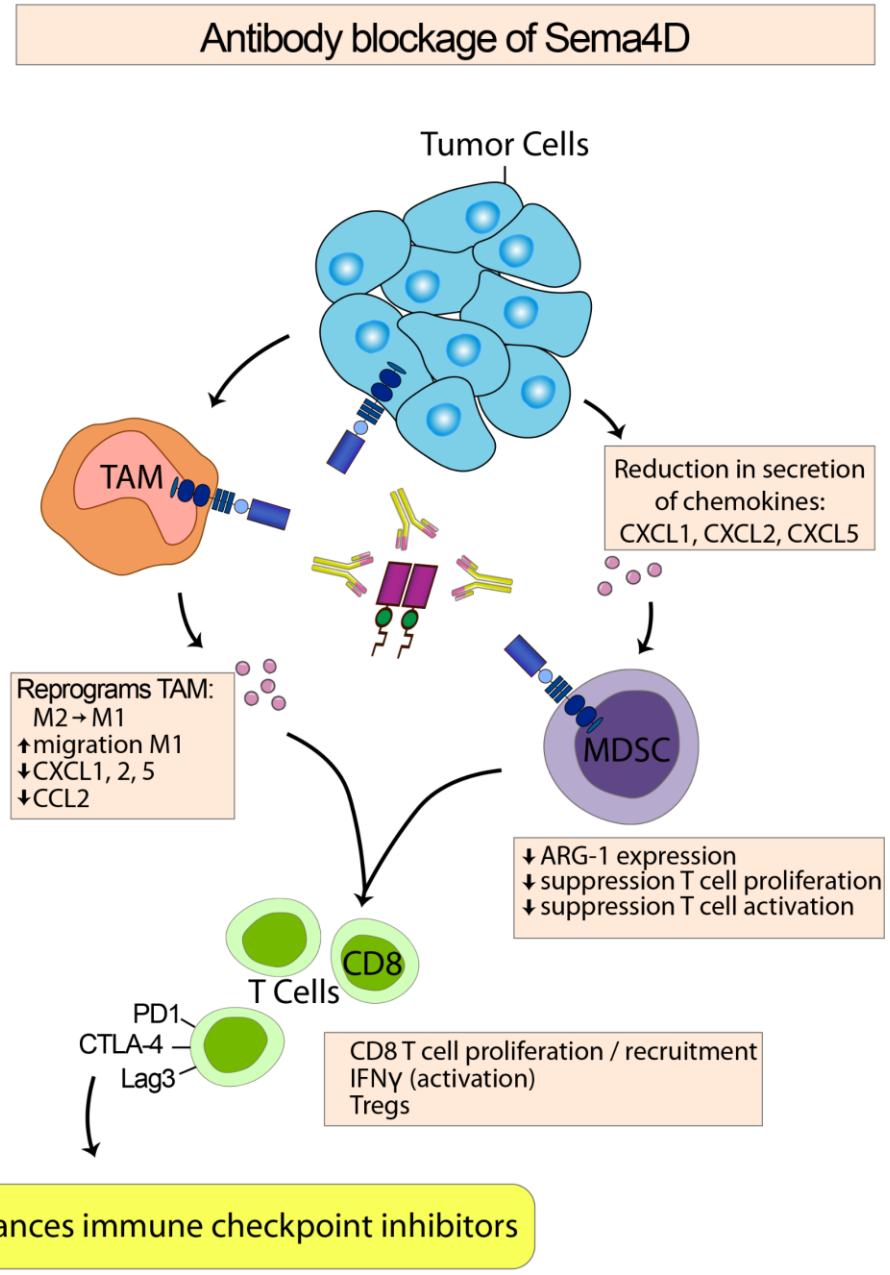
Proposed Mechanism of Action

- Semaphorin 4D signals through Plexin B1 and Plexin B2 receptors to regulate cellular cytoskeleton and function

- **Anti-SEMA4D shifts the balance of immune infiltration and myeloid suppression to promote anti-tumor T cell activity[1,2]**
  - Promotes infiltration of potent APC
  - Reverses recruitment and function of MDSC, M2 TAM and Treg
  - → Facilitates infiltration and activity of CD8+ T cells
- Pepinemab (VX15/2503), a humanized IgG4 with hinge modification, binds to SEMA4D and blocks its signaling activity



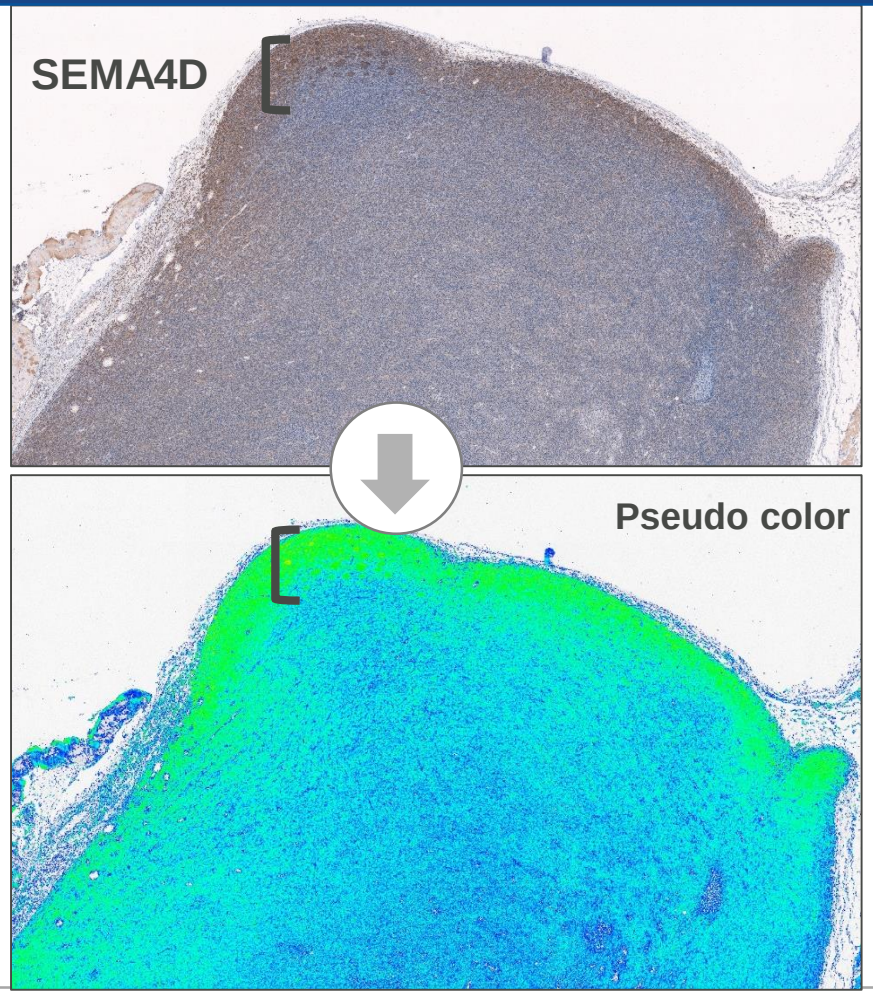




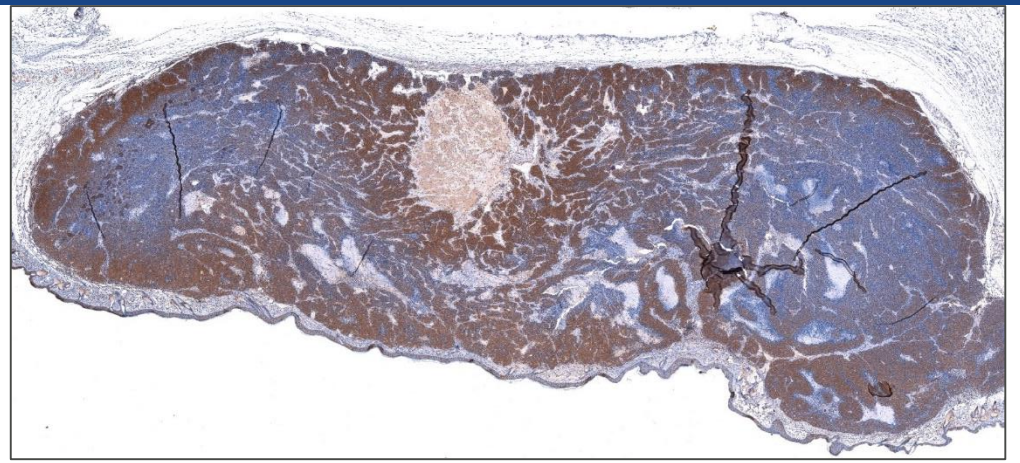
1. Evans EE et al. Cancer Immunol Research 2015
2. Clavijo et al. Cancer Immunol Research 2019

SEMA4D Expression is Concentrated at Invasive Margin of Tumor

Colorectal (Colon26)



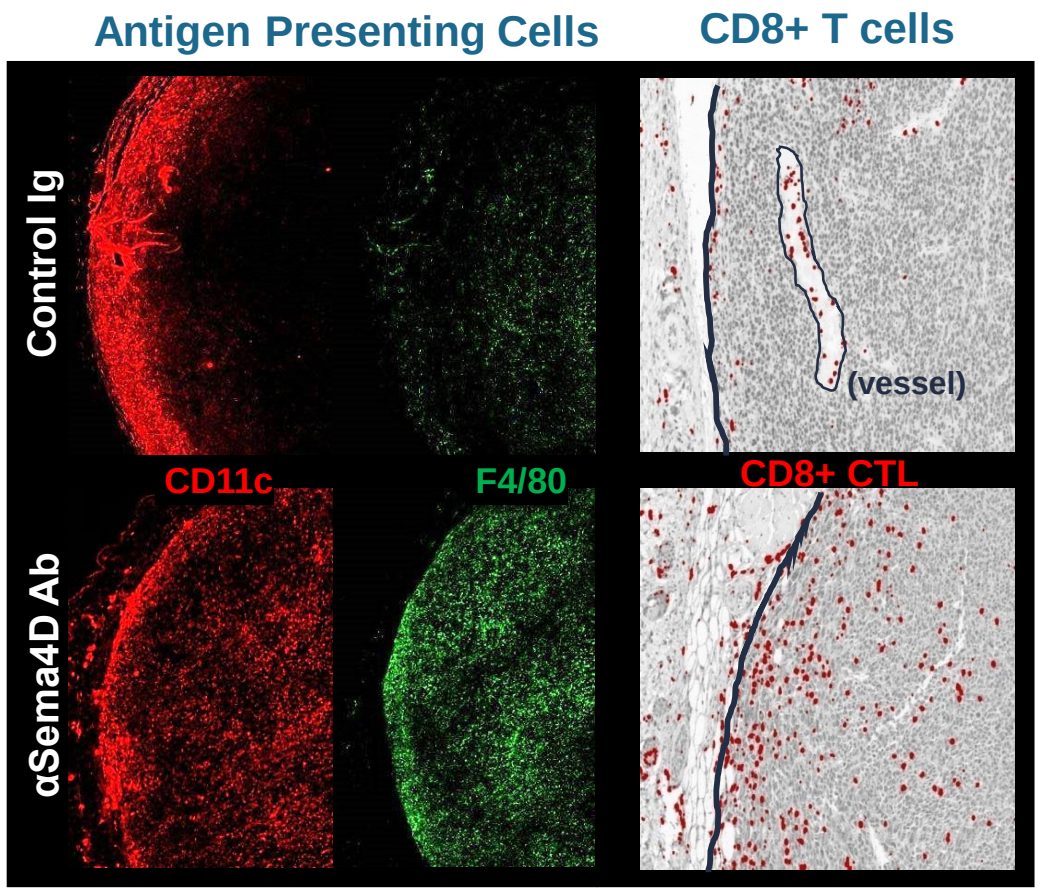
Mammary carcinoma (Tubo.A5)

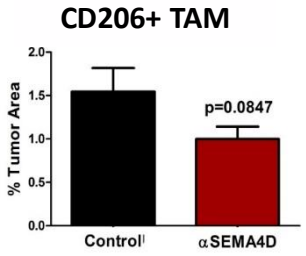


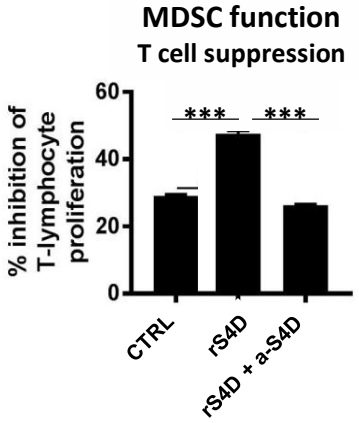
SEMA4D at the invasive margin of the tumor forms a barrier that restricts the infiltration of anti-tumor immune cells

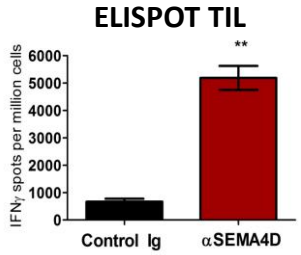
Antibodies against SEMA4D neutralize this barrier and "open the gates" of the tumor to the immune system

SEMA4D blockade reverses immune exclusion and myeloid suppression in TME









M2 TAM

MDSC

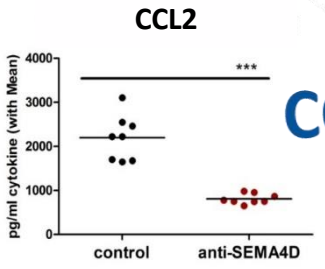
Teff

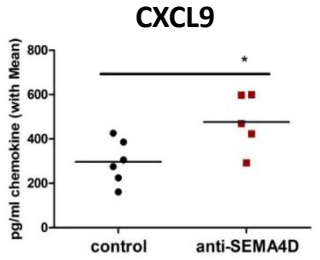
CCL2

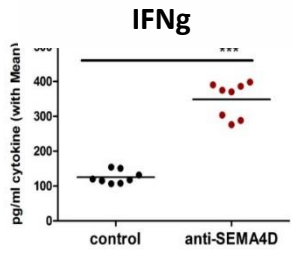
CXCL9

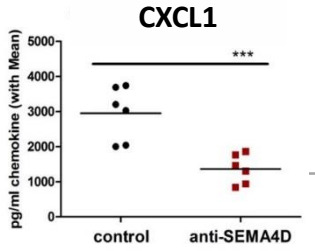
IFNg

CXCL1,2,5







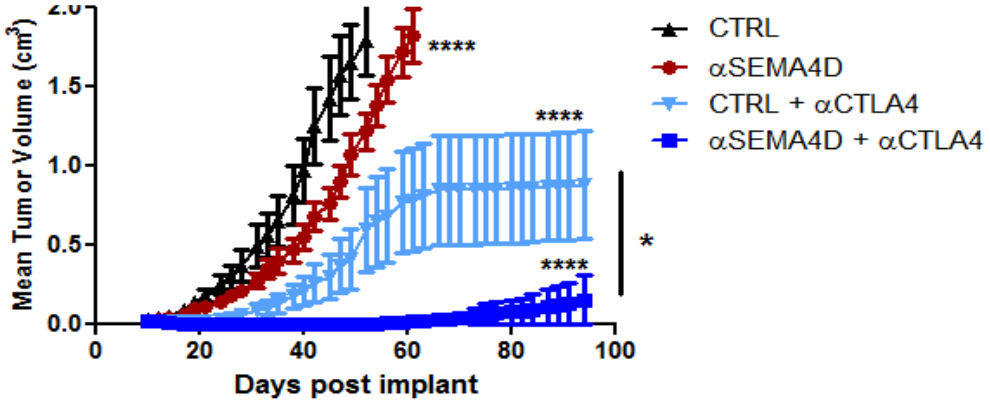


Colon26: Evans EE et al. Cancer Immunol Research 2015
MDSC and MOC1 HNSCC: Clavijo et al. Cancer Immunol Research 2019

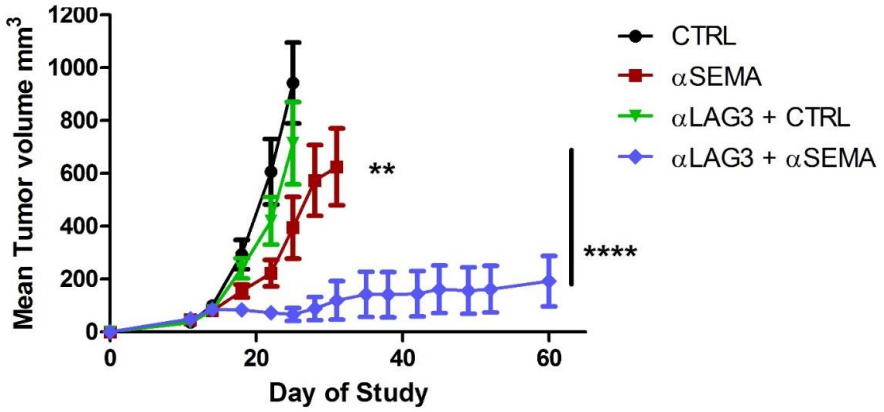
Anti-SEMA4D Antibody Enhances Activity of Immune Checkpoint Antibodies in Preclinical Syngeneic Models

anti-CTLA-4 Combination: MOC1 HNSCC

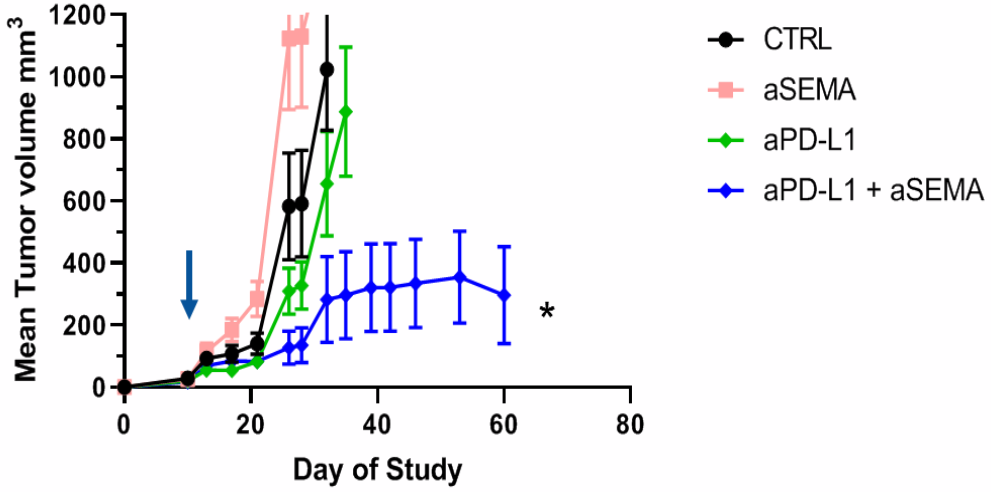
(Clint Allen, NIH)



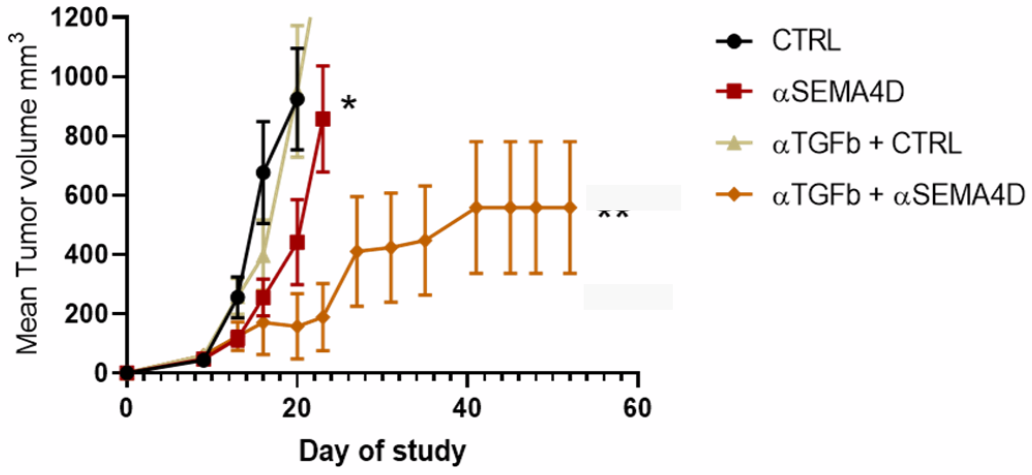
anti-LAG3 Combination: Colon26

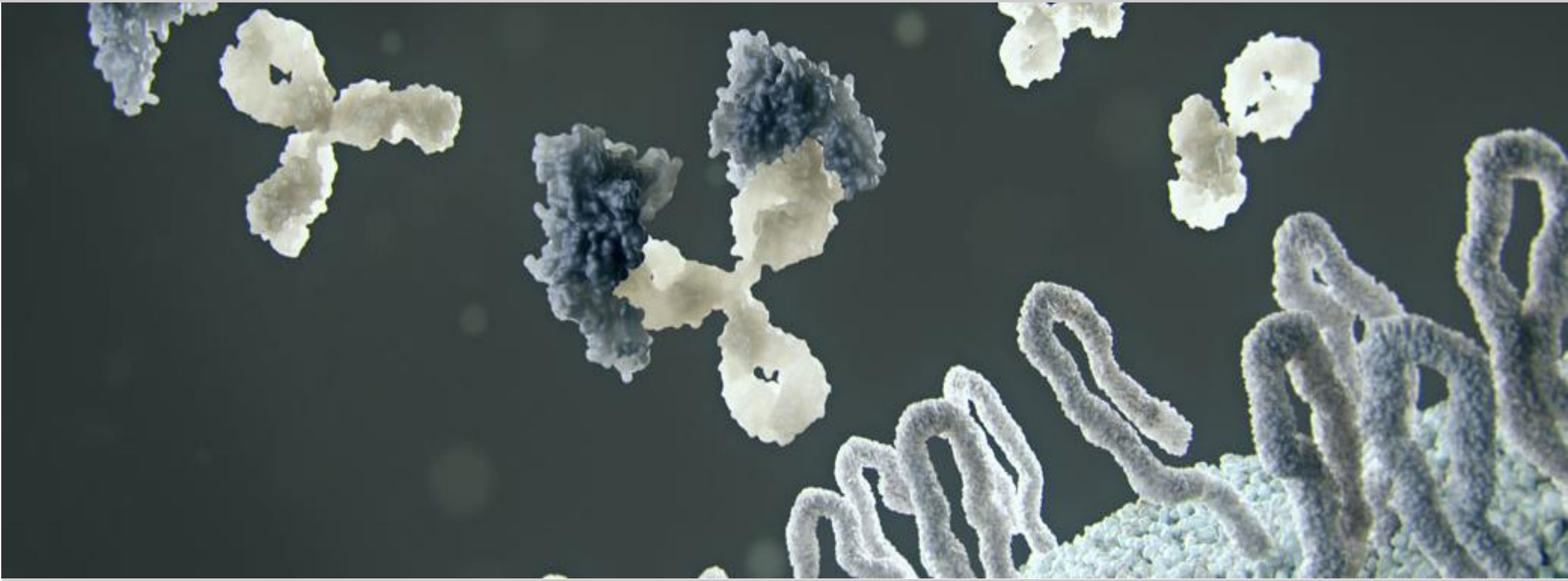


anti-PD-L1 Combination: Colon26



Anti-TGFβ: MC38





CLASSICAL-Lung Combination trial of Pepinemab with Avelumab

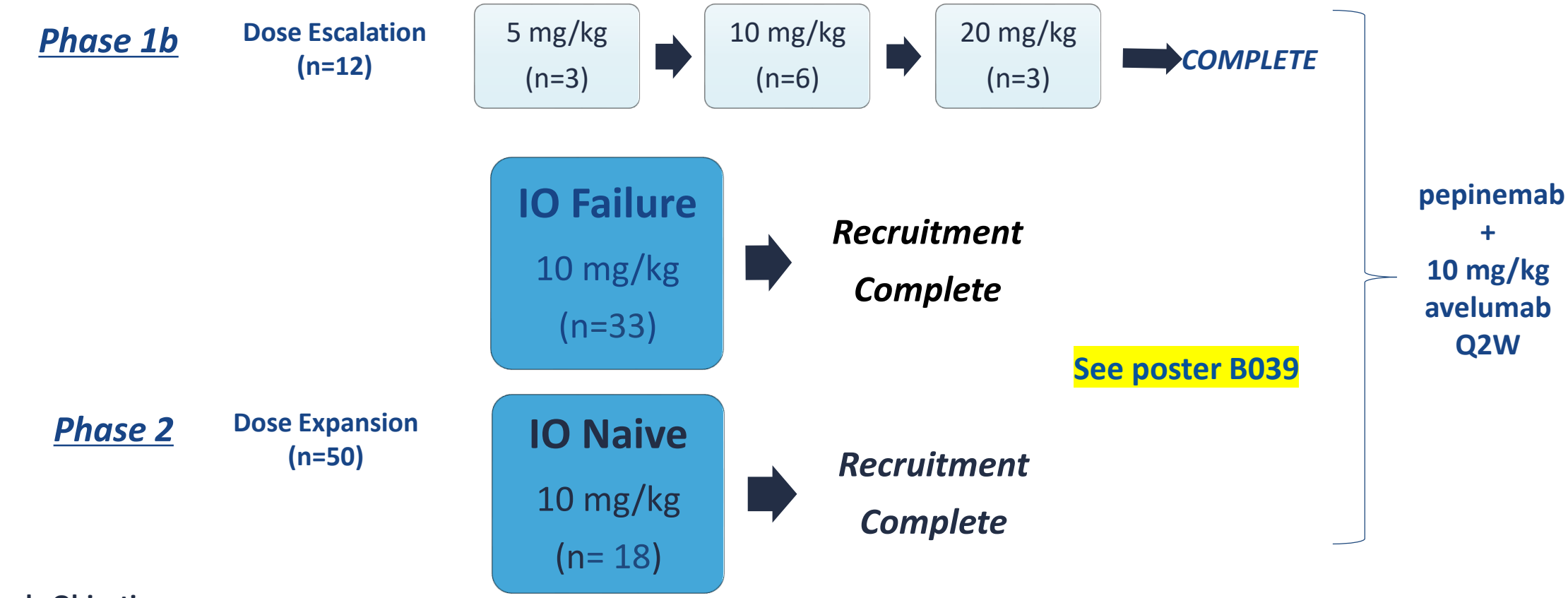
Co-funded by:

MERCK

Phase 1b/2 CLASSICAL- Lung Study Design

Combination Trial of Pepinemab with Avelumab in NSCLC

Co-funded by: MERCK



Study Objectives

- The primary objective of dose escalation is safety, tolerability, and identification of the RP2D for dose expansion.
- Secondary objectives include evaluation of efficacy, immunogenicity, and PK/PD, and an exploratory objective is to identify candidate biomarkers of activity

Safety Summary

CLASSICAL-Lung

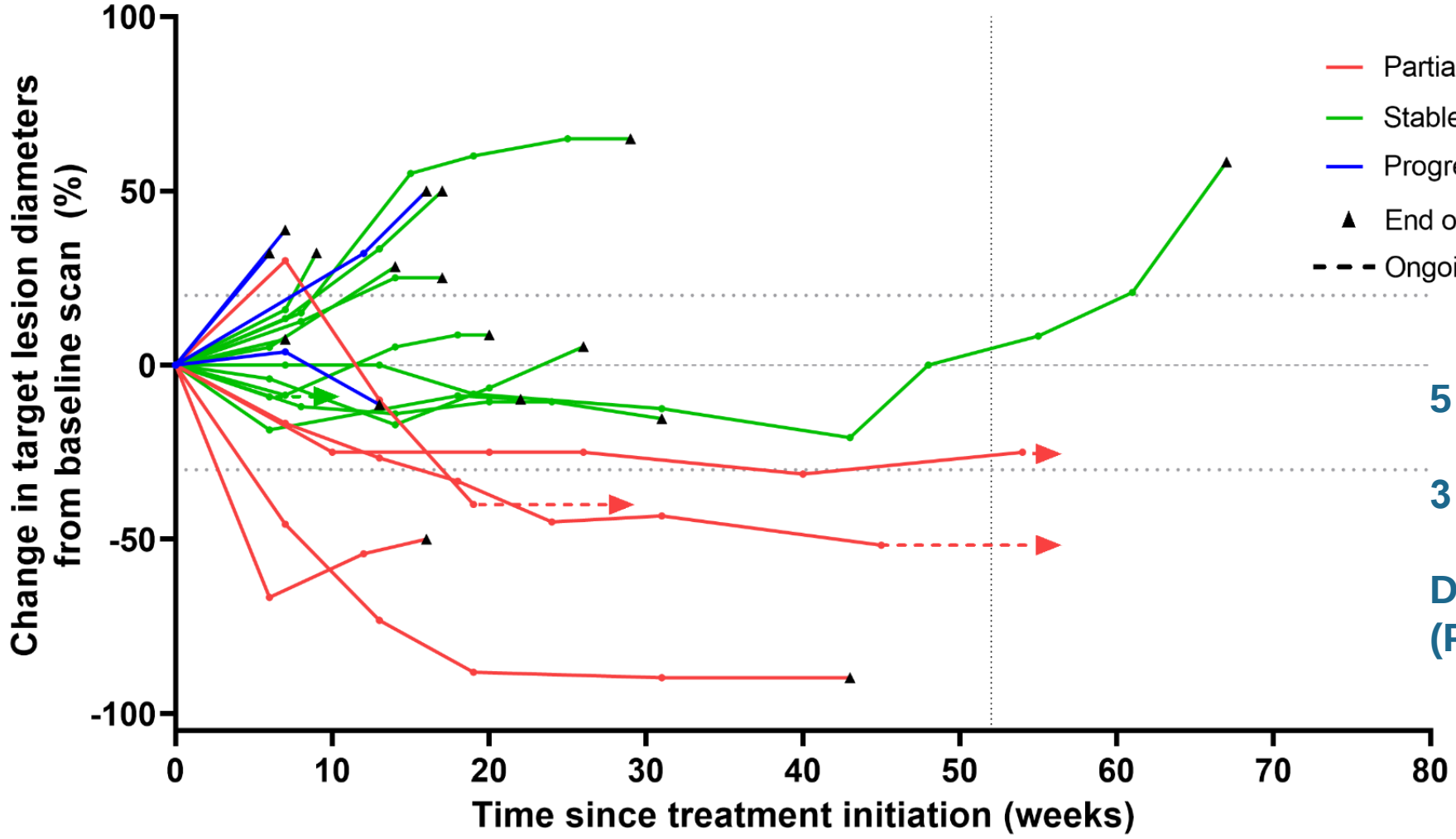
- The combination therapy of pepinemab plus avelumab is well tolerated at all dose levels, with no major safety signals identified to date.
  - One DLT, a grade 3 pulmonary embolism, occurred in the 10mg/kg pepinemab + 10mg/kg avelumab escalation cohort, resolved and did not recur in that same subject or additional subjects in any cohort.
  - Two immune-related Adverse Events (irAE): Myositis (grade3) and Diabetic ketoacidosis (grade4, related to avelumab only).
  - No grade 5 AEs related to the combination have been reported.
- Overall immunogenicity does not appear to be a concern with this combination.

Adverse Event Detail	Grade 3	Grade 4	Total Subjects
Abdominal Pain	1 [1]		1
Alanine Aminotransferase Increased	1 [1]		1
Aspartate Aminotransferase Increased	1 [1]		1
Lipase Increased	2 [2]		1
GGT Increased	1 [1]		1
Hyperprogression	1 [1]		1
Immune Mediated Diabetic Ketoacidosis	1 [1]		1
Myositis	1 [1]	1 [1]	1
Pulmonary Embolism	1 [1]		1
Systemic Inflammatory Response Syndrome	1 [1]		1
Wheezing	1 [1]		1
Total Events	**[11]**	**[1]**	**13 [13]**

Treatment-related Grade 3/4 AEs associated to combination, occurring in all subjects (n denotes the number of subjects, [x] denotes the number of events, (i.e. 2 [2]: 2 Subjects experienced 2 AEs).
Data cutoff 30AUG2019.

Percent Change in Target Lesion Diameter (IO Naïve Cohort)

Interim Analysis



5 Partial Responses

3 Subjects on study ≥ 1 year

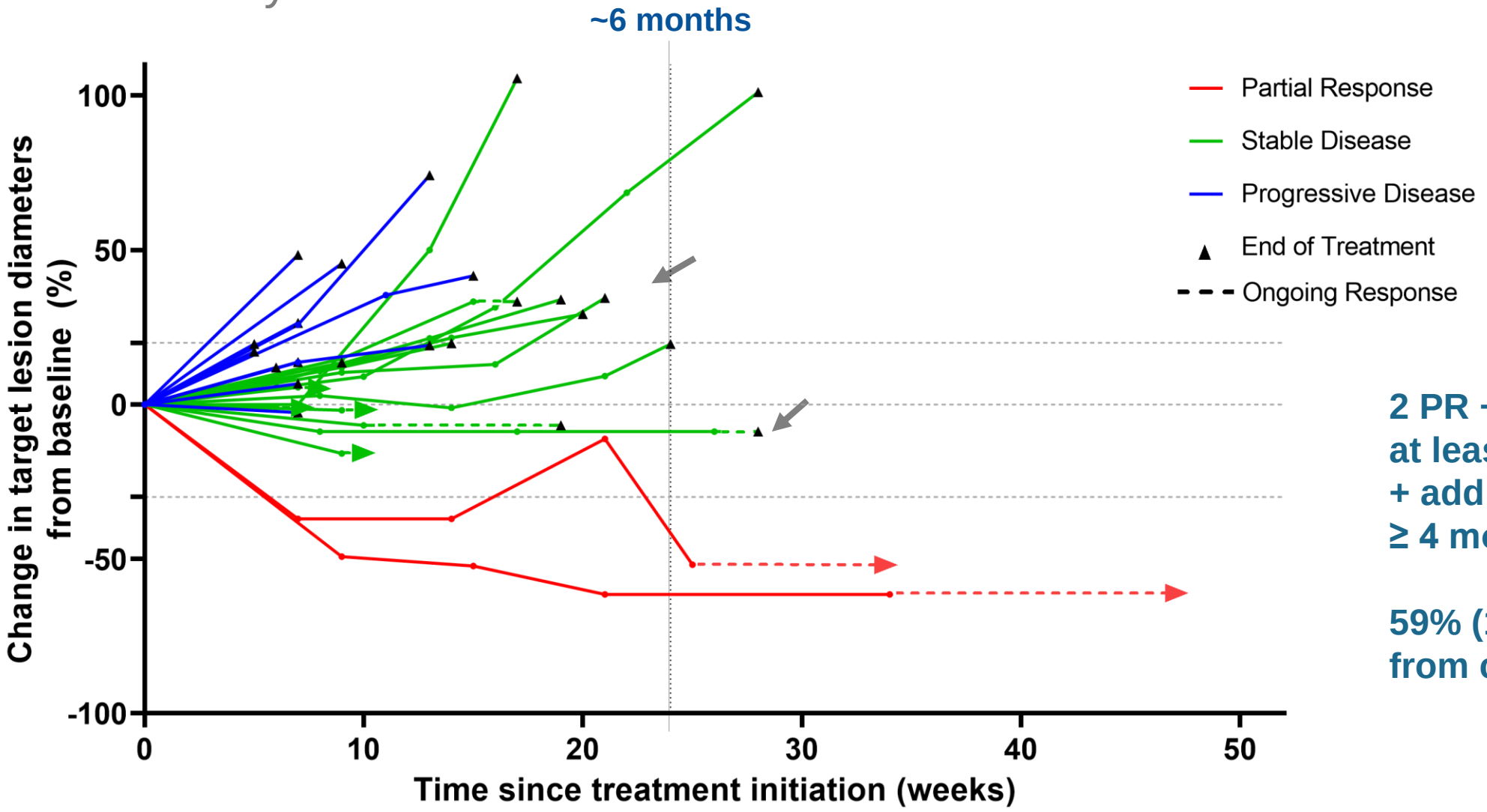
Disease control rate (PR+SD): 81%

Evaluable patients are shown (n=21)

Lines are color-coded based on best overall response

Percent Change in Target Lesion Diameter (IO Failure)

Interim Analysis



2 PR + 3 SD on study at least ~6 months + additional 5 SD ≥ 4 months

59% (17/29) benefitted from combo (SD or PR)

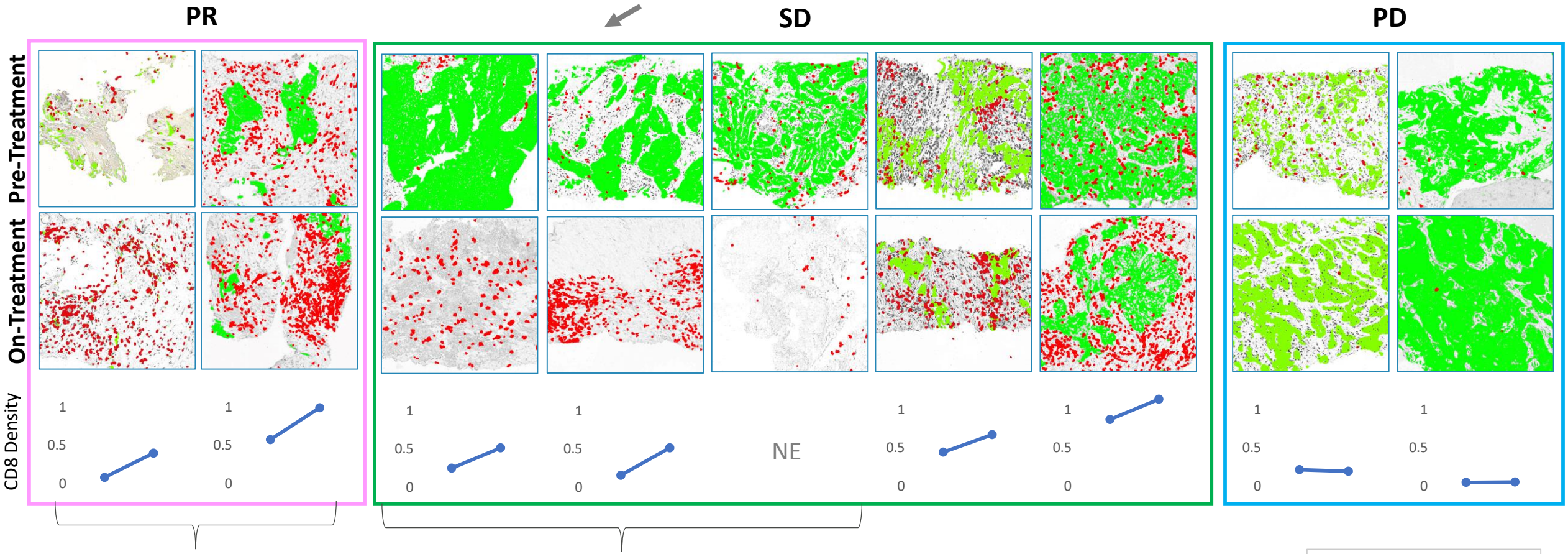
IO refractory

Lines are color-coded based on best overall response

Evaluable patients are shown (n=29)

CLASSICAL- Lung: IO Failure

Increase in CD8+ T cell infiltration



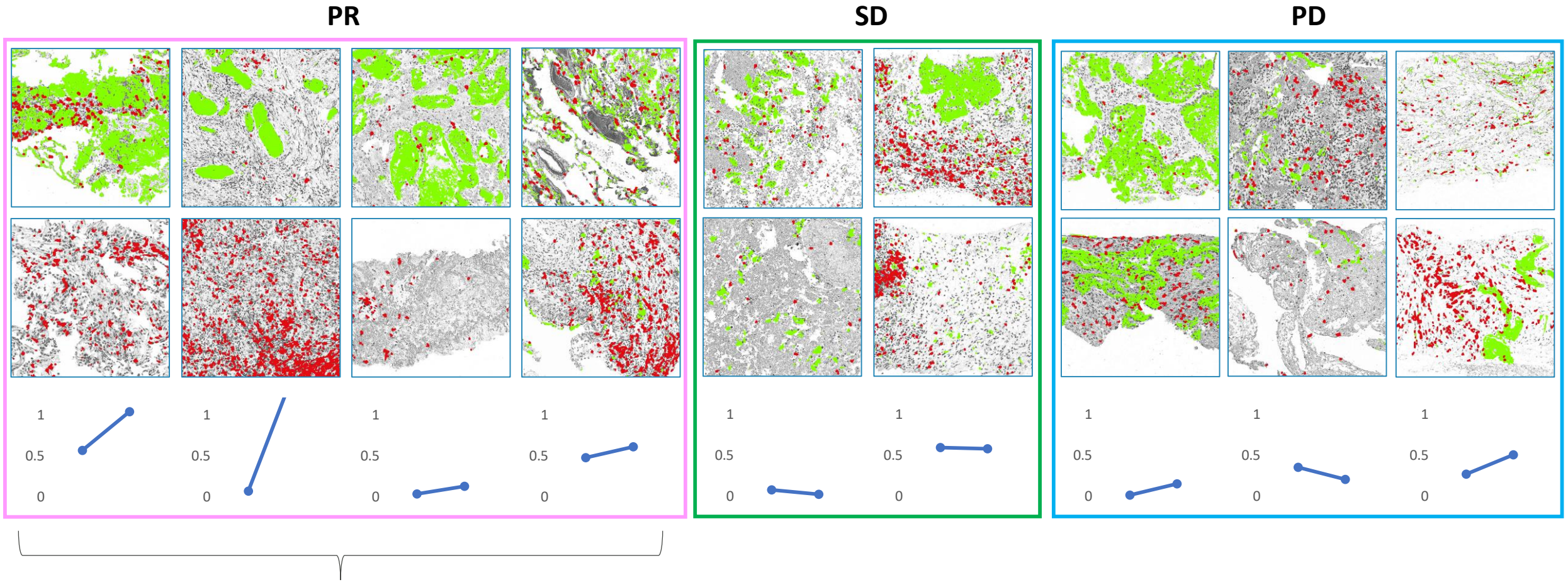
No or low tumor detected in these 2 biopsies from patients with PR

No tumor detected in these 3 biopsies from patients with stable disease
2 of these were PD-L1-negative

Tumor (Cytokeratin+)
CD8+ T cells
NE: not evaluable

CLASSICAL- Lung: IO Naive

Increase in CD8+ T cell infiltration



No or low tumor detected in these 4 biopsies from patients with PR

PD-L1 expression was low-negative in all samples

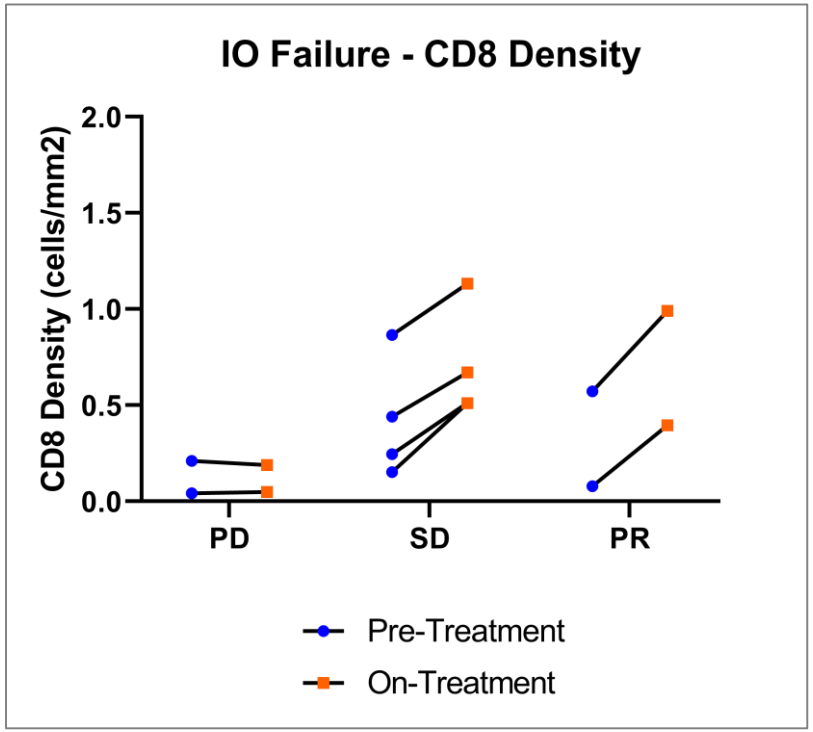
Tumor (Cytokeratin+) CD8+ T cells

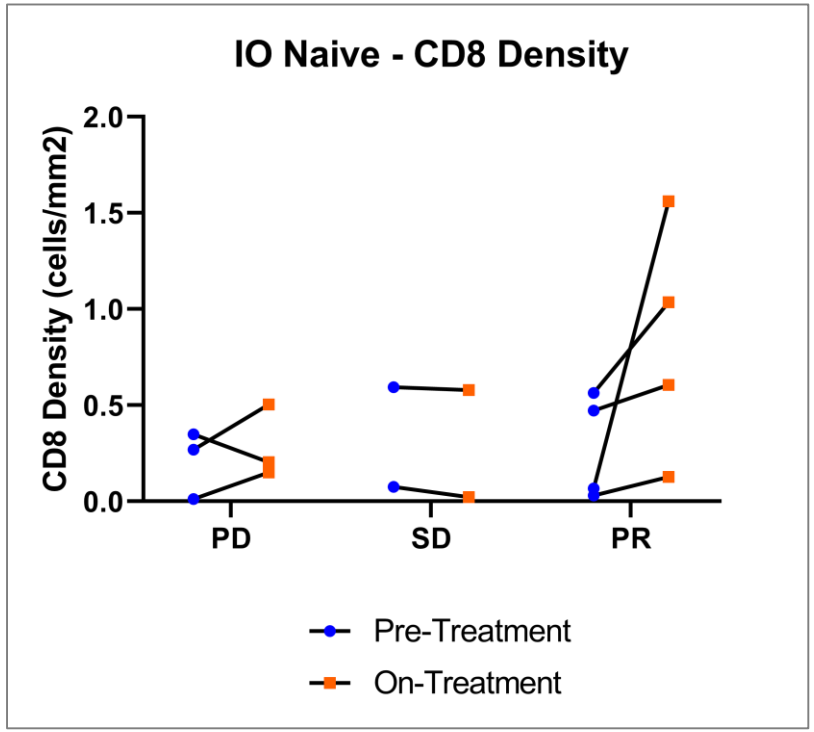
CD8 Density generally increased following treatment

CLASSICAL-Lung

- CD8 density in tumor generally increased following treatment with pepinemab + avelumab
- Higher CD8 density appears to correspond with beneficial clinical response

- Overall trends were similar in both IO naïve and IO failure cohorts
- → Additional analyses of myeloid and suppressor cell subsets are ongoing





- Matched pre and on-treatment from the same lesion
- On-treatment biopsies collected after ~ 5 weeks of treatment
- Core or needle biopsies
- Quantification of tumor bed across the entire biopsy section, excluding necrotic regions. Tumor bed was verified by pathologist review
- *For additional data on IO-naïve cohort, see poster B0309*

Pepinemab rapidly promotes T cell infiltration into tumor bed

MSS Colorectal cancer metastasis to liver – neoadjuvant/"window of opportunity" study

Winship Cancer Institute, Emory University

No treatment

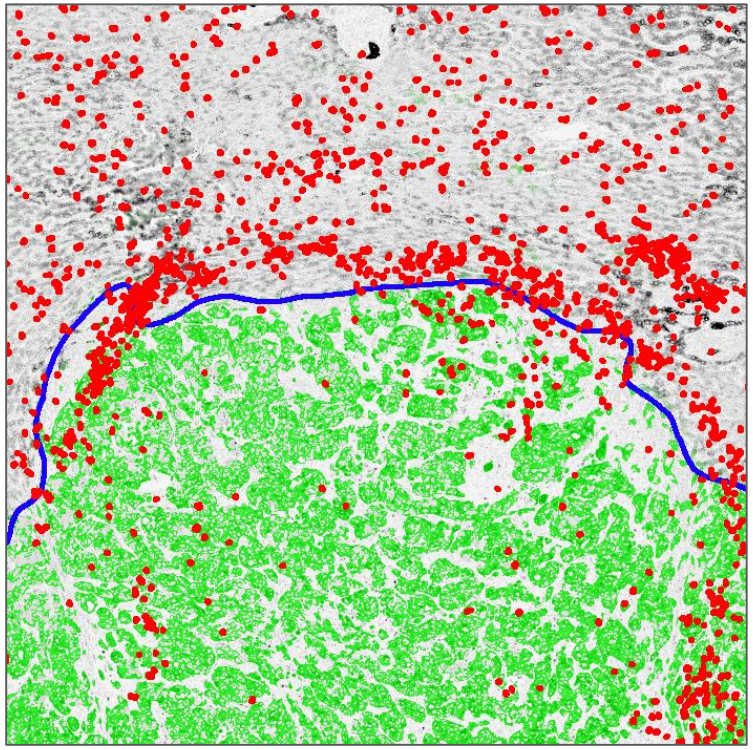
T cells are trapped at margin and are largely excluded from tumor bed

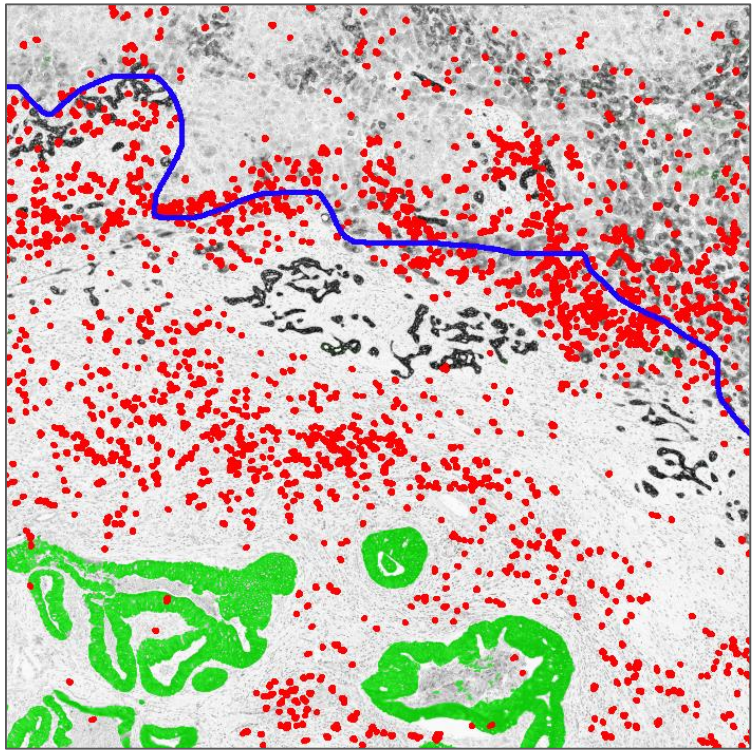
Pepinemab

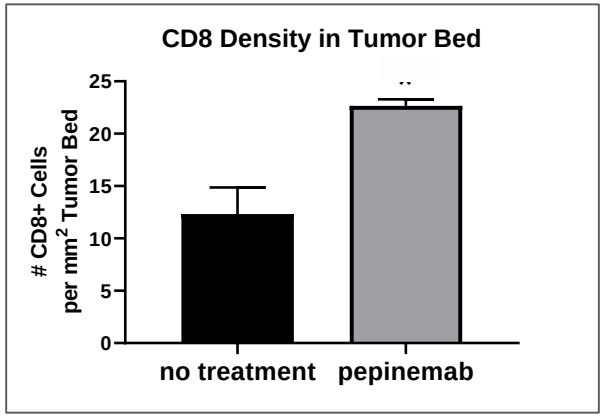
T cells penetrate into the tumor bed. Tumor content is reduced and appears to be replaced by stroma.

Normal liver

Tumor Bed







CD8 density was determined from entire tumor bed (n= 2 sections/patient).

CD8+ T cells
Margin of tumor bed
Tumor nodules

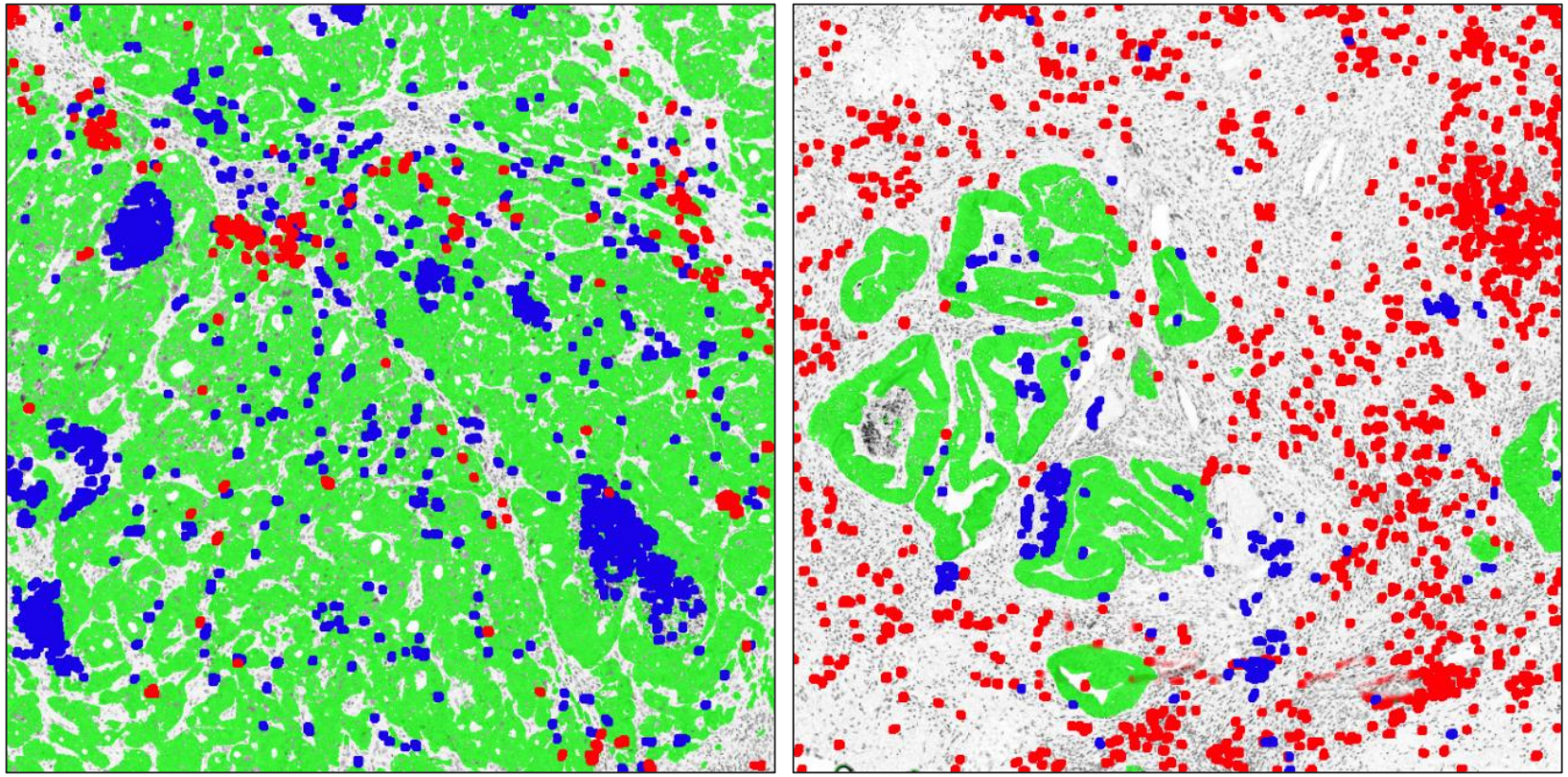
Patients received neoadjuvant chemo therapy before immunotherapy and surgery

Low MDSC and high CD8+ T cells following treatment with pepinemab

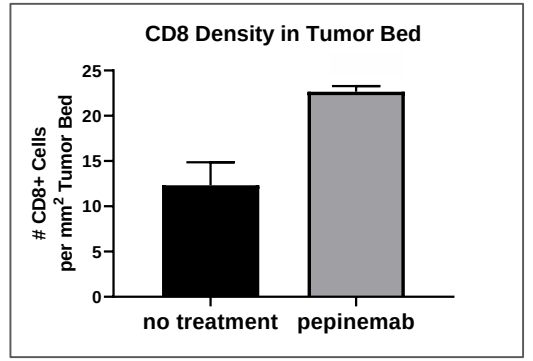
MSS Colorectal cancer metastasis to liver – neoadjuvant/"window of opportunity" study

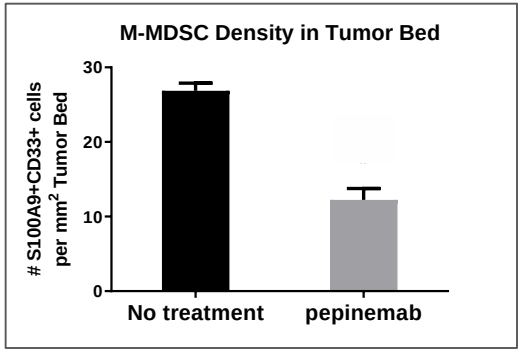
Winship Cancer Institute, Emory University

No treatment **Pepinemab**



Patients received neoadjuvant chemo therapy before immunotherapy and surgery





Density was determined from entire tumor bed (n= 2 sections/patient).

M-MDSC (S100A9+CD33+)
CD8+ T cells
Tumors (Cytokeratin+)

Summary

- Anti-SEMA4D shifts the immune balance in the TME to overcome immune exclusion and myeloid suppression
  - Increased T cell penetration and T cell activity
  - Reduced myeloid cells and reduced immune suppression
- The combination of pepinemab + avelumab is well tolerated in CLASSICAL-Lung trial.
- Further study is ongoing to determine the full extent and duration of treatment benefit.
  - Among evaluable IO naïve subjects (n=20) enrolled in either dose escalation or dose expansion, 5 immunotherapy naïve patients experienced a PR, 3 patients have durable responses over 1 year, and the Disease Control Rate (PR+SD) was 81%.
    - Quality of enrollment in this cohort suffered from 30% non-evaluable and only 7% (2/28) showed high PD-L1 expression.
  - 59% of evaluable patients (7/29) whose tumors had progressed during or following treatment with an anti-PD-x antibodies benefited from switching to the combination of pepinemab + avelumab, which appeared to induce a halt or reverse of tumor progression (SD or PR).
- Exploratory:
  - Increased CD8+ T cell density was observed in most tumors following treatment with pepinemab + avelumab. CD8+ T cell levels in tumor appear to correspond with response.
  - Tumor was absent or greatly reduced in 11/12 biopsies from subjects analyzed with PR or SD. Interestingly, no tumor was detected in biopsies analyzed from 3/6 subjects with PR and 3/7 subjects with SD. PD-L1 expression was negative in two of these three SD subjects, and all samples among IO naïve subjects were low or negative for PD-L1.
  - Additional studies are planned to interrogate the tumor microenvironment and peripheral immune compartment for lymphocyte and suppressor cell subset analysis.

See poster B039

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- Ernest Smith, CSO
- John Leonard, SVP
- Raymond Watkins, COO
- Scott Royer, CFO

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Ellen Giampoli & Jerome JeanGilles

Patients and their families

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