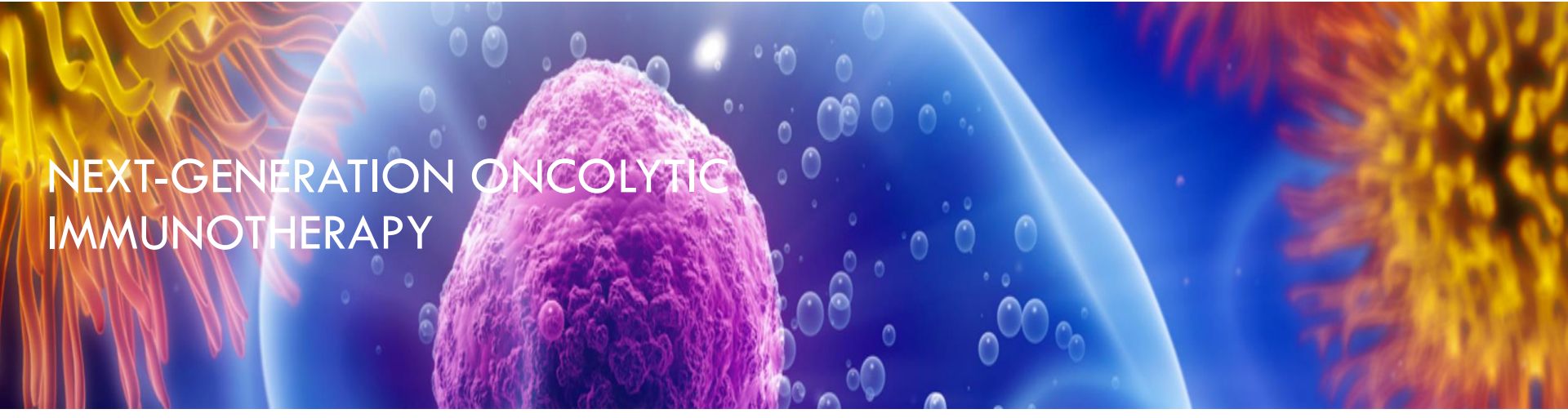
Replimune



August 2020

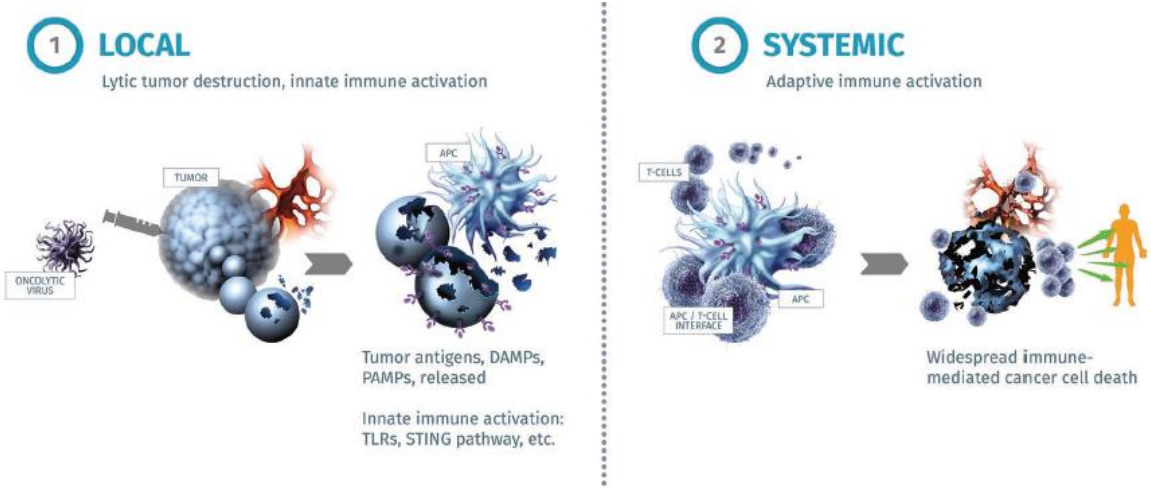
Safe harbor

Any statements contained herein that are not statements of historical facts may be deemed to be forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, including statements regarding the advancement of our clinical trials, patient enrollments in our existing and planned clinical trials and the timing thereof, the potential impact of COVID-19 on our milestones, the results of our clinical trials, the timing and release of our clinical data, our goals to develop and commercialize our product candidates, our expectations regarding the size of the patient populations for our product candidates if approved for commercial use and other statements identified by words such as "could," "expects," "intends," "may," "plans," "potential," "should," "will," "would," or similar expressions and the negatives of those terms. Forward-looking statements are not promises or guarantees of future performance, and are subject to a variety of risks and uncertainties, many of which are beyond our control, and which could cause actual results to differ materially from those contemplated in such forward-looking statements. These factors include risks related to our limited operating history, our ability to generate positive clinical trial results for our product candidates, the costs and timing of operating our in-house manufacturing facility, the timing and scope of regulatory approvals, changes in laws and regulations to which we are subject, competitive pressures, our ability to identify additional product candidates, political and global macro factors including the impact of the SARS-COV-2 coronavirus as a global pandemic and related public health issues, and other risks as may be detailed from time to time in our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, and other reports we file with the Securities and Exchange Commission. Our actual results could differ materially from the results described in or implied by such forward-looking statements. Forward-looking statements speak only as of the date hereof, and, except as required by law, we undertake no obligation to update or revise these forward-looking statements.

- Proprietary 'Immulytic' oncolytic immunotherapy platform
  - Intended to maximally activate the immune system against a patient's cancer
  - Intended to establish Replimune's products as the second cornerstone of immuno-oncology
- RP1 – in multiple clinical trials, with current focus on immune-responsive tumors
  - Lead indication – advanced cutaneous squamous cell carcinoma (CSCC) is a commercially attractive indication
    - Strong efficacy signal from single arm data in combination with Opdivo
    - 240 patient registration directed randomized trial in combination with Libtayo enrolling
    - Single agent study in organ transplant recipients contra-indicated for anti-PD1 enrolling
  - Anti-PD1 refractory melanoma
    - Strong efficacy signal with RP1 combined with Opdivo; 125 patient potential registration cohort enrolling
  - 30 patient lung cancer cohort expected to initiate by year end 2020
- RP2 & RP3 - intended to treat less immune-responsive tumors
  - Initial clinical safety & efficacy data with single agent RP2 & combined with Opdivo expected by end 2020
  - RP3 intended to enter the clinic by end 2020
- Well capitalized to deliver; $262m in cash as of 30 June 2020; runway to mid 2023

Oncolytic immunotherapy

- The use of viruses that selectively replicate in & kill tumors to treat cancer
  - ✓ Highly inflammatory
  - ✓ Activates both innate and adaptive immunity
  - ✓ Releases the full array of tumor antigens into an inflamed environment
  - ✓ Systemically activates the immune system against the tumor & neo-antigens released
  - ✓ Can be 'armed' with additional genes to increase efficacy
- Single agent T-Vec is FDA approved for the treatment of advanced melanoma



Replimune

Replimune's platform

1. A potent underlying virus strain

Replimune believes HSV to be the most potent, versatile & clinically validated virus species for oncolytic use

There is great diversity among clinical HSV strains

29 new clinical strains were tested & the most effective engineered for oncolytic use

2. Increased tumor killing & spread

Armed with GM-CSF & a potent fusogenic protein (GALV-GP R-)

Increases direct & immunogenic tumor killing*

Intended for immune responsive tumor types

3. Delivery of potent immune stimulatory proteins

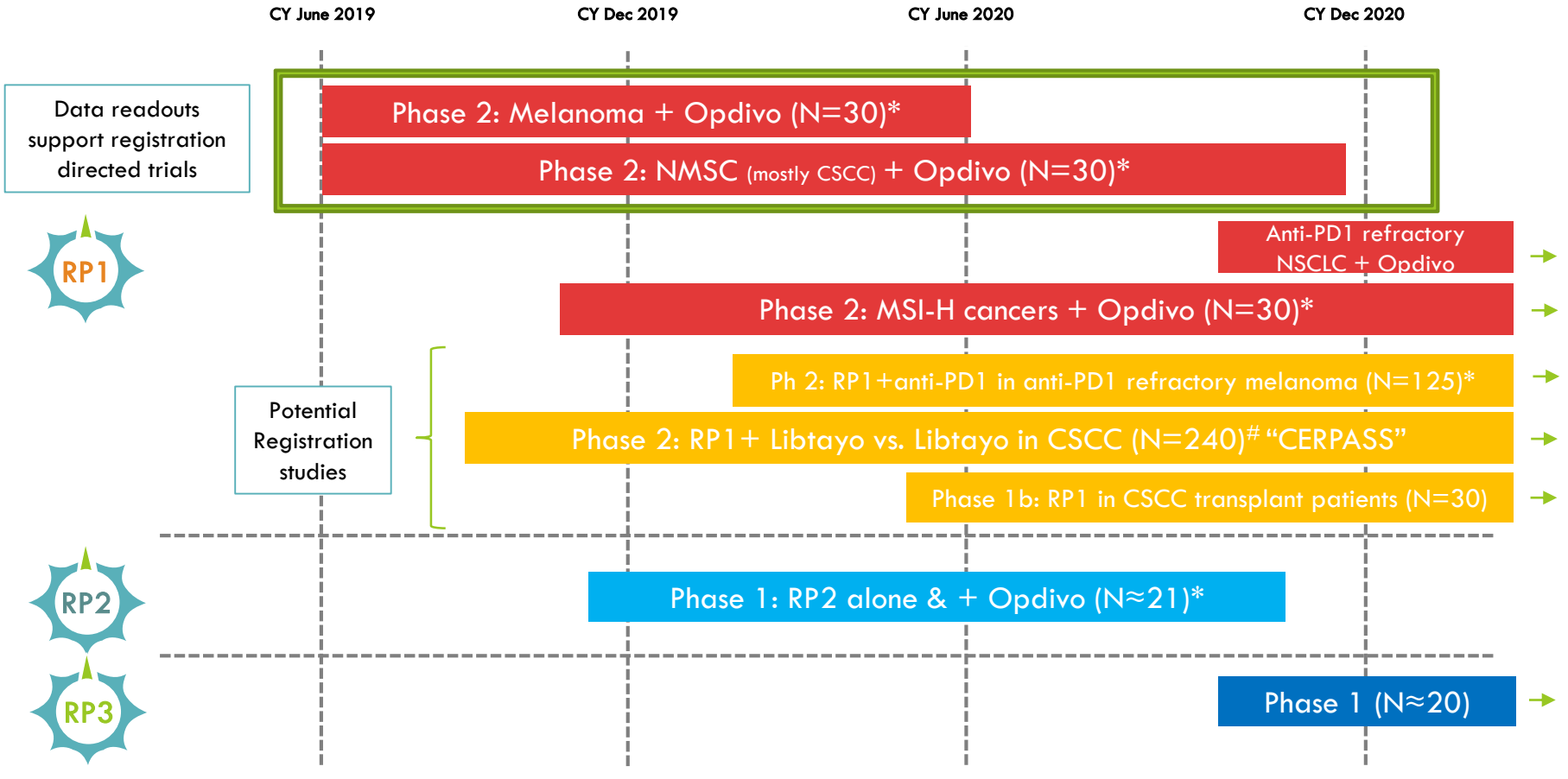
Focus on *clinically validated* pathways which function at the time & place of immune response initiation, but where systemic engagement is sub-optimal

- Anti-CTLA-4
- Immune-costimulatory pathway activators
- Aims to *increase efficacy* while *reducing toxicity*

Intended for less & non-immune responsive tumor types

* Replimune pre-clinical data published in Thomas et at JITC 2019

Replimune's development plan

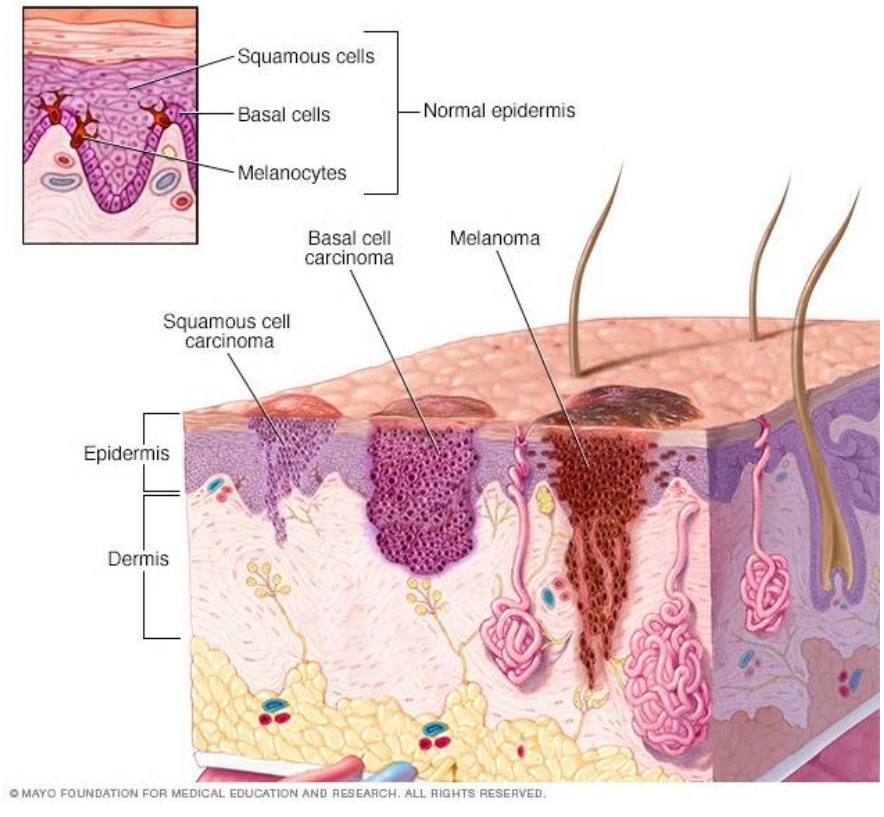


* Under clinical trial collaboration & supply agreement with BMS for the supply of Opdivo – full commercial rights retained by Replimune

Under clinical trial collaboration agreement with Regeneron; 50:50 sharing of clinical trial costs – full commercial rights retained by Replimune

Lead indication overview: CSCC

- The second most common skin cancer with ≈700,000 patients annually in the U.S.[1]
- Occurs when DNA damage from exposure to ultraviolet radiation or other agents triggers abnormal changes to squamous cells
- 10% have 'high risk' disease (recurs following initial surgery)
- Approximately 7,000-15,000 US deaths annually[1-3]
  - Most conservative addressable population
  - 80% of patients die from locoregional progression, not metastatic disease[4,5]
- Potential US market estimated at 7,000-28,000 patients annually[1-4]
- Approved anti-PD-1 therapies:
  - Libtayo (Regeneron) 2018
  - Keytruda (Merck) 2020



[1]Rogers et al JAMA Dermatol **10** 2015
[2]Clayman et al JCO **23** 2005
[3]Mansouri et al J Am Acad Dermatol **153** 2017
[4]Schmults et al JAMA Dermatol **149** 2013
[5]Motaparthi et al Adv Anat Pathol **24** 2017

Single agent anti-PD1 data in advanced CSCC

	Libtayo				Keytruda	Opdivo
Patient population	Locally advanced		metastatic		47 locally advanced + 58 metastatic	4 locally advanced, 16 locoregional, 4 metastatic
Number of patients	37 (per label, 2018)	33 (ASCO 2020)	75 (per label, 2018)	59 (ASCO 2020)	105 (ESMO 2019)	24 (ASCO 2020)
ORR	48.5%	45%	46.7%	51%	34.3%	54.5%
CR	0%	13%	5.3%	20%	3.8%	0%

Replimune

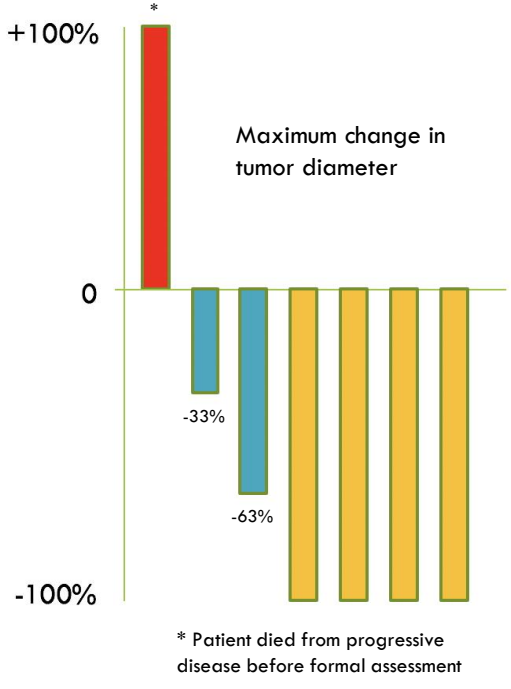
Lead indication: CSCC – the CERPASS study

- Registration-directed randomized controlled trial in collaboration with Regeneron
  - 240 patients
  - Randomized 2:1 (RP1+ Libtayo vs. Libtayo alone)
  - Primary endpoint ORR
  - Secondary endpoints include CR rate, duration of response, PFS, OS
- Aim to show 15% delta improvement in ORR
  - Control arm ORR expectation based on anti-PD1 single agent data 34-51%
  - Control arm CR expectation based on anti-PD1 single agent data <10% at data cut off
- Aim to also improve durability and show multi-fold (2-3x) improvement in CR rate

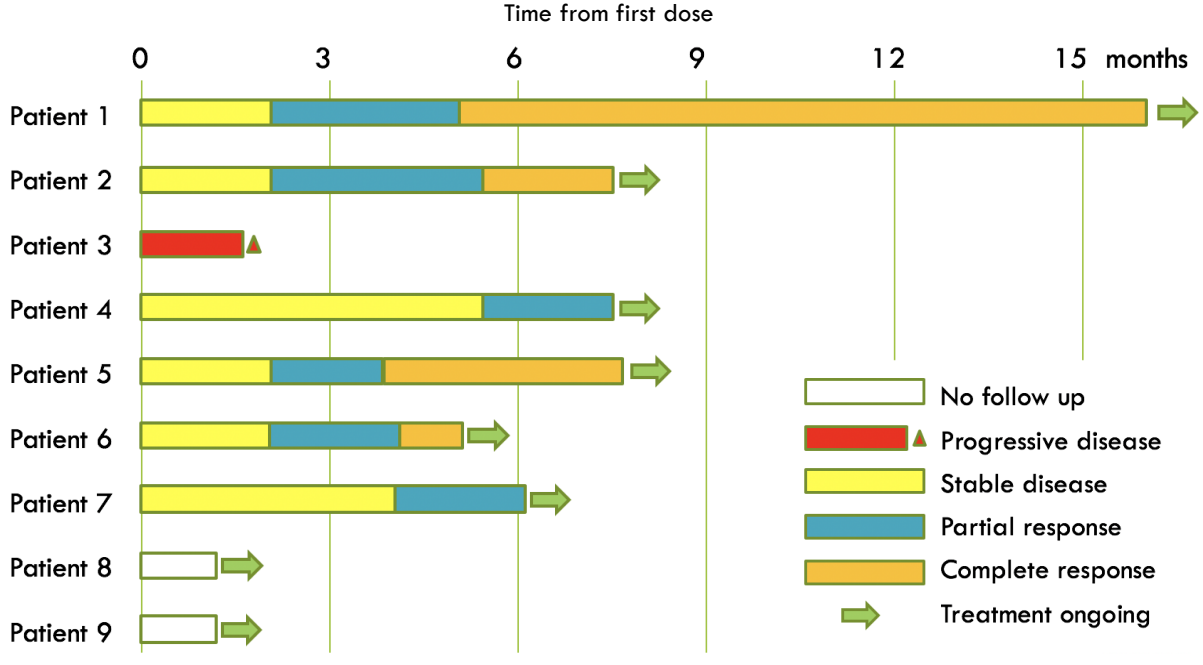
CSCC data

- As of May 2 (latest data cut off) six of seven patients with follow up treated with RP1+Opdivo were in response
  - All ongoing
- Four of seven patients with ongoing CRs
  - Unprecedented rate of complete response in patients with advanced disease
    - Including of uninjected distant tumors
  - Systemic activity demonstrated to be robust and durable
  - Clear differentiation from anti-PD1 monotherapy
  - Supportive biomarker data

Responses are deep & all are ongoing to date

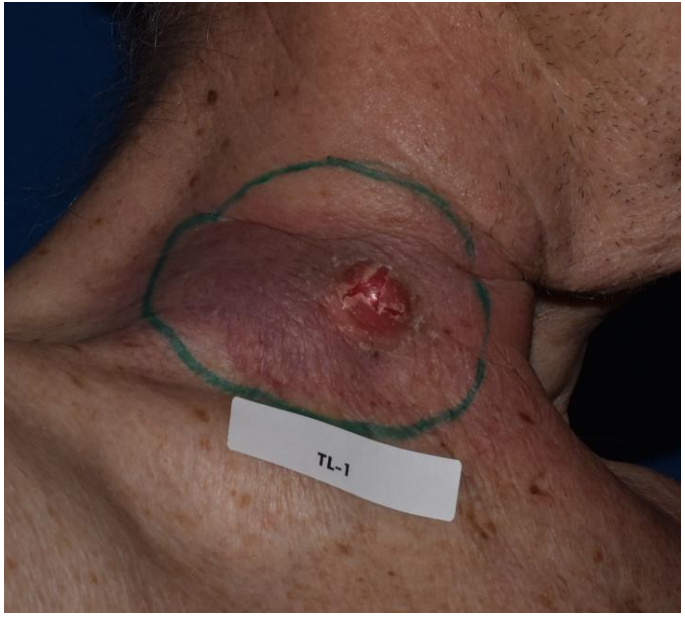


* Patient died from progressive disease before formal assessment

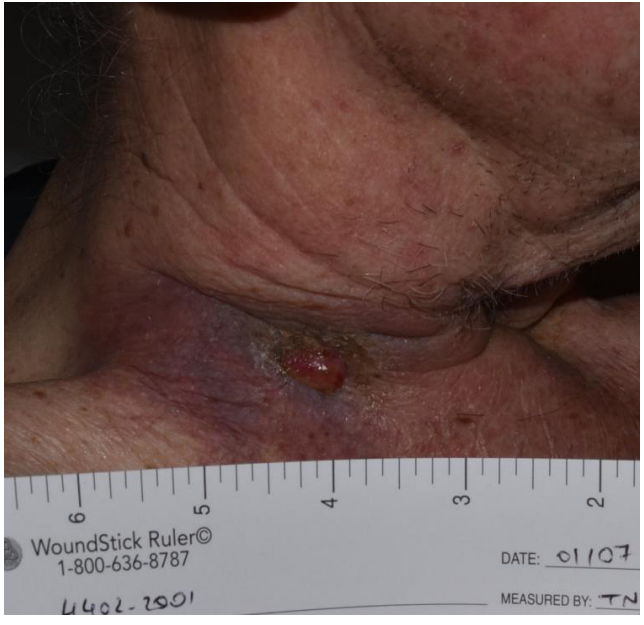


Patient 2 (4402-2001): Ongoing CR

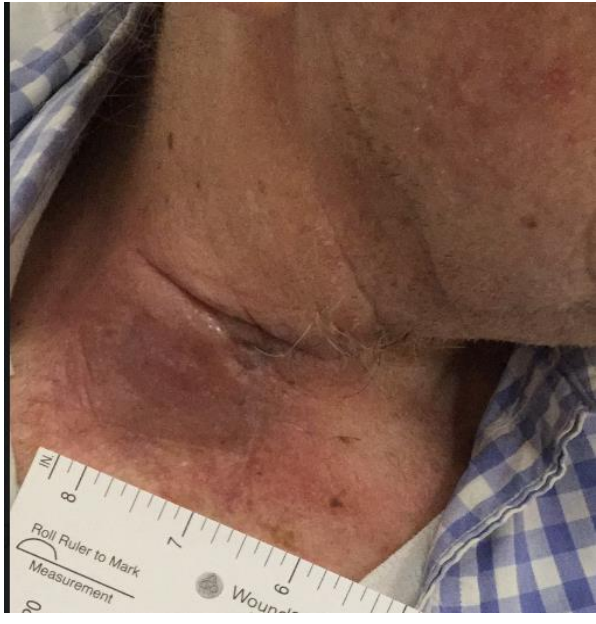
16th June 2019
(baseline)



1st July 2019
(post one dose of RP1, no Opdivo)



16th July 2019
(post 2 doses of RP1 & 1 dose of Opdivo)

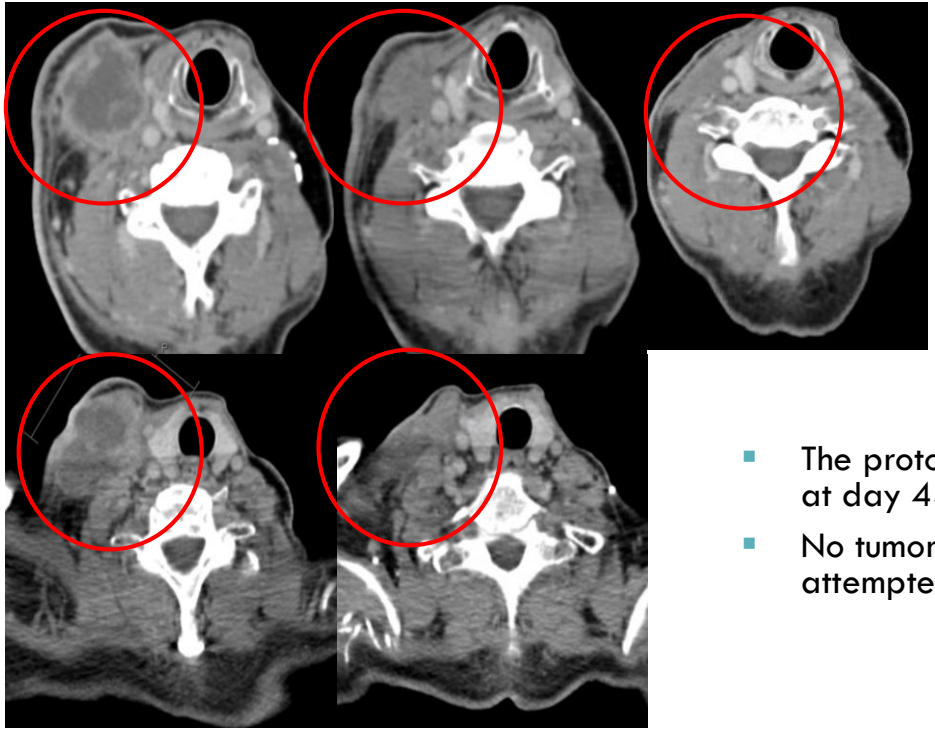


- Patient with recurrent CSCC of the neck (bilateral, right injected), retroperitoneal nodes & bone metastases (not injected)
- Previously treated with cisplatin-based chemoradiation & carboplatin/5-FU
- Both the large injected tumor & the smaller contralateral tumor in the neck reduced considerably before the first Opdivo dose, i.e. after the first dose of RP1, followed by resolution of all disease

Patient 2 (4402-2001): Ongoing CR

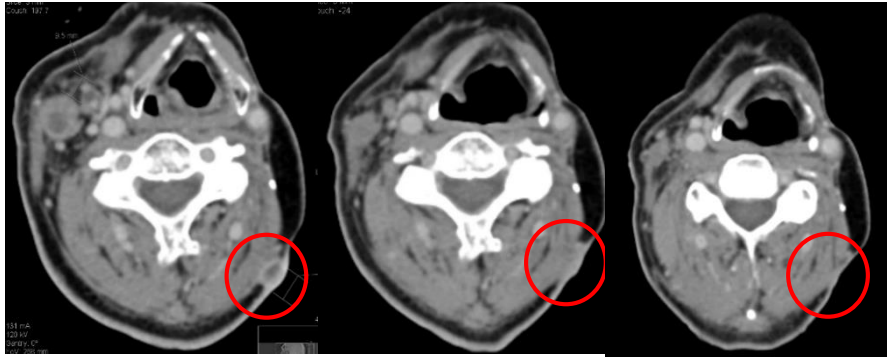
Right neck (injected)

Baseline 8 weeks 24 weeks



Left neck (not injected)

Baseline 8 weeks 16 weeks

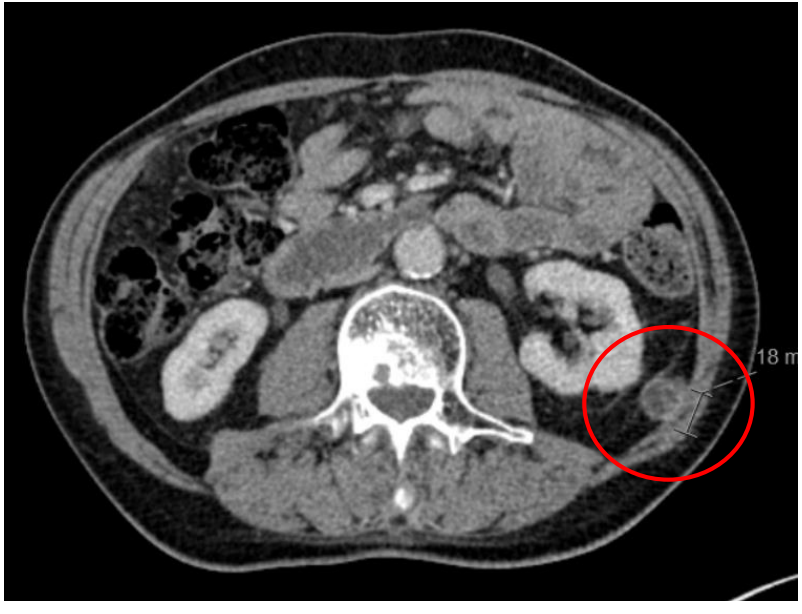


- The protocol mandated biopsy of the injected tumor taken at day 43 was tumor free
- No tumor was found to remain when a biopsy was attempted from the left neck

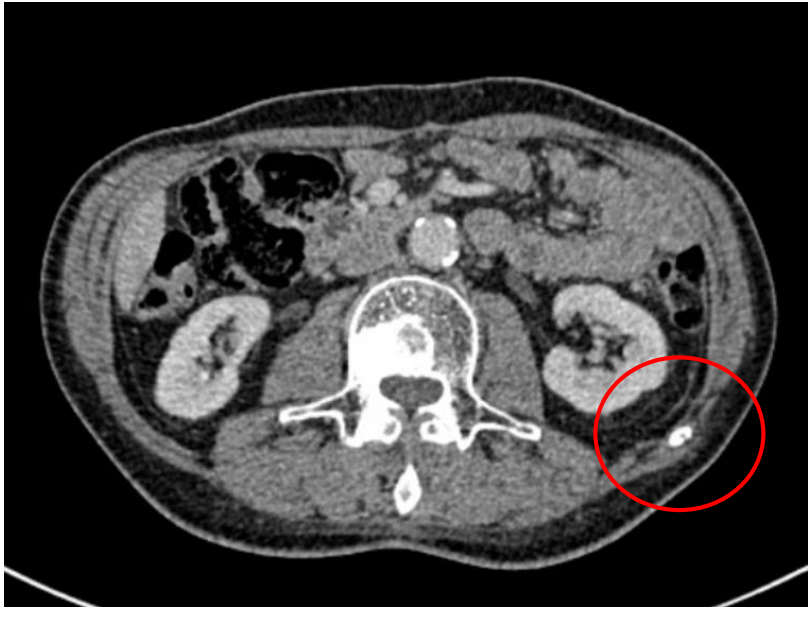
Replimune

Patient 2 (4402-2001): Ongoing CR

Baseline

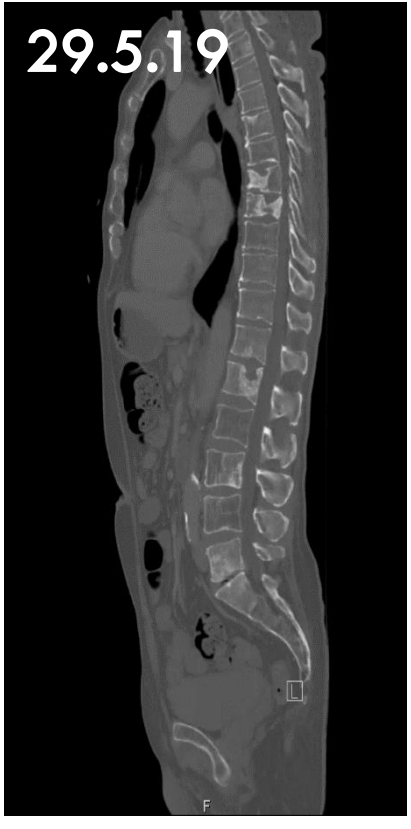


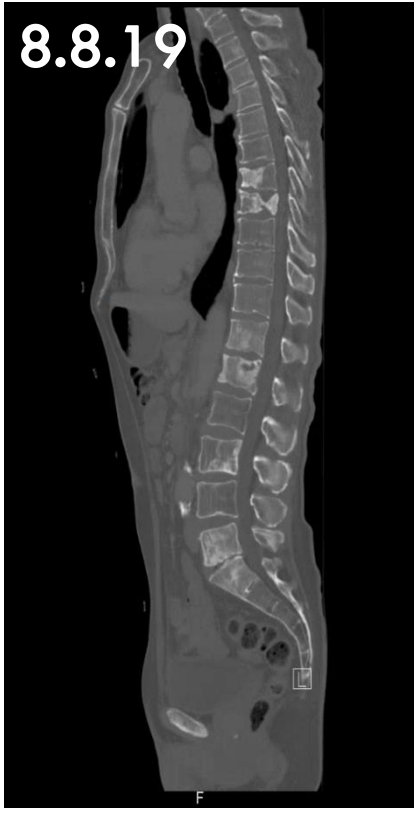
16 weeks

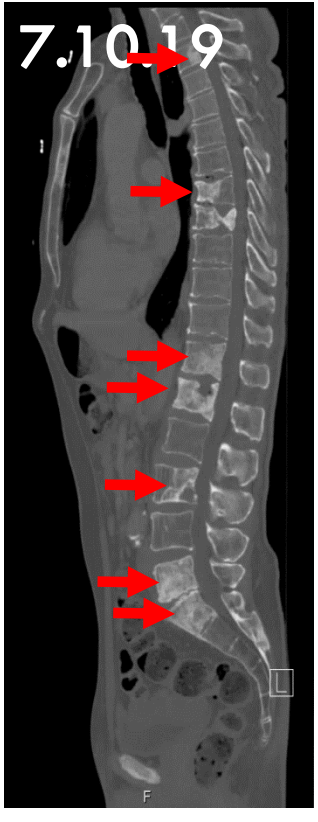


- The patient also had baseline retroperitoneal tumors which have completely resolved

Patient 2 (4402-2001): Ongoing CR







Complete sclerosis of all bone lesions with no areas of active disease. Declared radiological CR. Confirmed by PET scan (next slide)

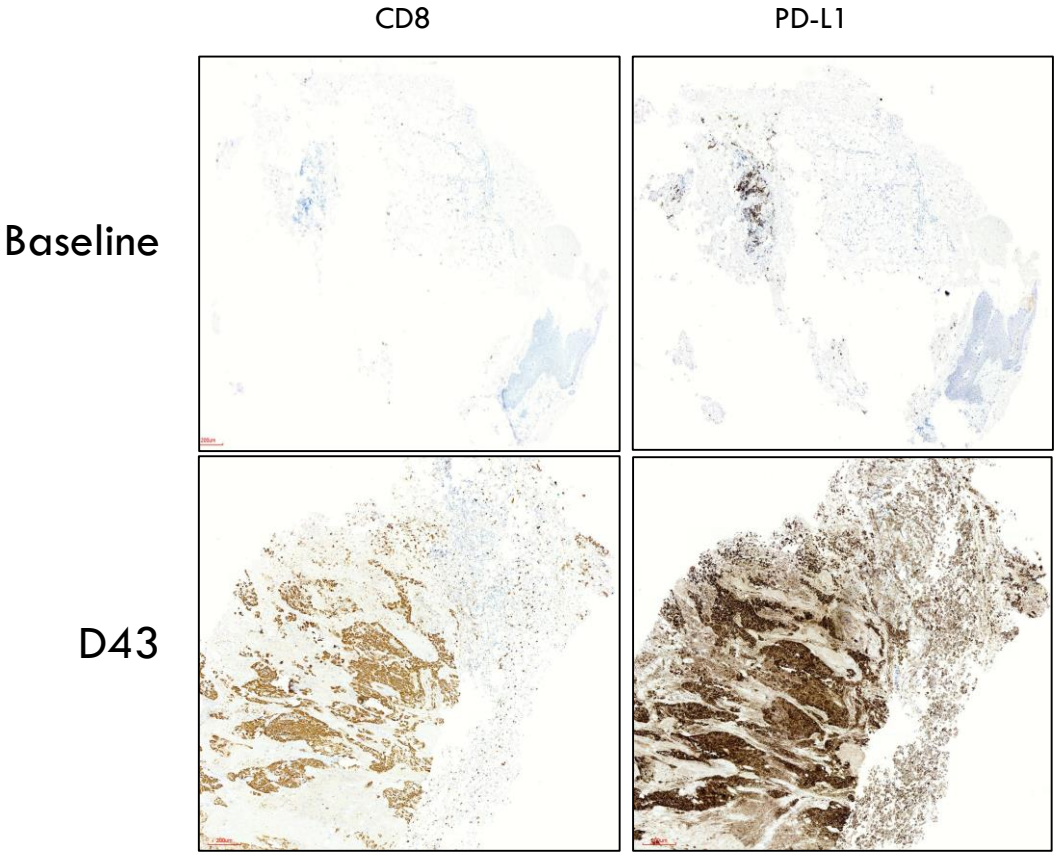
→ Indicates area of increased bony sclerosis, indicative of healing response of lytic metastases

Patient 2 (4402-2001): Ongoing CR

Bone metastases had substantially increased by CT between the prior PET scan (June 2018) and initiating the trial (June 2019), but no PET scan was performed at screening.

The PET scan to confirm CR of bone mets performed Feb 2020 showed no active disease

Patient 2 (4402-2001): CD8 T cell & PD-L1 staining



Replimune

Anti-PD1 refractory melanoma – market opportunity

- Approximately half of advanced melanoma patients still die of their disease, despite multiple approved therapies now being available
  - Anti-PD1, anti-CTLA-4, combined anti-CTLA-4/anti-PD1, BRAF targeted agents
- Approximately 7,230 US deaths annually from metastatic melanoma[1]
- Approximately 62,000 deaths annually world-wide

- High unmet medical need for patients with baseline resistance to checkpoint therapy
- 40-65% of all metastatic melanoma are primary refractory to initial anti-PD1 therapy[2]
- The expected response rate to retreatment with anti-PD1 therapy following progression on single agent anti-PD1 is 6-7%[3]
- The expected response rate to Yervoy having failed initial single agent anti-PD1 is 13%[4]

[1] https://seer.cancer.gov (2019 data)

[2] Gide et al Clin. Cancer Res **24** 2018

[3] Ribas et al Lancet Oncology **19** 2018; Hodi et al JCO **34** 2016

[4] Pires de Sliva et al ASCO 2020

Anti-PD1 refractory melanoma data

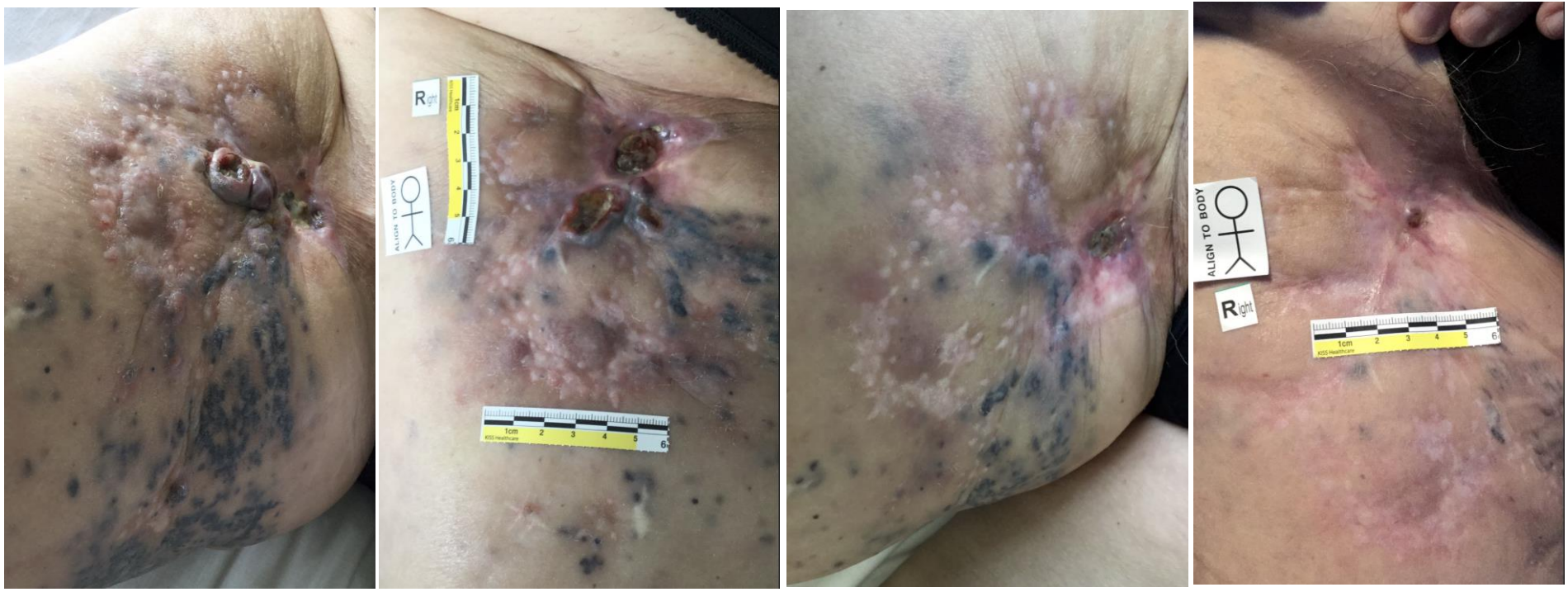
- 36 melanoma patients have been enrolled & treated with RP1 combined with Opdivo, with the last patient enrolled on Jan 7th 2020*
- As of May 2nd 2020 (data cut off), the status of the anti-PD1 refractory cutaneous melanoma (N=16) patients in this immature data set was:
  - 87.5 percent stage m1b/c
    - very late stage visceral disease population
  - Nine patients showed initial clinical benefit**
  - Five patients so far have met the formal criteria for response***
    - four of which had previously failed both anti-PD1 and anti-CTLA 4 therapies
  - Two further patients remain on treatment with the opportunity for response
  - The minimum final objective response rate (ORR) for these patients will therefore be 31%
  - Clinical data supported by biomarker data including reversal of T cell exclusion
- Responses also seen in anti-PD1 refractory uveal and mucosal melanoma

*Phase 1 expansion cohort & phase 2 melanoma cohort combined **SD or better with evidence of anti-tumor activity

***RECIST other than PD requires confirmation on successive scans

Patient #: 4403-1003 (Yervoy/Opdivo refractory melanoma) – Ongoing PR

10th June 2019 | 24th June 2019 (pre Opdivo) | 2nd September 2019 | 16th March 2020



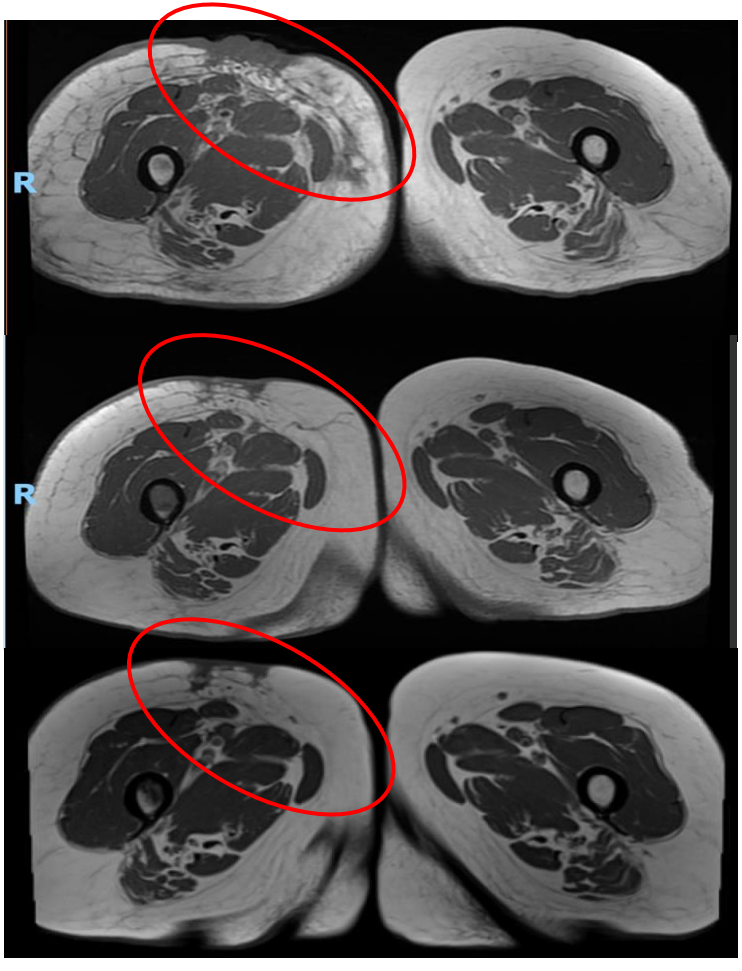
- Baseline disease in the thigh, groin & lungs
- Tumors in the thigh flattened after the first dose of RP1, i.e. prior to Opdivo & extensive oedema rapidly reduced

Patient #: 4403-1003 (Yervoy/Opdivo refractory melanoma) – ongoing PR

May 2019 (Baseline)

August 2019

December 2019

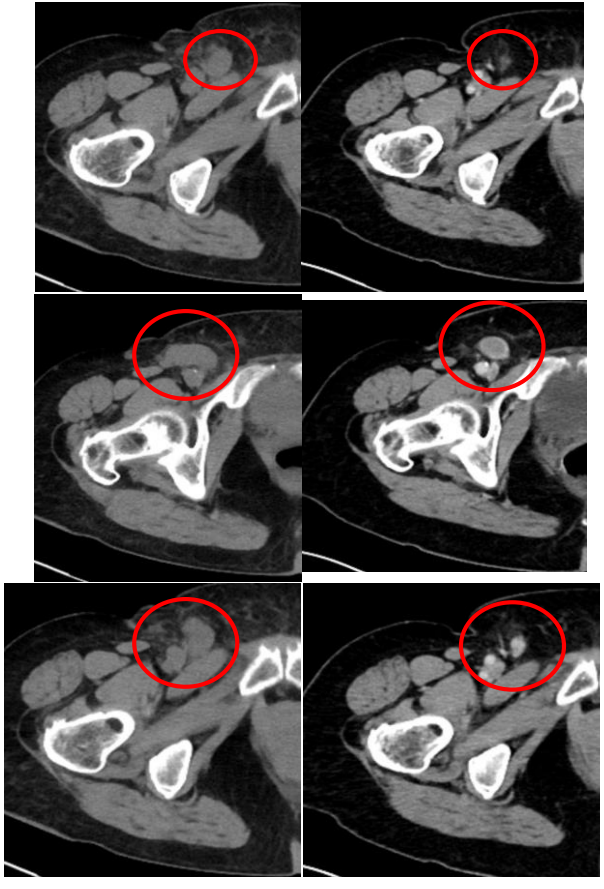


- Patient quality of life has also greatly improved, from being essentially immobile to being fully mobile
- Patient remains on treatment at 10 months

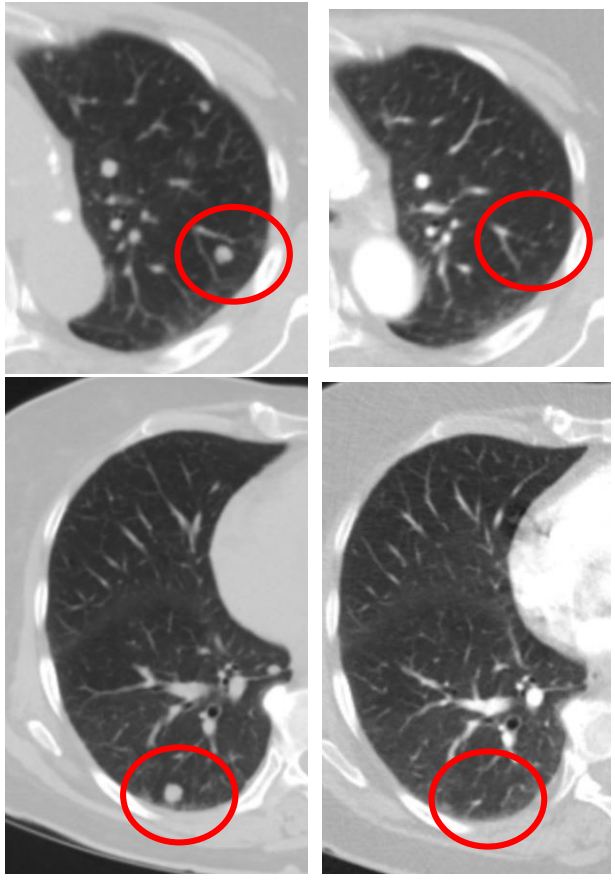
Replimune

Patient #: 4403-1003 (Yervoy/Opdivo refractory melanoma) – Ongoing PR

22nd May 2019 16th March 2020



22nd May 2019 16th March 2020



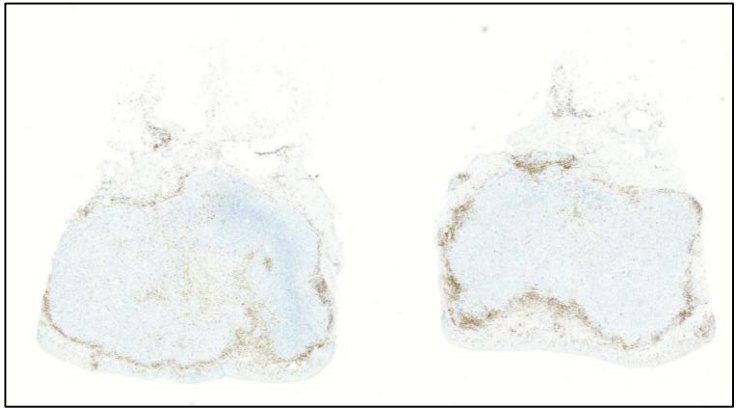
Reduction of uninjected lung lesions

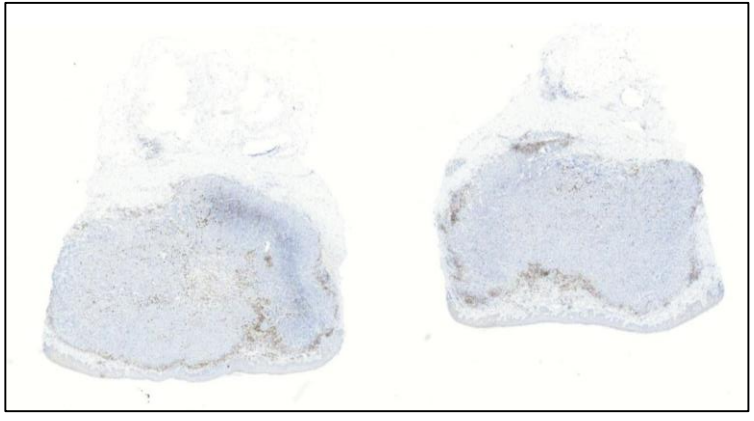
Patient #: 4403-1003: Reversal of T cell exclusion with RP1 combined with Opdivo

CD8

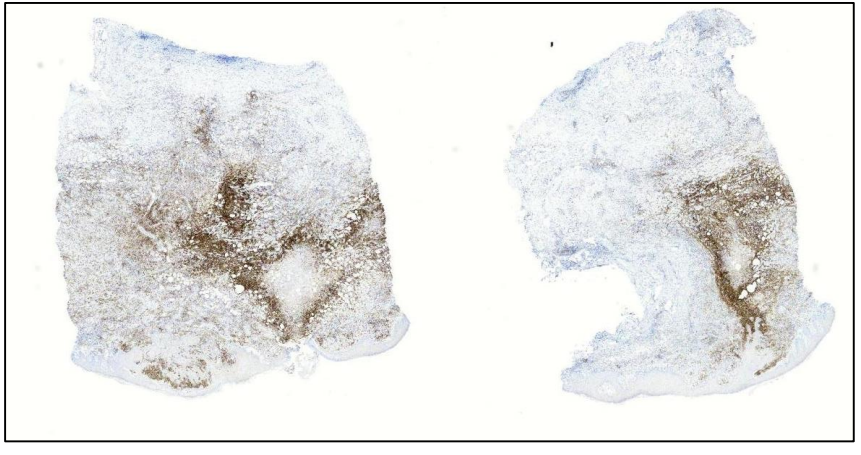
PD-L1

Baseline





Day 43 biopsy



Anti-PD1 refractory melanoma; 125 patient study underway

- Enrollment of a 125 patient potentially registrational cohort underway
  - RP1 combined with Opdivo
  - Hurdle for success intended to be discussed with FDA late 2020
  - ORR to a second line of anti-PD1 is estimated at **6-7%**[1]
- Targeting patients with primary/acquired resistance to anti-PD1 therapy
  - Treated with anti-PD1or anti-PD1/anti-CTLA-4 for at least 12 weeks with progression confirmed on successive scans
  - Includes patients failing anti-PD1 adjuvant therapy
  - Very unlikely to respond to further treatment with single agent anti-PD1
  - High un-met medical need

[1]Ribas et al Lancet Oncology **19** 2018; Hodi et al JCO **34** 2016

New cohort in anti-PD1 refractory NSCLC

- Anti-PD1 refractory NSCLC is an area of considerable un-met need, with no SOC/viable options
- RP1 combined with Opdivo has demonstrated the ability to shrink lung metastases
- RP1 combined with Opdivo shows activity in anti-PD1 refractory melanoma
- RP1 has been administered safely into lung tumors in multiple patients using imaging guidance
- The lung is an 'immune responsive' site
- Enrollment expected to begin into 30 patient cohort later this year

RP2 & RP3: anti-CTLA-4 & co-stimulatory pathway agonist delivery

- Focus on delivery of proteins which act <u>as the immune response is being generated</u>
  - Systemic antibody approaches probably don't act at the right place or the right time
  - Potential for toxicity
- 

  - Delivery of anti-CTLA-4 directly into the tumor
  - Blocks Treg activation/inhibition of T cell activation at the site of immune response initiation
  - Retain the efficacy of Yervoy alone & in combination with anti-PD1 but reduce toxicity
    - Phase 1 trial alone & combined with Opdivo underway – initial data expected late 2020
- 

  - Delivery immune co-stimulatory pathway activating ligands
  - RP3 encodes anti-CTLA-4, CD40L & 4-1BBL
    - CD40L: Broadly activates both innate & adaptive immunity
    - 4-1BBL: Promotes the expansion of cellular & memory immune responses
    - Phase 1 trial alone & combined with anti-PD1 expected to initiate this year

Replimune

Critical focus on manufacturing

- For registration directed studies & commercialization, in-house manufacturing in place
- The team has extensive manufacturing experience
- 63,000 ft^2 manufacturing facility leased in July 2018 in Framingham, MA, appropriate for multi-product production
  - State of the art facility
  - Fully fitted out; first tech transfer run successfully completed
  - Scale sufficient to cover full global commercialization of Replimune's products at full capacity
- Product expected to be released in 2021 to incorporate in studies intended for approval

Looking ahead: Targeted milestones for the remainder of 2020*

- RP2 - Initial clinical data from phase 1 trial of RP2 alone & combined with Opdivo
- RP1 - CSCC
  - Complete recruitment of 30 patient NMSC cohort with Opdivo
  - First patients dosed in single agent transplant study
  - Plan for neoadjuvant study
- RP1 - Anti-PD1 refractory melanoma
  - Discuss potential path to market with FDA
  - Report mature data set from 30 patient completed cohort with Opdivo
- RP1 - Finalize planning for anti-PD1 refractory NSCLC cohort
- RP3 - Phase 1 clinical trial to initiate

*The COVID-19 pandemic has delayed, and we expect it may continue to delay, the timing of patient enrollment and treatment in certain of our ongoing clinical studies.

Replimune