

Mupadolimab SITC Data and Company Update

Conference Call and Webcast, November 12, 2021



Forward-Looking Statements / Safe Harbor



This presentation and the accompanying oral presentation contain “forward-looking” statements, including statements related to the potential safety and efficacy of mupadolimab, CPI-818, ciforadenant such as whether mupadolimab is well positioned to improve patient outcomes based on its mechanism of inhibiting immunosuppressive adenosine in the tumor microenvironment and by enhancing immune responses to the tumor; the Company’s ability and Angel Pharmaceutical’s ability to develop and advance product candidates into and successfully complete preclinical studies and clinical trials, including the Company’s Phase 1b/2 clinical trial of mupadolimab, Angel’s plans to initiate Phase 2 clinical trial of CPI-818, the timing of the availability and announcement of clinical data and certain other product development milestones, and the sufficiency of the Company’s cash resources. All statements other than statements of historical fact contained in this press release are forward-looking statements. These statements often include words such as “believe,” “expect,” “anticipate,” “intend,” “plan,” “estimate,” “seek,” “will,” “may” or similar expressions. Forward-looking statements are subject to a number of risks and uncertainties, many of which involve factors or circumstances that are beyond the Company’s control. The Company’s actual results could differ materially from those stated or implied in forward-looking statements due to a number of factors, including but not limited to, risks detailed in the Company’s Quarterly Report on Form 10-Q for the quarter ended September 30, 2021, filed with the Securities and Exchange Commission on November 1, 2021, as well as other documents that may be filed by the Company from time to time with the Securities and Exchange Commission. In particular, the following factors, among others, could cause results to differ materially from those expressed or implied by such forward-looking statements: the Company’s ability to demonstrate sufficient evidence of efficacy and safety in its clinical trials of mupadolimab, CPI-818 and ciforadenant; the accuracy of the Company’s estimates relating to its ability to initiate and/or complete preclinical studies and clinical trials; the results of preclinical studies may not be predictive of future results; the unpredictability of the regulatory process, regulatory developments in the United States and other foreign countries; the costs of clinical trials may exceed expectations; and the Company’s ability to raise additional capital. Although the Company believes that the expectations reflected in the forward-looking statements are reasonable, it cannot guarantee that the events and circumstances reflected in the forward-looking statements will be achieved or occur, and the timing of events and circumstances and actual results could differ materially from those projected in the forward-looking statements. Accordingly, you should not place undue reliance on these forward-looking statements. All such statements speak only as of the date made, and the Company undertakes no obligation to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise.

This presentation concerns products that are under clinical investigation and which have not yet been approved for marketing by the U.S. Food and Drug Administration. Such products are currently limited by Federal law to investigational use, and no representation is made as to its safety or effectiveness for the purposes for which it is being investigated.

Agenda

- Review of mupadolimab properties
 - B cell activation
 - Enzyme inhibition
 - Comparison to other antibodies
- SITC poster presentation: Phase 1 clinical data in NSCLC and HNSCC
- Plans for randomized Phase 2/3
- Company update
- Q&A

B cells - Important Predictors of IO Response and Prognosis

Article

B cells and tertiary lymphoid structures promote immunotherapy response

Article

Tertiary lymphoid structures improve immunotherapy and survival in melanoma



ARTICLE

<https://doi.org/10.1038/s41467-021-23355-4> OPEN


B cell signatures and tertiary lymphoid structures contribute to outcome in head and neck squamous cell carcinoma

Ayana T
Sheryl R.
Zengbiak
Robert L.
Tullia C.

Article

Defining HPV-specific B cell responses in patients with head and neck cancer

<https://doi.org/10.1038/s41586-020-2931-3>
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 Check for updates

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Tumours often contain B cells and plasma cells but the antigen specificity of these intratumoral B cells is not well understood^{1–4}. Here we show that human papillomavirus (HPV)-specific B cell responses are detectable in samples from patients with HPV-positive head and neck cancers, with active production of HPV-specific IgG antibodies in situ. HPV-specific antibody secreting cells (ASCs) were present in the tumour microenvironment, with minimal bystander recruitment of influenza-specific cells, suggesting a localized and antigen-specific ASC response. HPV-specific ASC responses correlated with titres of plasma IgG and were directed against the HPV proteins E2, E6 and E7, with the most dominant response against E2. Using intratumoral B cells and plasma cells, we generated several HPV-specific human monoclonal antibodies, which exhibited a high degree of somatic hypermutation, consistent with chronic antigen exposure. Single-cell RNA sequencing analyses detected activated B cells, germinal centre B cells and ASCs within the tumour microenvironment. Compared with the tumour parenchyma, B cells and ASCs were preferentially localized in the tumour stroma, with well-formed clusters of activated

Current in
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Article

B cells are associated with survival and immunotherapy response in sarcoma

ORIGINAL ARTICLE

Presence of B Cells in Tertiary Lymphoid Structures Is Associated with a Protective Immunity in Patients with Lung Cancer

Claire Germain^{1,2,3}, Sacha Grjatic^{4,5}, Fella Tamzali^{1,2,3}, Samantha Knockaert^{1,2,3}, Romain Remark^{1,2,3}, Jérôme Goc^{1,2,3}, Alice Lapelle^{1,2,3}, Etienne Becht^{1,2,3}, Sandrine Katschian^{6,7}, Geoffrey Bizouard⁸, Pierre Validire^{1,8}, Diane Damotte^{1,2,3,9}, Marco Alfano¹⁰, Pierre Magdeleinat^{10,11}, Isabelle Cremer^{1,2,3}, Jean-Luc Teillaud^{1,2,3}, Wolf-Herman Fridman^{1,2,3,12}, Catherine Sautès-Fridman^{1,2,3}, and Marie-Caroline Dieu-Nosjean^{1,2,3}

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 frontiers
in Immunology

ORIGINAL RESEARCH
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Tertiary Lymphoid Structure-B Cells Narrow Regulatory T Cells Impact in Lung Cancer Patients

Claire Germain^{1,2,3,4,5,6}, Priyanka Devi-Marulkar^{3,4,5}, Samantha Knockaert^{3,4,5,6}, Jérôme Biton^{3,4,5,6}, Hélène Kaplan^{3,4,5,6}, Laila Letalef^{1,2,3,4,5}, Jérôme Goc^{3,4,5,6}, Agathe Seguin-Givélet^{2,6,7}, Dominique Gossot^{2,6}, Nicolas Girard⁸, Pierre Validire^{4,9}, Marine Lefèvre^{2,6,8}, Diane Damotte^{3,4,5,10}, Marco Alfano^{3,4,5,11}, François M. Lemoine^{1,2}, Keith E. Steele¹², Jean-Luc Teillaud^{1,2,3,4,5}, Scott A. Hammond¹³ and Marie-Caroline Dieu-Nosjean^{1,2,3,4,5,6}

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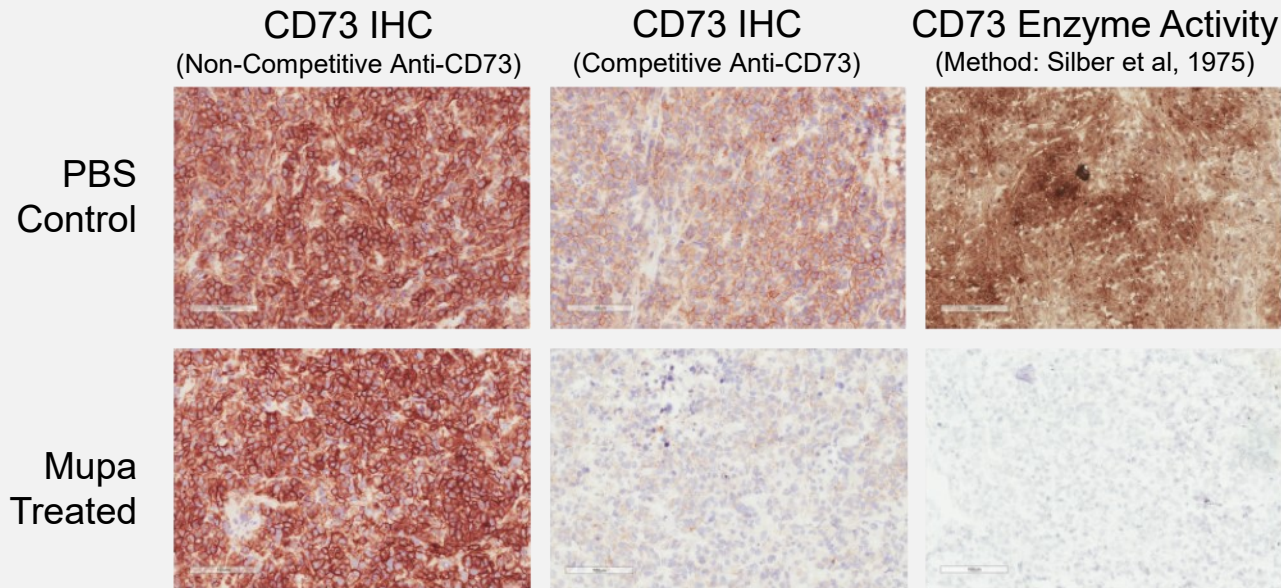
The presence of tertiary lymphoid structures (TLS) in the tumor microenvironment is associated with better clinical outcome in many cancers. In non-small cell lung cancer (NSCLC), we have previously showed that a high density of B cells within TLS (TLS-B cells) is positively correlated with tumor antigen-specific antibody responses and increased intratumor CD4⁺ T cell clonality. Here, we investigated the relationship

- B cells are found in tumors of responders^{1,2,3}
- The B lineage signature in tumors was the dominant parameter for overall survival²
- Activated B cells and antibody secreting cells specific for tumor-specific antigens found in the tumor microenvironment in HPV⁺ head and neck patient samples^{4,5}
- High density B cells within tertiary lymphoid structure promote CD4⁺ T cell response and are associated with superior clinical outcomes in NSCLC patients^{6,7}

1. Helmink et al, Nature, 2020; 2. Petitprez et al, Nature 2020; 3. Cabrita et al, Nature 2020; 4. Weiland et al, Nature 2020; 5. Ruffin et al, Nat. Commun. 2021; 6. Germain et al, Am. J. Respir. Crit. Care. Med. 2014; 7. Germain et al, Front Immunol. 2021

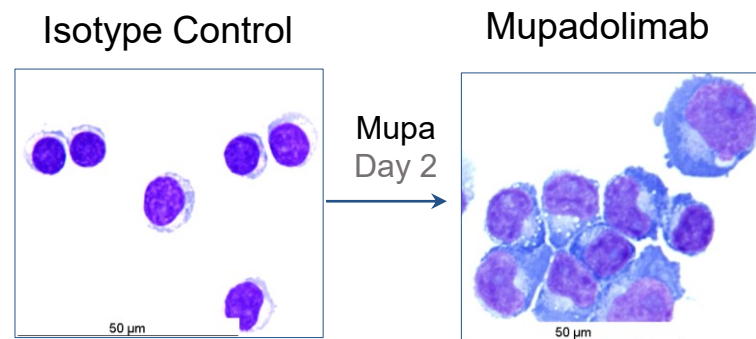
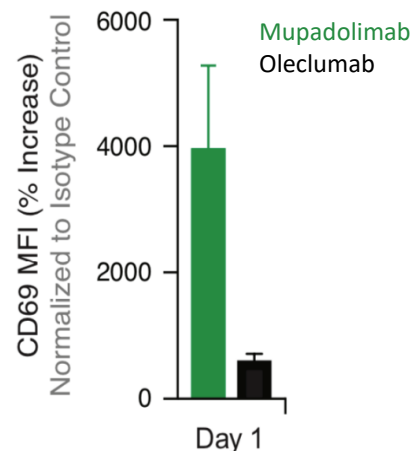
Mupadolimab is an Anti-CD73 Antibody with Dual Functions

B cell activation and adenosine blockade



CD73 Enzymatic Activity Blockade

- Mupadolimab binds to tumor cells and blocks the production of adenosine as demonstrated by immunohistochemistry (IHC)
- Mupadolimab treatment does not cause loss of CD73 by internalization



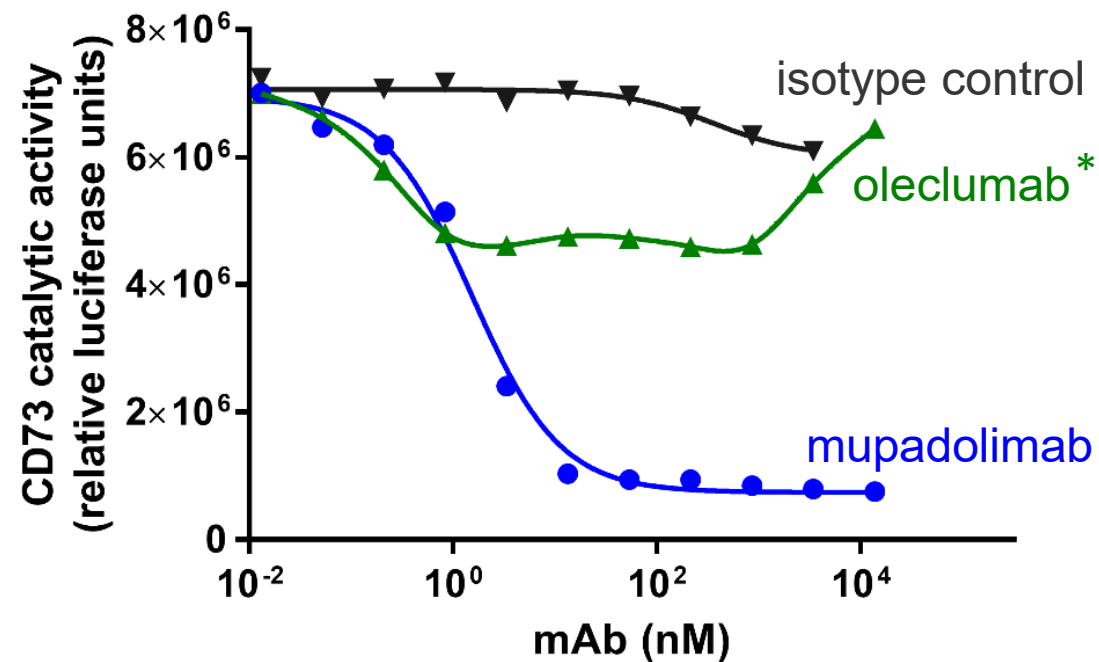
B Cell Activation & Differentiation

- Mupadolimab demonstrates a potent B cell stimulation compared to oleclumab, an adenosine blocking anti-CD73 antibody
- Mupadolimab activates B cells, resulting in morphological and surface marker changes consistent with B cell differentiation

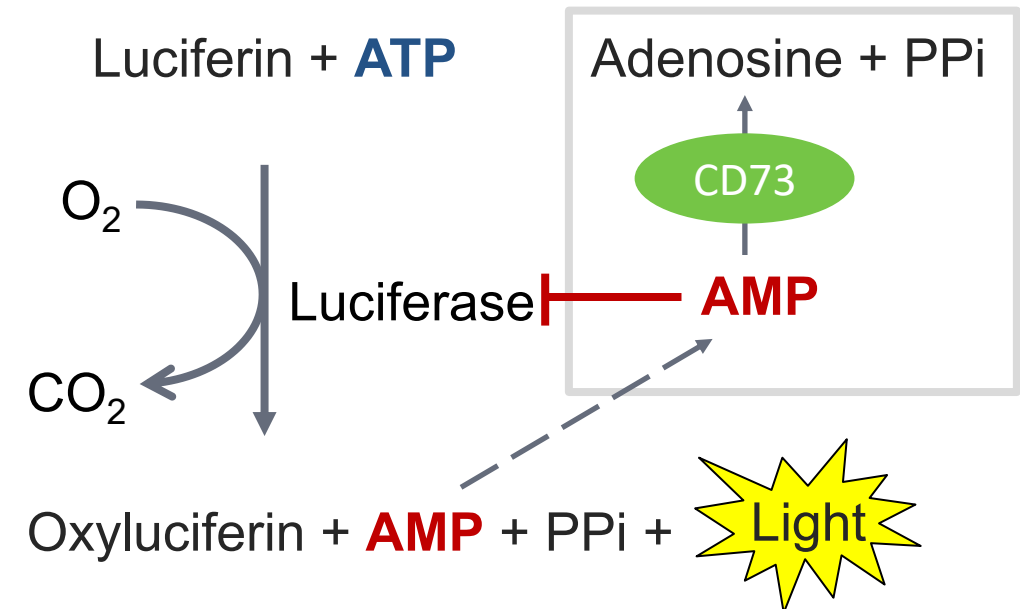
Mupadolimab Fully Inhibits CD73 Enzymatic Activities

No hook effect observed

CD73 Catalytic Activity
Tumor Cell line MDA-MB-231



Measure CD73 activity as decreased inhibition
Of luciferase enzymatic reaction









- Hook effects are observed due to the stoichiometry of antigen-antibody complexes

Corvus is a Leader with a Differentiated Antibody

Anti-CD73 competitive landscape



Company	Program	Adenosine Blockade	B Cell Activation	Status
	Mupadolimab	Full	Strong*	Phase 2/3 ready
	Oleclumab	Partial	Weak	Phase 2
	Uliledlimab	Full	Moderate	Phase 1
	BMS-986179	Partial	Not reported	Phase 1
	NZV930	Partial	Not reported	Phase 1
	INCA00186	Partial	Not reported	Preclinical

* Also shown to activate T cells and antigen presenting cells

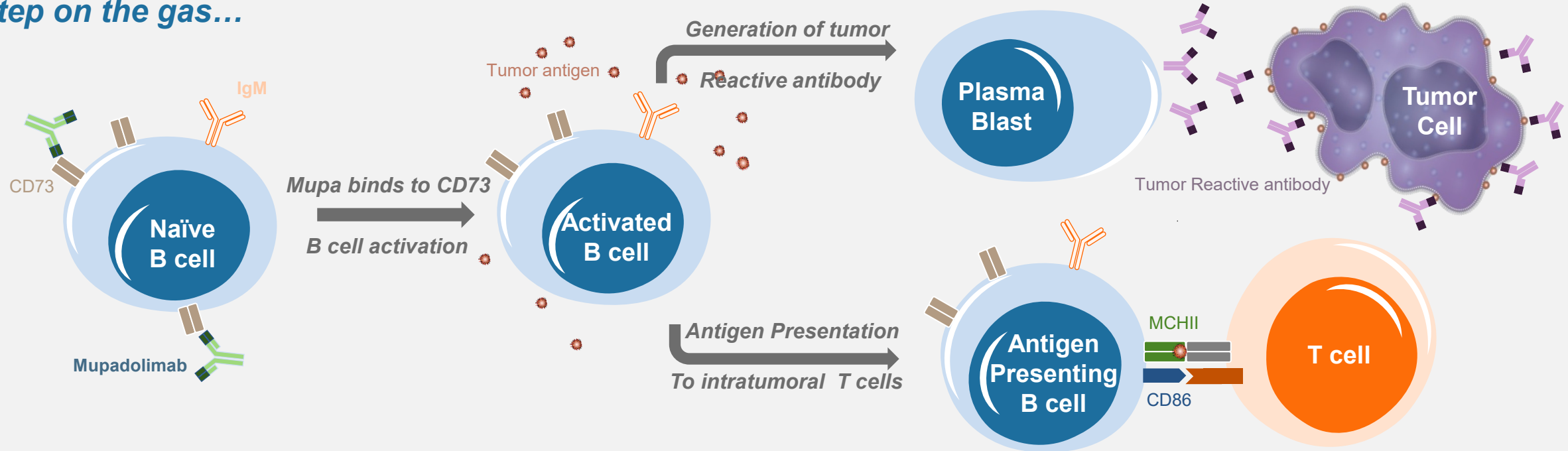
Comparison of Mupadolimab to Oleclumab

Property	Mupadolimab	Oleclumab
Isotype	IgG1 (No FcR binding)	IgG1 (No FcR binding)
Affinity	Picomolar	Picomolar
Epitope	Carboxyl Terminal	Amino Terminal
Enzyme Inhibitor	Competitive	Allosteric
Hook Effect	None, complete inhibition	Hook effect, incomplete inhibition
Internalization	No	Yes
B Cell Activation	Strong	Weak

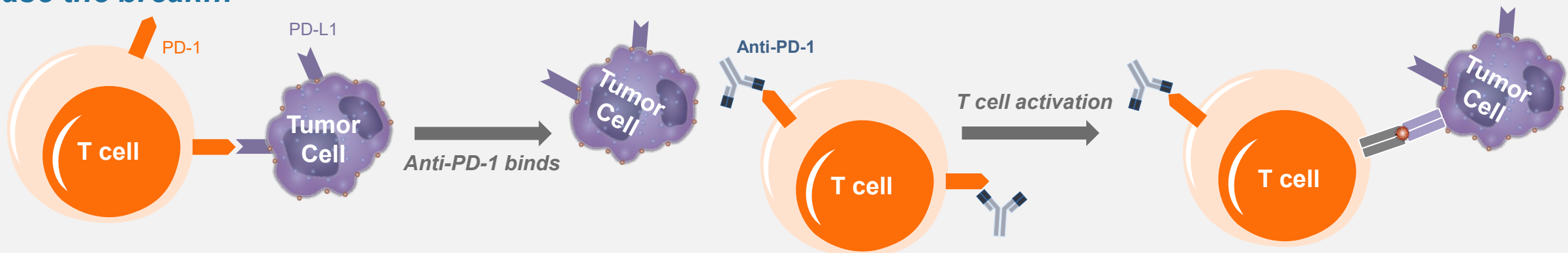
Targeting B Cells and T Cells: Mupa, anti-PD(L)1 Combo

Step on the gas and release the brake...

Step on the gas...



Release the brake...



Phase 1/1B Protocol Design Summary

Expansion cohorts of NSCLC and HNSCC is ongoing



- Phase 1/1b clinical trial (NTC03454451), mupadolimab alone and in combination with ciforadenant (A2A receptor antagonist) and/or pembrolizumab in patients with advanced refractory cancer
- A dose of ≥ 12 mg/kg intravenous every 3 weeks is well tolerated and leads to complete CD73 target occupancy
- Treatment induced rapid changes in blood B and T cells
- Additional NSCLC and HNSCC patients are being evaluated in ongoing expansion cohort

NSCLC and HNSCC Patient Characteristics and AE Summary

Doses of ≥ 12 mg/kg are well tolerated

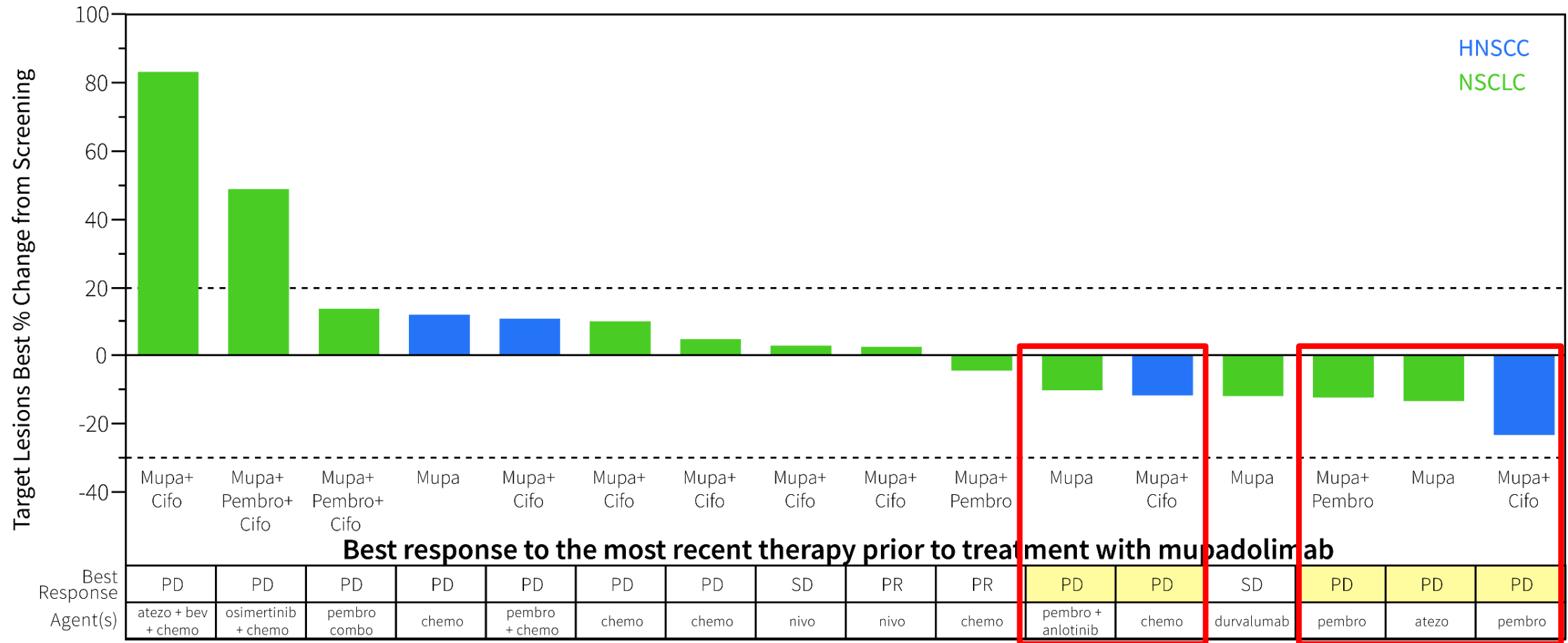


	Subjects (N)	Age (yrs) Median (range)	Gender, male N (%)	No. of Prior Therapy Median (range)	Prior PD-(L)1 Therapy N (%)
HNSCC	10	65 (43, 87)	9 (90)	3 (1,5)	10 (100)
NSCLC	15	64 (53, 80)	6 (40)	3 (2,4)	14 (93)

- Treatment related adverse events (AEs) were reported in 17 (68%) of the NSCLC and HNSCC patients
- Severe AEs (grade 3 or above) were reported in 4 (16%) patients
- Treatment related serious AEs were reported in 2 (8%) patients
- No changes in serum quantitative immunoglobulin were observed

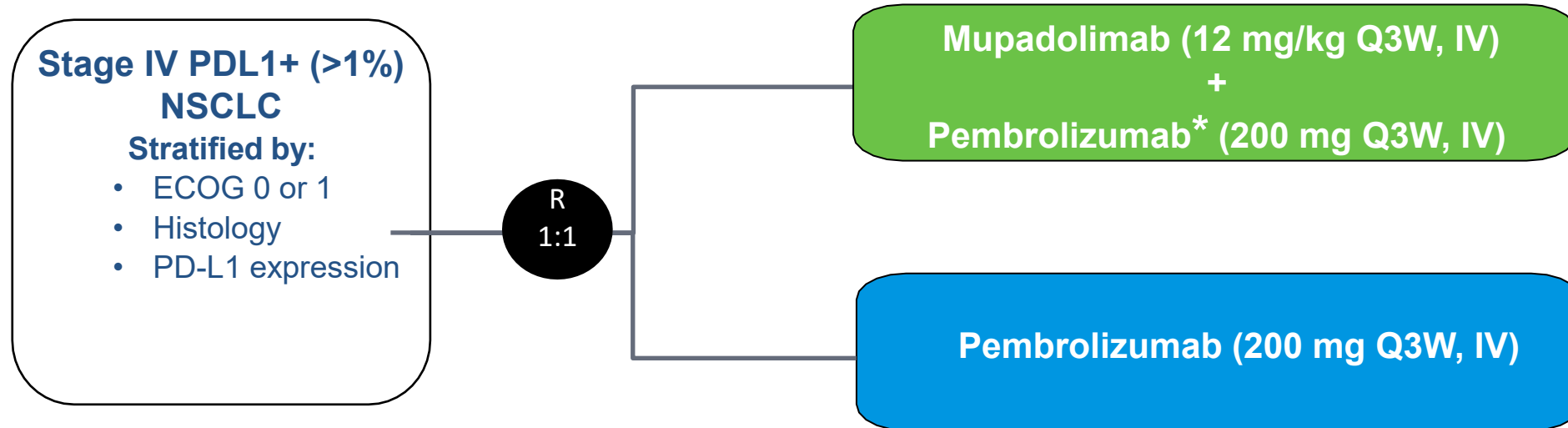
Anti-tumor Activity in HNSCC and NSCLC Pts with ≥ 12 mg/kg

Tumor regression in pts with PD as best response to prior therapy



- Cifo = ciferadenent (A2AR antagonist), pembro = pembrolizumab (anti-PD-1), atezo = atezolizumab (anti-PD-L1), bev = bevacizumab (anti-VEGF), chemo = chemotherapy, nivo = nivolumab (anti-PD-1)
- PD = progressive disease; SD = stable disease; PR = partial response

Proposed Randomized Ph 2/3 study of Mupadolimab in NSCLC



Primary Endpoint	<ul style="list-style-type: none">• Progression free survival (PFS)
Secondary Endpoints	<ul style="list-style-type: none">• Objective response rate (ORR) by RECIST 1.1• Duration of Objective Response (DOR)• Overall survival (OS)• Safety and tolerability

*Other anti-PD1s under consideration

Mupadolimab Unique Opportunity

1

Novel immunotherapy approach based on B cell activation and adenosine blockade

2

SITC data suggests mupadolimab may overcome resistance to anti-PD(L)1 therapies

3

Positioning for Phase 2/3 (combination with anti-PD(L)-1) in NSCLC in 2022

Significant Near-Term Opportunities

Mupadolimab HNSCC and NSCLC

1

- Differentiated anti-CD73 mAb
- Potential broad applications in cancer and infectious disease

CPI-818 for T-cell Lymphomas

2

- Angel Pharmaceuticals initiating Phase 2 study in China
- Potential to address significant T cell lymphoma population in China

Ciforadenant for frontline RCC

3

- Safety, biomarker and significant clinical experience
- Collaboration with Kidney Cancer Consortium