



NEXT-GENERATION ONCOLYTIC
IMMUNOTHERAPY

July 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 results of our plans to initiate new clinical trials, 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, our expectations regarding commercialization of our product candidates, our expectations with respect to our own in-house manufacturing capabilities, 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 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.

We have filed with the Securities and Exchange Commission (SEC) a registration statement on Form S-3 (including a prospectus) and will file with the SEC a prospectus supplement to the prospectus for the offering to which this presentation relates. Before you invest, you should read the prospectus supplement and the accompanying prospectus in that registration statement and the documents incorporated by reference or filed as exhibits to the registration statement for more complete information about Replimune Group, Inc. and this offering. You may get these documents and other documents for free by visiting EDGAR on the SEC website. Alternatively, copies of the preliminary prospectus supplement and the accompanying prospectus, when available, may be obtained from J.P. Morgan Securities LLC, Attention: Broadridge Financial Solutions, 1155 Long Island Avenue, Edgewood, NY 11717, by telephone at (866) 803-9204, or by e-mail at prospectus-eq_fi@jpmorgan.com; or SVB Leerink LLC, Attention: Syndicate Department, One Federal Street, 37th Floor, Boston, MA 02110, by telephone at (800) 808-7525, ext. 6218, or by e-mail at syndicate@svbleerink.com.

This presentation shall not constitute an offer to sell or the solicitation of an offer to buy any securities, nor shall there be any sale of these securities in any jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of such state or jurisdiction.

Offering summary

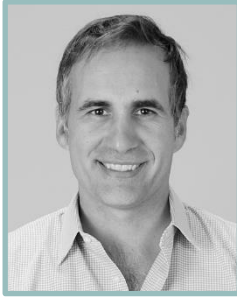
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Issuer:	Replimune Group, Inc.
Ticker (Exchange):	REPL (Nasdaq)
Base offering size:	\$80mm of common stock and pre-funded warrants (100% primary)
Over-allotment option:	15% (100% primary)
Use of proceeds:	<p>Together with our existing cash and cash equivalents and short-term investments:</p> <ul style="list-style-type: none">• to fund the development of RP1 through the completion of our ongoing clinical trials in RP1;• to fund clinical development with RP2 and RP3; and• the remainder for general corporate purposes, including working capital requirements and operating expenses.
Lock-up:	<ul style="list-style-type: none">• 60 days for Company and certain shareholders, directors and officers• 90 days for nearly all directors and officers
Bookrunners:	J.P.Morgan SVBLEERINK BMO  Capital Markets®
Lead manager:	 WEDBUSH

- Proprietary 'Immulytic' oncolytic immuno-gene therapy 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 with meaningful long-term market opportunity
 - Strong efficacy signal from single arm data in combination with Opdivo – data updated June 3
 - Ongoing 240 patient registration directed randomized trial in combination with Libtayo
 - Single agent study in organ transplant recipients contra-indicated for anti-PD1 enrolling
 - Anti-PD1 refractory melanoma
 - 125 patient cohort enrolling
 - Strong signal from current RP1 combined with Opdivo melanoma cohort – data updated June 3
- RP2 & RP3 - intended to treat less immune-responsive tumors
 - Ongoing Phase 1 clinical trial of RP2 alone & combined with Opdivo
 - Safety & efficacy with single agent RP2 & initial data combined with Opdivo expected by end 2020
 - RP3 intended to enter the clinic in H2 2020

The most experienced oncolytic immunotherapy team

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PHILIP ASTLEY-SPARKE

Chief Executive Officer
CEO BioVex, Chairman at uniQure



ROB COFFIN

President and Chief R&D Officer
Founder & CTO at BioVex, VP at Amgen



COLIN LOVE

Chief Operating Officer
SVP BioVex; VP at Amgen through T-Vec BLA filing



JEAN M. FRANCHI

Chief Financial Officer
*CFO Merrimack Pharmaceuticals;
CFO Dimension Therapeutics*



PAMELA ESPOSITO

Chief Business Officer
VP BD at BioVex; CBO at Ra Pharmaceuticals

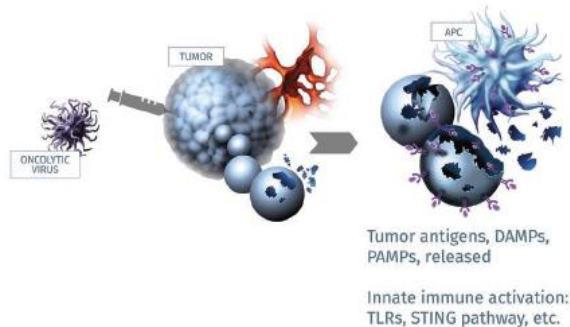
Oncolytic immunotherapy

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- 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

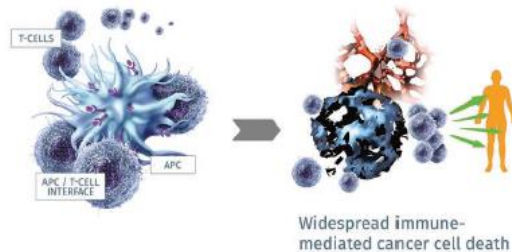
1 LOCAL

Lytic tumor destruction, innate immune activation



2 SYSTEMIC

Adaptive immune activation



Replimune's differentiated approach

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Our platform offers significant advantages compared to competing approaches, such as cell-based therapies, including TILs, and personalized vaccines

Competitive dimension	Cell-based therapy (including TILs)	Personalized Vaccines	Replimune's Immulytic Platform
"Off the shelf" – no patient-specific manufacturing	✗	✗	✓
Commercially attractive COGS	✗	✗	✓
Incorporates multiple modalities (incl innate and adaptive immunity)	✗	✗	✓
Desirable safety profile, without a high frequency of high grade side effects including death	✗	✓	✓
Potentially applicable to nearly all patients with solid tumors	✗	✗	✓

Replimune's platform

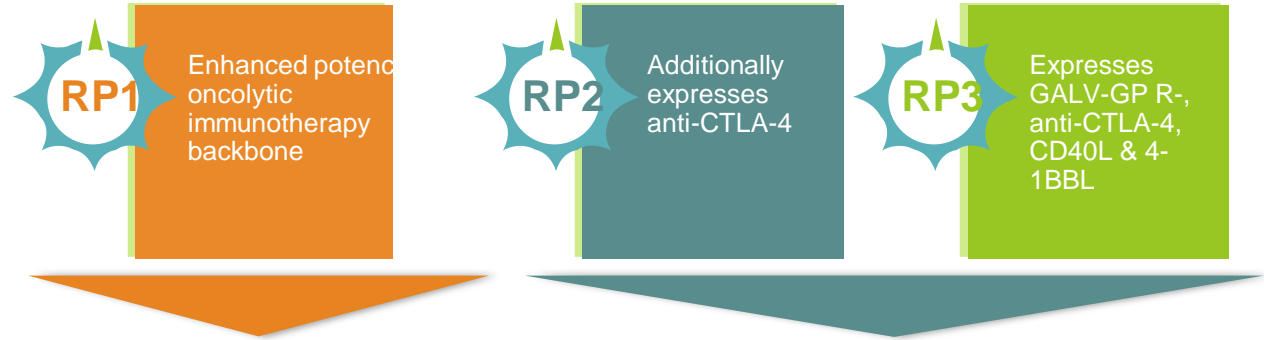
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1. A potent underlying virus strain

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

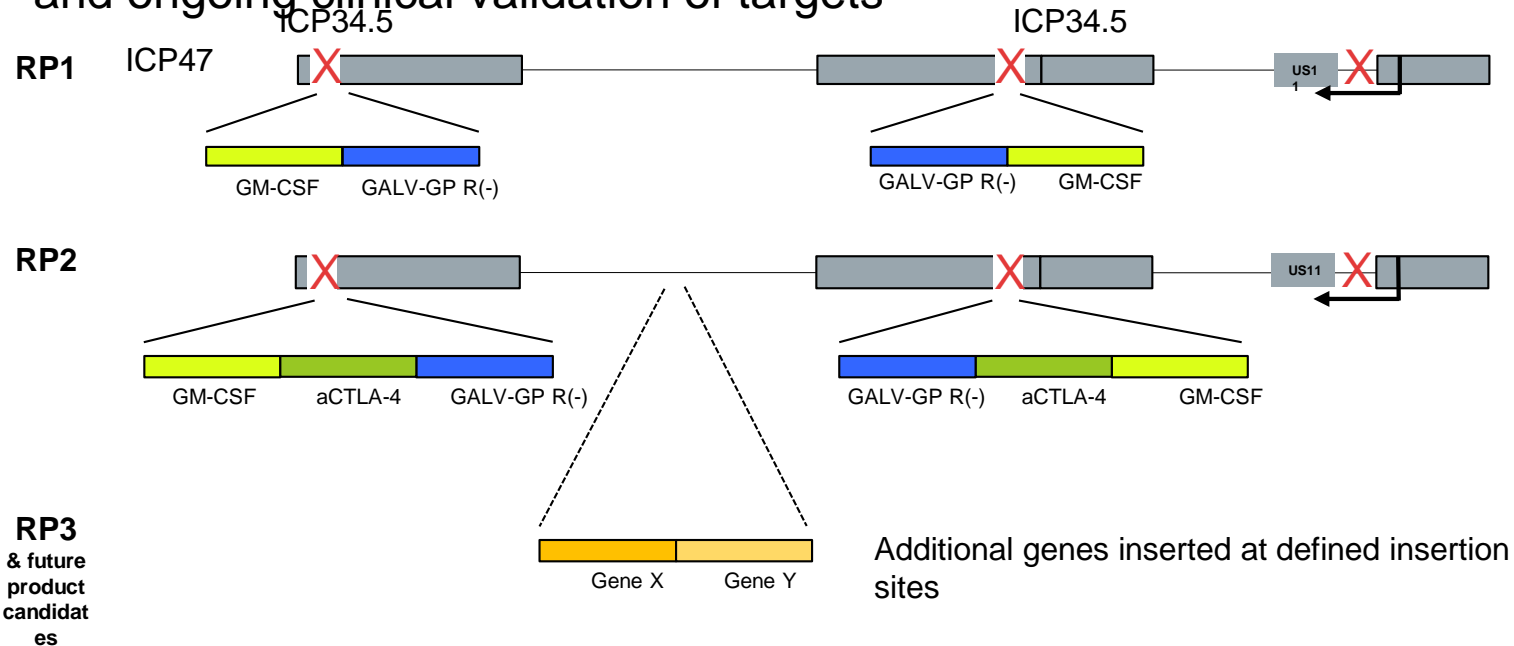
- Anti-CTLA-4
- Immune-costimulatory pathway activators
- *Aims to increase efficacy while reducing toxicity*

Intended for less & non-immune responsive tumor types

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

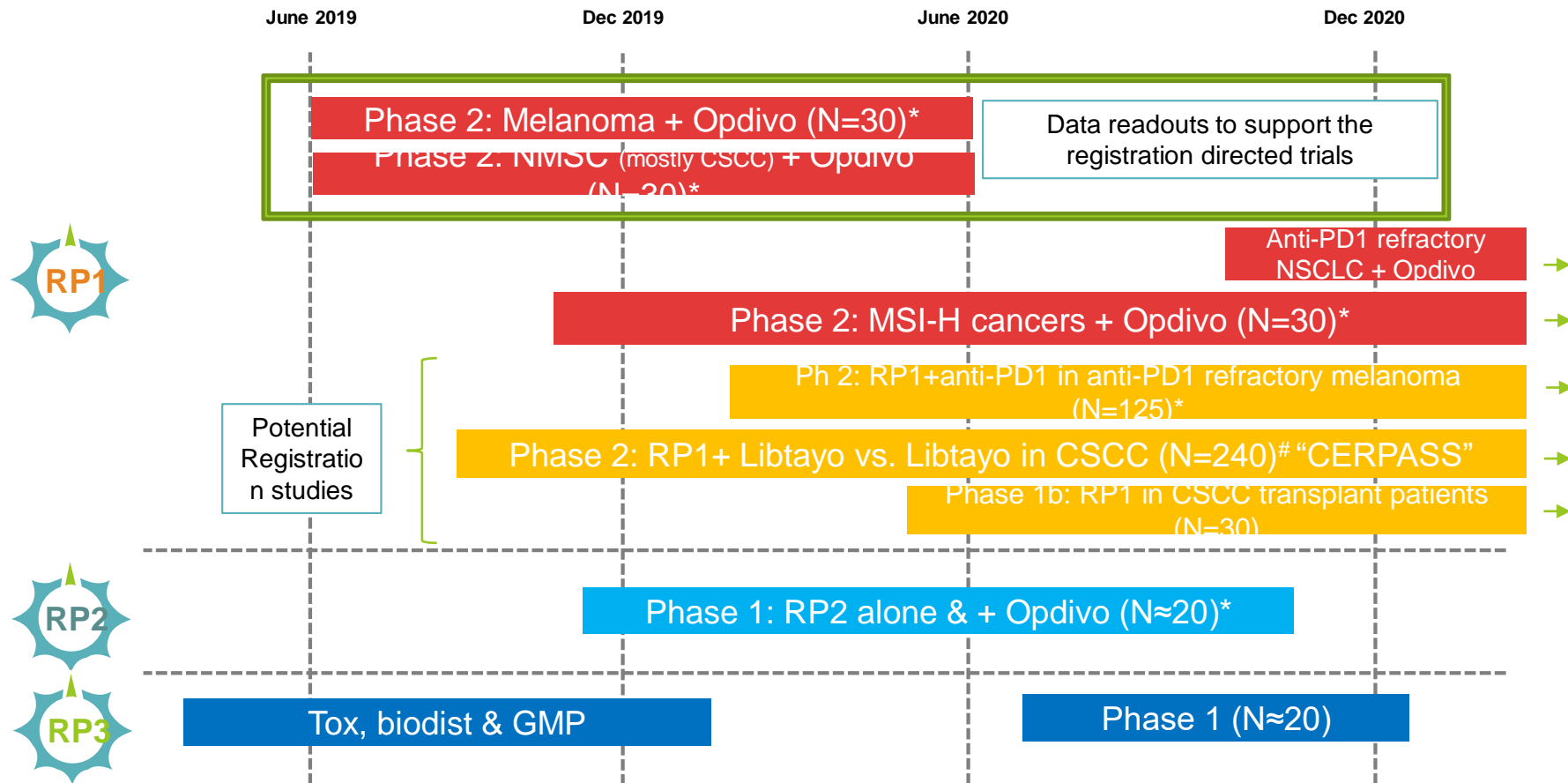
Our “plug and play” platform approach

- New products candidates encoding new therapeutic genes can be rapidly developed from conception to initiation of clinical trials in <18 months
- Future therapeutic genes driven by evolving scientific understanding, and ongoing clinical validation of targets



Replimune's development plan

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* 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

Summary of data presented on June 3

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Data presented continues to support the current registration-directed clinical trials

Cutaneous squamous cell carcinoma data update

- Six of seven patients with follow up treated with RP1+Opdivo have ongoing PRs or CRs → **Response rate never seen before with historical approaches in this indication**
- Four patients with ongoing CRs (including of uninjected distant tumors): *Clear differentiation from anti-PD1 monotherapy*
- Data continues to highlight RP1 is well tolerated, demonstrates immune activation & continues to drive durable and deep responses in patients with CSCC → **Systemic activity demonstrated to be robust and durable**

Anti-PD1 refractory cutaneous melanoma data update illustrates promising activity providing significant opportunity for an effective approach

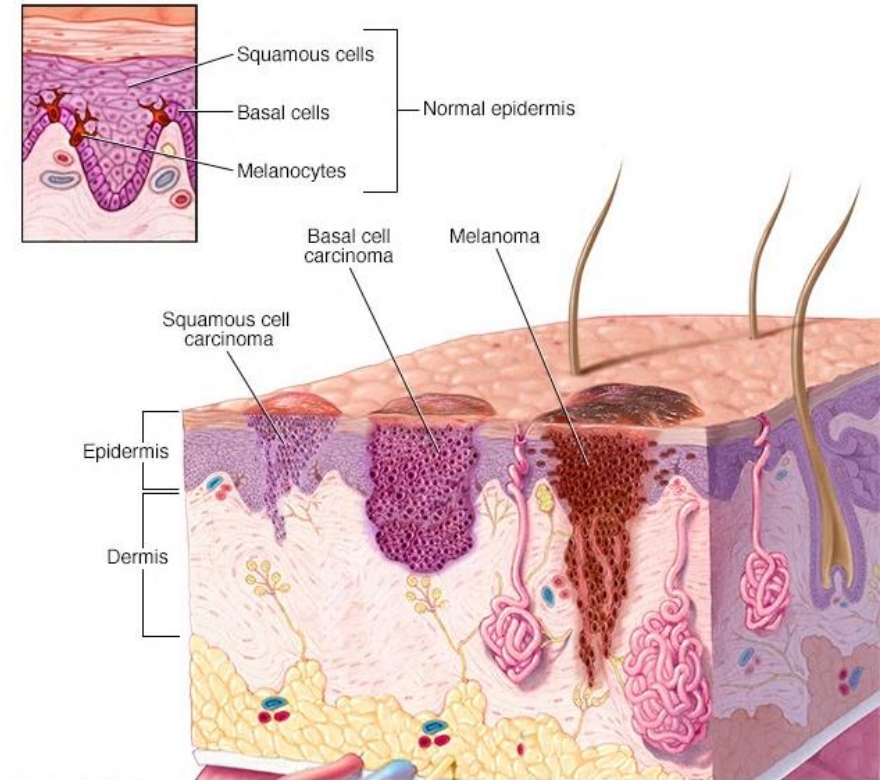
- 16 patients treated with RP1 in combination with Opdivo
 - 5 patients in response - 2 further patients remain on treatment with the opportunity for response
 - These responses (which include patients with extensive visceral disease) wouldn't be expected with a second line of anti-PD1; 4/5 patients had failed prior combined Yervoy/Opdivo

CSCC opportunity overview

Lead indication overview: CSCC

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- The second most common skin cancer with $\approx 700,000$ 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 annually¹⁻³
 - 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 annually¹⁻⁴
- Only approved anti-PD-1 therapy:



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¹Rogers et al JAMA Dermatol **10** 2015

²Clayman et al JCO **23** 2005

³Mansouri et al J Am Acad Dermatol **153** 2017

⁴Schmults et al JAMA Dermatol

149 2013

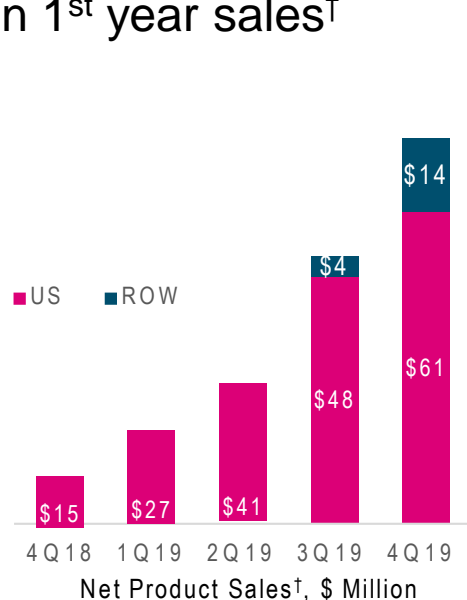
⁵Motaparthy et al Adv Anat Pathol **24**

2017

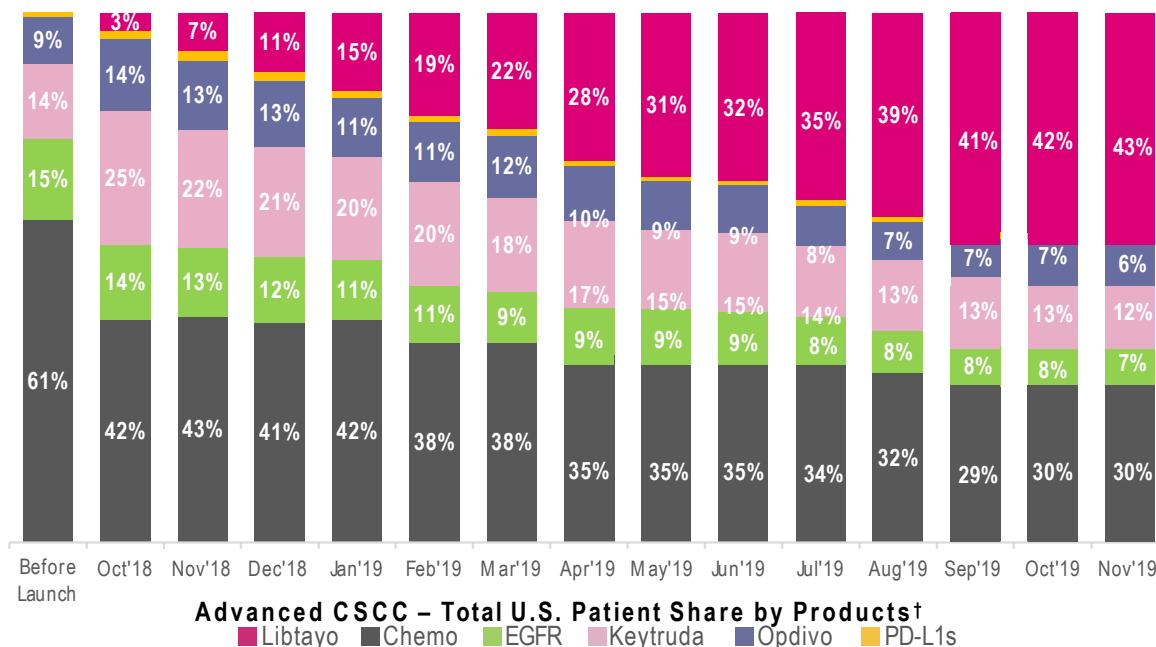
Regeneron has paved the way in CSCC

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Libtayo generated ~\$200M in 1st year sales†



Libtayo captured market share of systemic therapies



CSCC – Cutaneous Squamous Cell Carcinoma
 † Source: Regeneron Q1 2020 Corporate Presentation
 Updated IQVIA – Claims through Nov'19

Single agent anti-PD1 data in advanced CSCC

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	Libtayo				Keytruda	Opdivo
Patient population	Locally advanced		metastatic		47 locally advanced + 58 metastatic	4 locally advanced, 16 locoregional, 4 metastatic
Number of patients	33 (per label, 2018)	78 (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%

Lead indication: CSCC – the CERPASS study



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- 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

Additional clinical trials in CSCC

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- 30 patient clinical trial of single agent RP1 open for enrollment in solid organ transplant recipients (liver & kidney)
 - Organ transplant recipients are at increased risk of malignancy, with CSCC most prevalent
 - 70% of patients develop CSCC within 20 years¹
 - Anti-PD1 therapy contra-indicated due to the risk of organ rejection in around 40% of patients
 - Clinical data indicates that RP1 has single agent activity in CSCC
- Intend expansion of the CSCC program to also include neoadjuvant use

¹Fisher et al J Am Acad Dermatol **82** 2020

RP1 + Opdivo data summary in advanced CSCC

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So far, nine patients have been treated with RP1 + Opdivo:

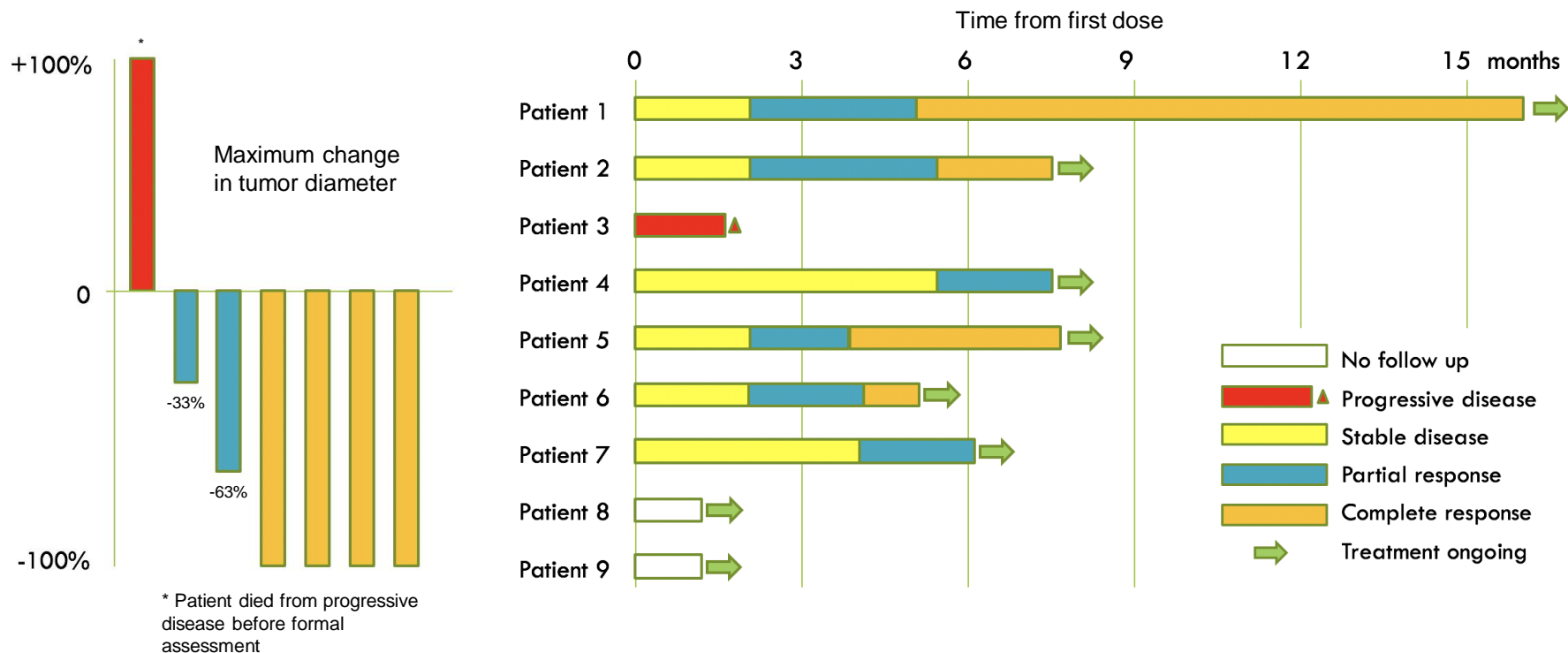
- 4 locally advanced, 5 metastatic, 56% had prior systemic therapy
- 6/7 patients with follow up in ongoing response
 - Patient 1: Ongoing CR
 - Patient 2: Ongoing CR (previously PR)
 - Patient 3: PD
 - Patient 4: Ongoing PR
 - Patient 5: Ongoing CR
 - Patient 6: Ongoing CR (new)
 - Patient 7: Ongoing PR (new)
 - Patient 8: Initiated dosing 24th April 2020 (no follow up)
 - Patient 9: Initiated dosing 28th April 2020 (no follow up)

Other NMSC patients enrolled:

- BCC: N=2 (PD, no follow up yet)
- Merkel cell carcinoma: N=1 (PD)
- Angiosarcoma: N=2 (PR, no follow up yet)

Responses are deep & all are ongoing to date

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Anti-PD-1 refractory melanoma opportunity overview



Anti-PD1 refractory melanoma – market opportunity

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- 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 melanoma¹
- 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 therapy²
- 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; 125 patient study underway



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- 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-PD1 or 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

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

Melanoma data summary

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- 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 [8 having had prior anti-CTLA-4 and anti-PD1]) patients in this immature data set was:
 - 87.5% patients with stage M1b/c (visceral disease)
 - 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

*Phase 1 expansion cohort & phase 2 melanoma cohort combined

**SD or better with evidence of anti-tumor activity

Melanoma data summary (cont.)

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- As of May 2nd 2020 (data cut off), the status of the patients in this immature data set was:
 - Anti-PD1 naive cutaneous melanoma (N=8):
 - Eight patients showed initial clinical benefit*
 - Four so far having met the formal definition of response
 - Two further patients remaining on treatment with the opportunity for response
 - Mucosal melanoma (N=6):
 - Three patients showed initial clinical benefit*
 - Two met the formal definition of response** (one anti-PD1 naive, one having had prior anti-PD1)
 - Uveal melanoma (N=6):
 - Five patients showed initial clinical benefit* (all anti-PD1 refractory)
 - Two ongoing (extensive liver disease, both refractory to combined Opdivo and Yervoy)
 - One patient having a 27.3% reduction by RECIST (uni-dimensional measurement) / 61% reduction by WHO (bi-dimensional measurement)

*SD or better with evidence of anti-tumor activity

Safety of RP1 combined with Opdivo in patients with skin cancers

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Treatment related treatment emergent adverse events (TEAEs) N=41				
Preferred term	Grade 1-2 (>15%) # (%)	Grade 3 (all) # (%)	Grade 4 (all) # (%)	Grade 5 (all) # (%)
Pyrexia	17 (41.5)	1 (2.4)	0	0
Chills	16 (39.0)	0	0	0
Influenza like symptoms	11 (26.8)	0	0	0
Fatigue	8 (19.5)	5 (12.2)	0	0
Decreased appetite		1 (2.4)	0	0
Dehydration		1 (2.4)	0	0
Hypotension		1 (2.4)	0	0
Lipase Increased		1 (2.4)	0	0
Localised oedema		1 (2.4)	0	0
Lymph node pain		1 (2.4)	0	0
Oedema		1 (2.4)	0	0
Rash		1 (2.4)	0	0
Seroconversion test positive		1 (2.4)	0	0
Total	34 (82.9)	8 (19.5)	0	0
Patients who discontinued due to TEAE	4 (9.8)			

- Patients in the melanoma & NMSC phase 2 cohorts treated with RP1 combined with Opdivo as of 1st May 2020
- There continues to be a good safety profile, with most AE's being Grade 1/2 constitutional-type symptoms
- Injections into visceral tumors practical and well tolerated, with clinical activity seen

New cohort in anti-PD1 refractory NSCLC

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- 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
- Agreed with BMS to 'swap in' an anti-PD1 relapsed/refractory NSCLC cohort in place of the bladder cancer cohort

**Beyond immune responsive tumor
types:
RP2 & RP3**

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

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- Focus on delivery of proteins which act as the immune response is being generated



- Systemic antibody approaches probably don't act at the right place or the right time
- Potential for toxicity

■ RP2

- 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

■ RP3

- Delivery immune co-stimulatory pathway activating ligands
- RP3 encodes anti-CTLA-4, CD40L & 4-1BBL
 - CD40L: Broadly activates both innate & adaptive immunity

Critical focus on manufacturing

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- RP1-RP3 currently manufactured by a CMO for ongoing clinical development
- For later stage development & commercialization, in-house manufacturing in place
- The team has extensive manufacturing experience
- 63,000 ft² 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



Conclusions from June 3 data: *“Building the Second Cornerstone of IO”*

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- RP1 - CSCC
 - Significant expected commercial opportunity
 - Clear path to market
 - Frequency of CRs provides clear differentiation to anti-PD1 alone
 - Biomarkers (CD8 T cells & PD-L1) supportive
- RP1 - Anti-PD1 refractory melanoma
 - Significant expected commercial opportunity
 - Clear activity in Yervoy/Opdivo failed patients, including with extensive visceral disease
 - Biomarkers (CD8 T cells & PD-L1) supportive
 - Activity also seen in mucosal & uveal melanoma patients
- RP1 - Early indications of activity seen beyond skin cancers
- Clinical testing of RP1 combined with Opdivo in anti-PD1 refractory NSCLC planned

Looking ahead: Targeted milestones for the remainder of 2020*

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- RP1 - CSCC
 - Complete recruitment of 30 patient NMSC cohort with Opdivo
 - Present data from 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
- RP2 - Initial data from phase 1 trial of RP2 alone & combined with nivolumab
- RP3 - Phase 1 clinical trial to initiate

*COVID-19 has impacted & is expected to continue to impact accrual & therefore the number of patients from whom data is expected to be available during 2020, with average expected length of follow up also expected to be reduced.

Example CSCC patients

Patient 2 (4402-2001): Ongoing CR

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16th June 2019
(baseline)



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



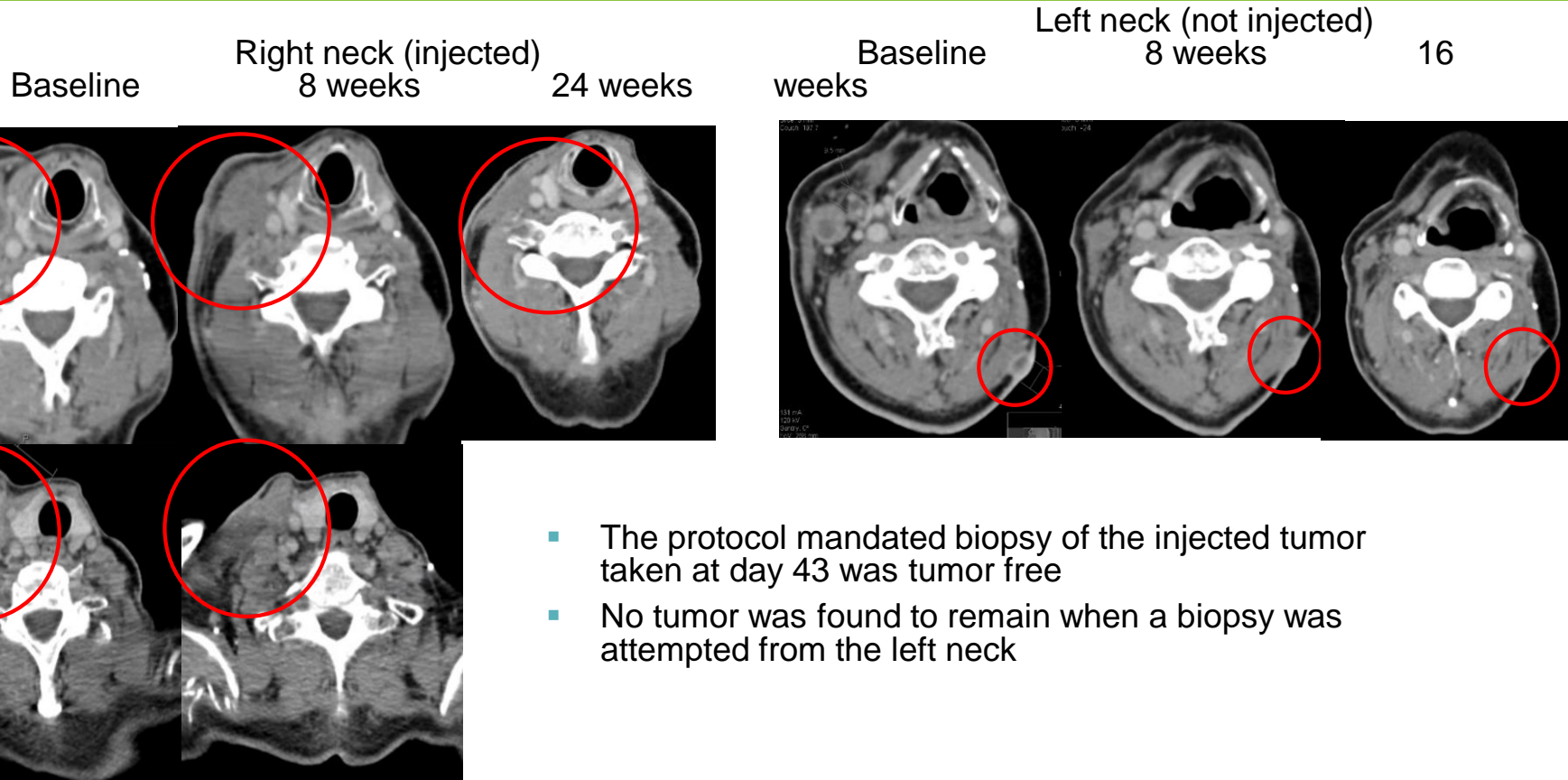
16th July 2019
(post 2 doses of RP1 & 1
dose of Opdivo)



- 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

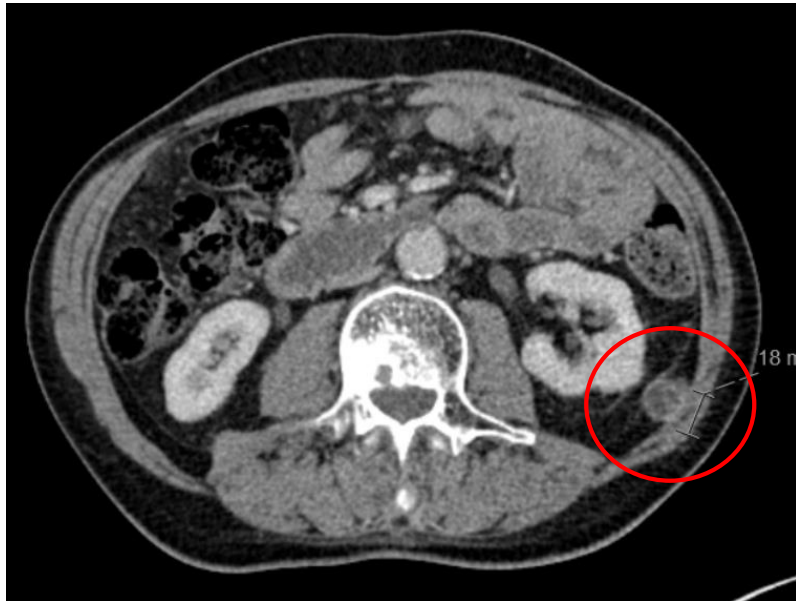
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Patient 2 (4402-2001): Ongoing CR

35

Baseline



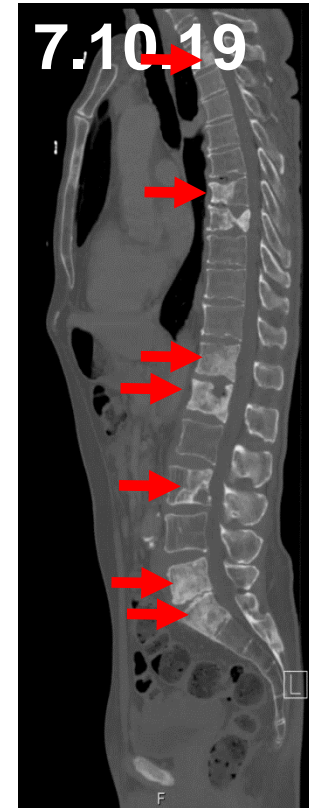
16 weeks



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

Patient 2 (4402-2001): Ongoing CR

36

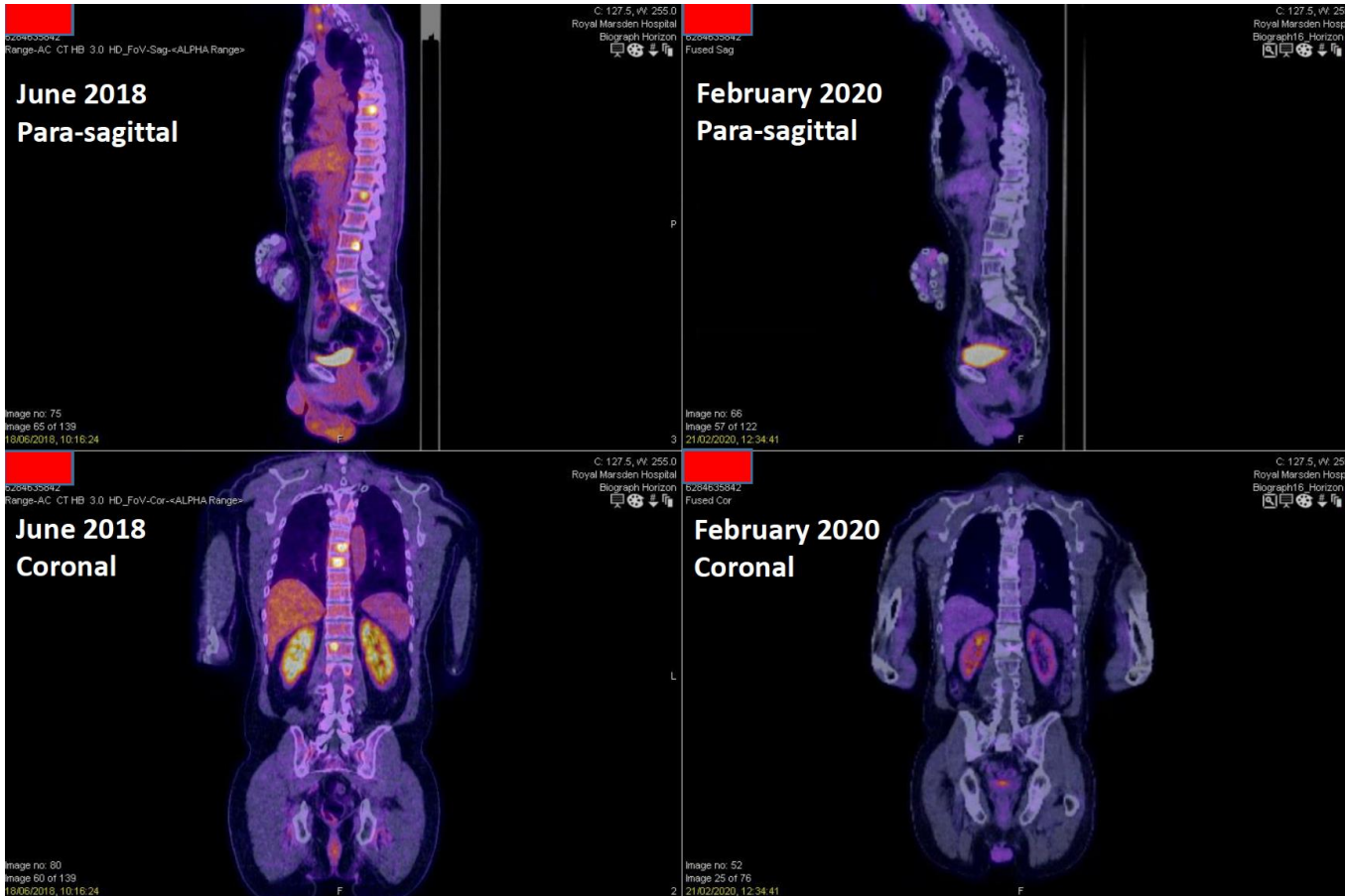


Complete sclerosis of all bone lesions with no areas of active disease. Declared radiological CR. Confirmed by PET scan (next slide)

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

Patient 2 (4402-2001): Ongoing CR

37

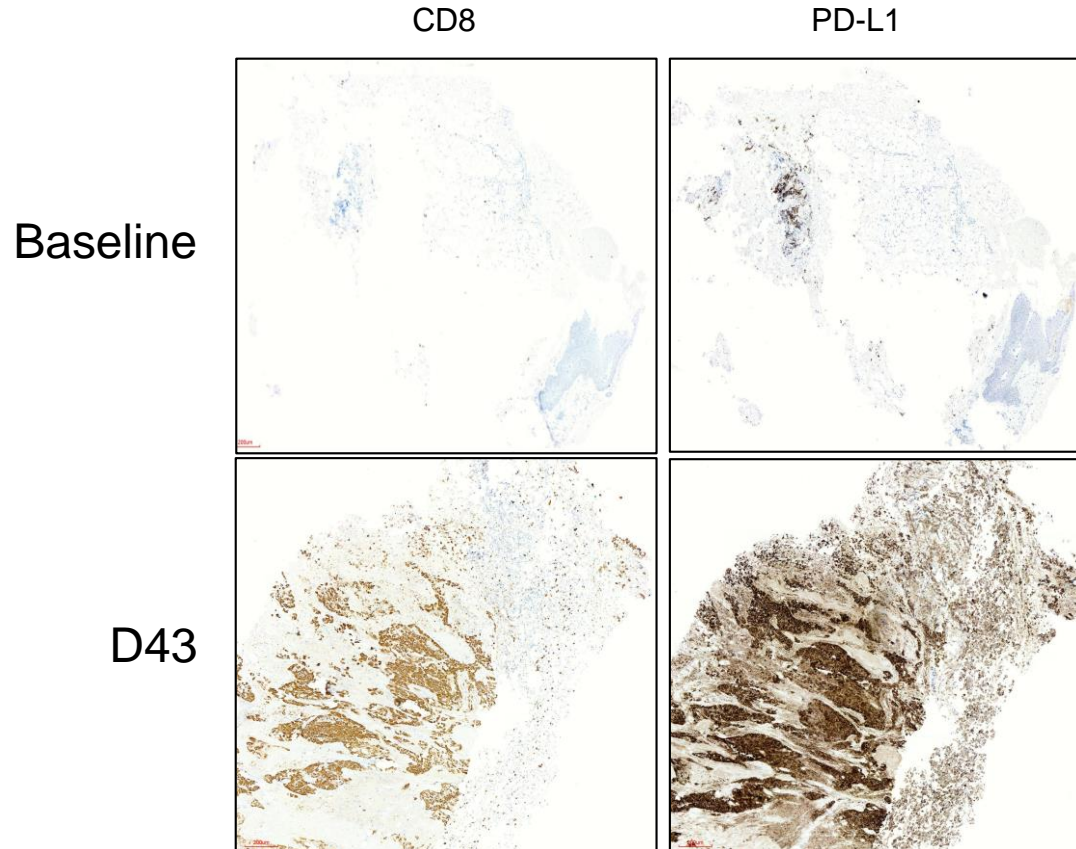


Bone metastases had substantially increased by CT between the prior PET scan (June 2018) and initiating the trial (June 2019), but no PET scan was performed at screening.

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

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Patient 4 (4402-2004): Ongoing PR

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2nd Sept 2019
(pre-dosing)

16th Sept
(post single RP1 dose, no Opdivo)

15th Oct

2nd Dec

13th Jan



Baseline scan

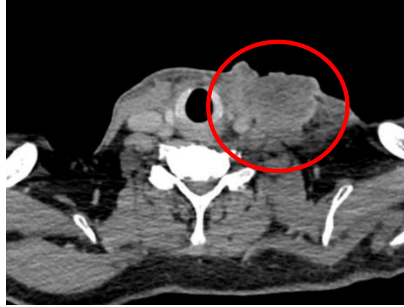


- Recurrent CSCC of the neck (injected) and lung metastases (not injected)
- Previously treated with radiotherapy with immediate relapse
- The large injected tumor in the neck flattened considerably after the first dose of RP1 (i.e. before the first Opdivo dose), & continued to reduce thereafter

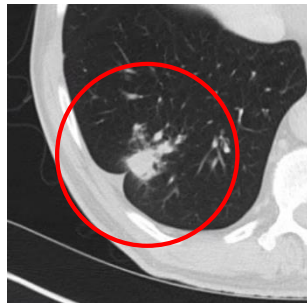
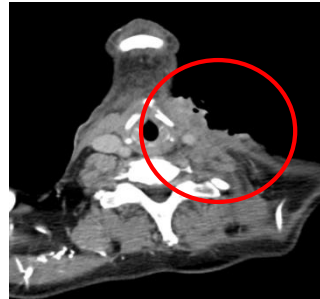
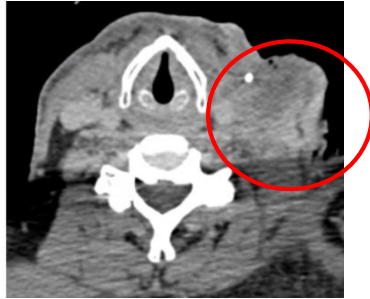
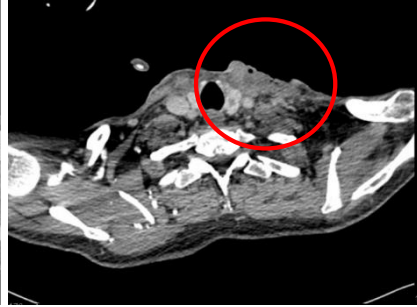
Patient 4 (4402-2004): Ongoing PR

40

28th August 2019



25th October 2019



- The only other sites of disease were lesions in the lung, which have also significantly reduced

Patient 5 (4402-2005): Ongoing CR

41

25th Sep 2019
(Baseline)

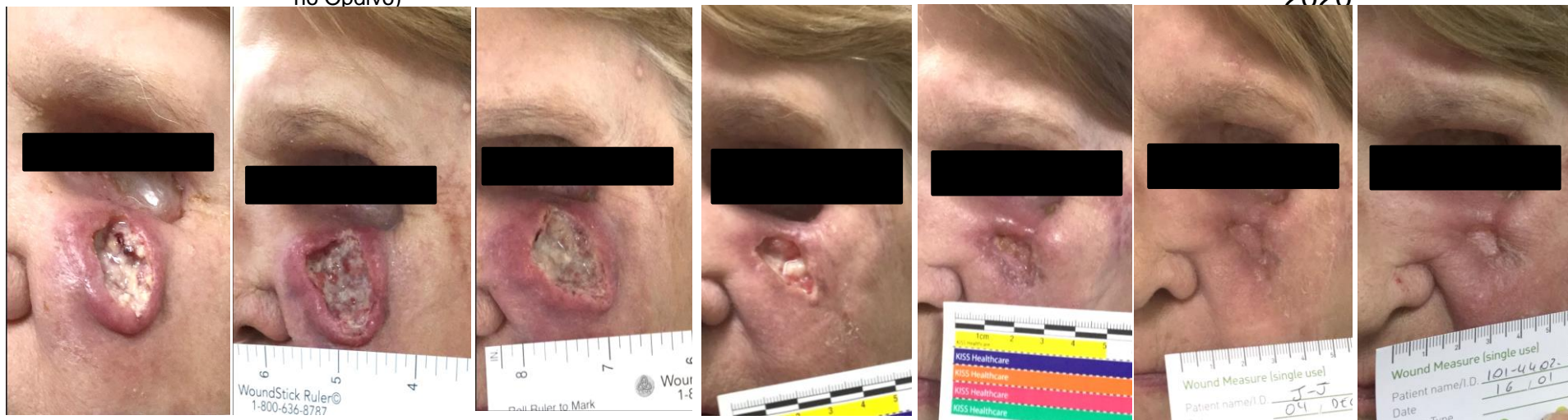
9th Oct 2019
(post single RP1 dose,
no Opdivo)

23rd Oct 2019

6th Nov 2019 20th Nov 2019

4th Dec 2019
2020

16th Jan



- Recurrent, rapidly progressing CSCC of the left cheek with bone invasion through the maxillary region, previously treated with surgery & radiation before trial entry
- The lesion flattened considerably after the first dose of RP1, and continued to reduce after the first dose of Opdivo
- CR confirmed by biopsy in December

Patient 6 (4402-2006): Ongoing CR

42

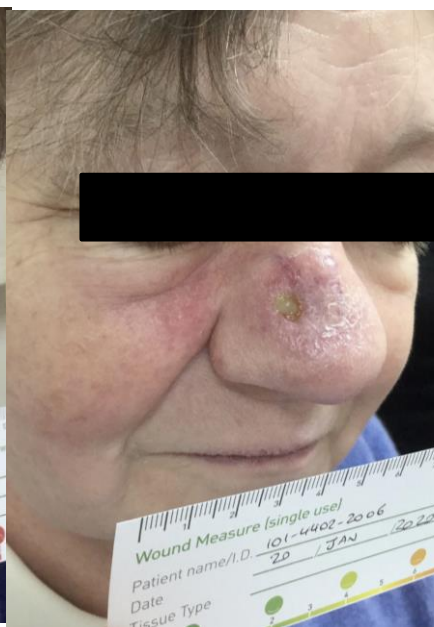
23rd December
2019



6th January 2020
(post single RP1 dose, no Opdivo)



20th January 2020



2nd March 2020



- Recurrent, rapidly progressing CSCC of the nasal region (3.5cm tumor), previously treated with carboplatin & radiation before trial entry

Patient 6 (4402-2006): Ongoing CR

43

Baseline



Day 57



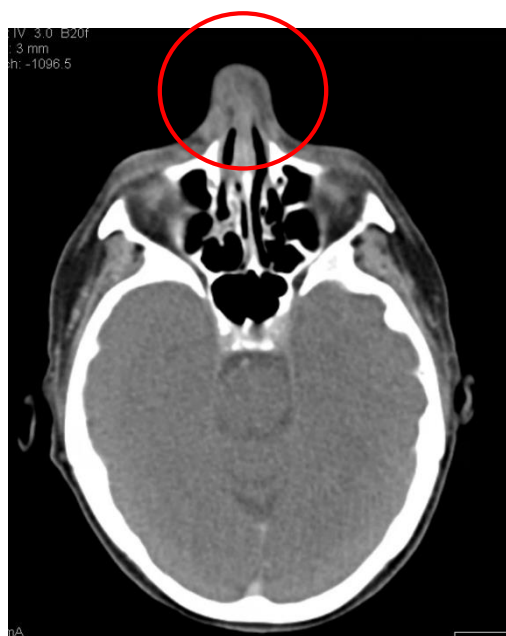
Patient 6 (4402-2006): Ongoing CR

44

18th Dec 2019
(Screening)



2nd Feb 2020



14th April 2020*

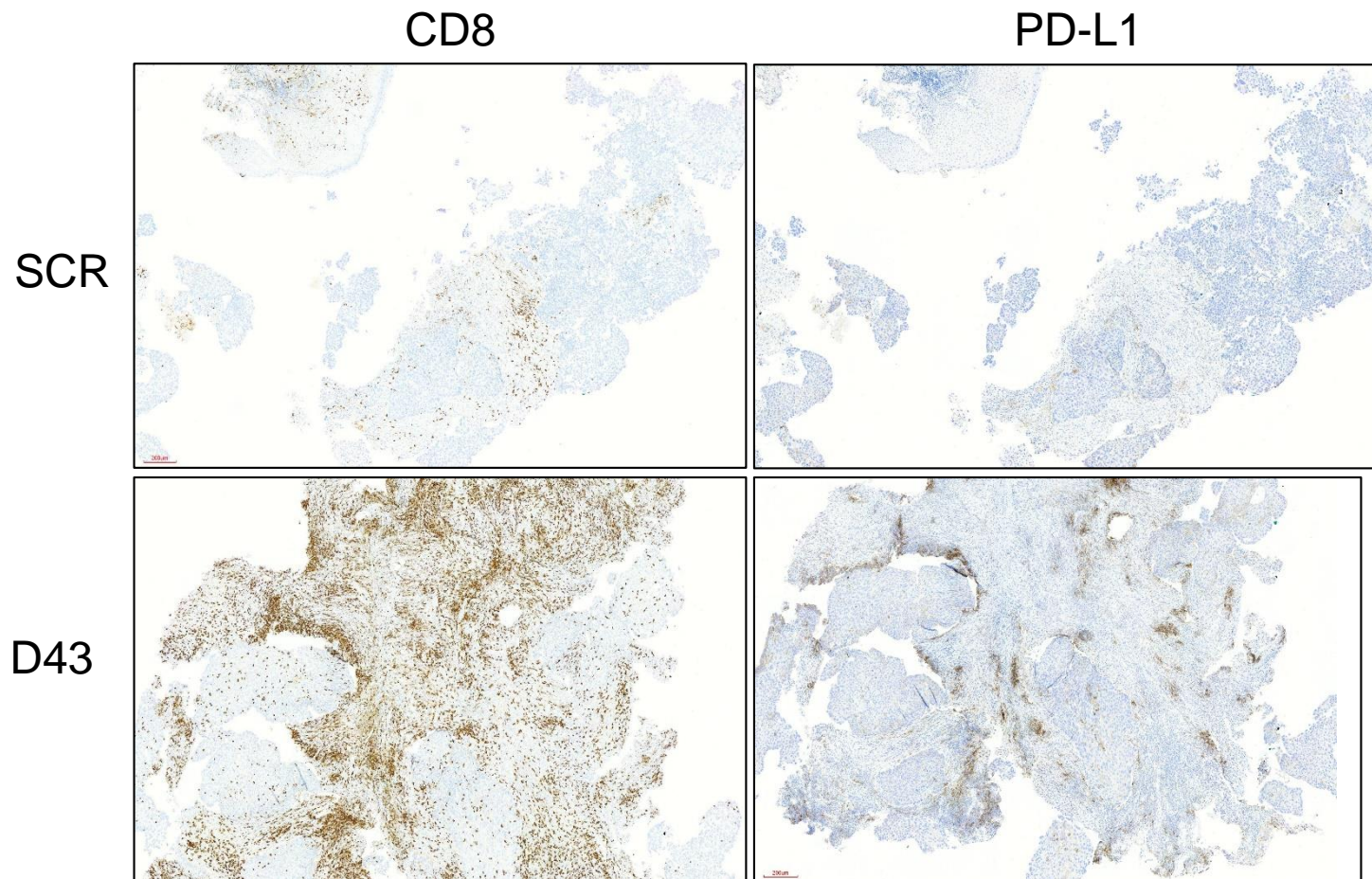


- The alternative to study treatment was rhinectomy

* CT done in a different plane to prior scans to maximally capture the affected area

Patient 6 (4402-2006): Ongoing CR

45



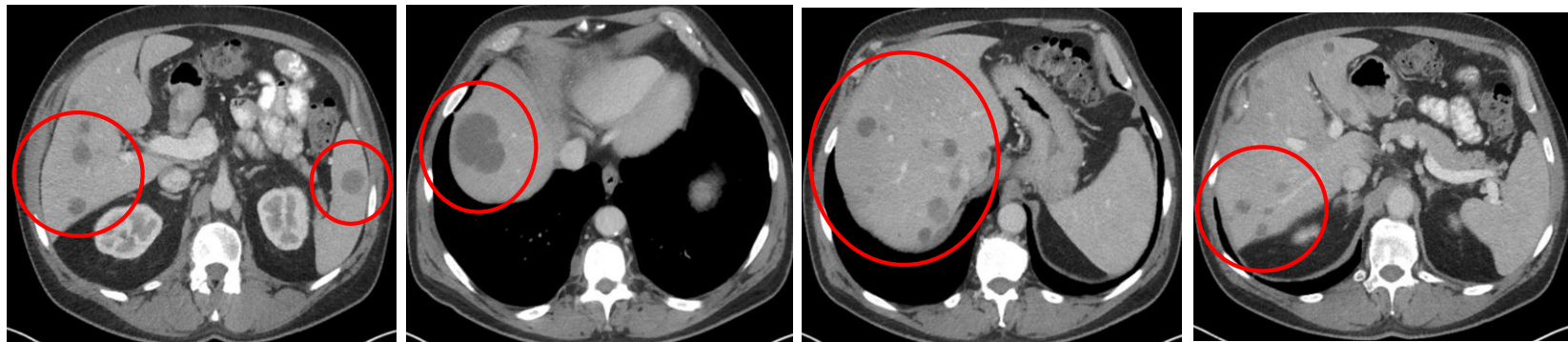
Example melanoma patients

Anti-PD1 refractory cutaneous melanoma patients

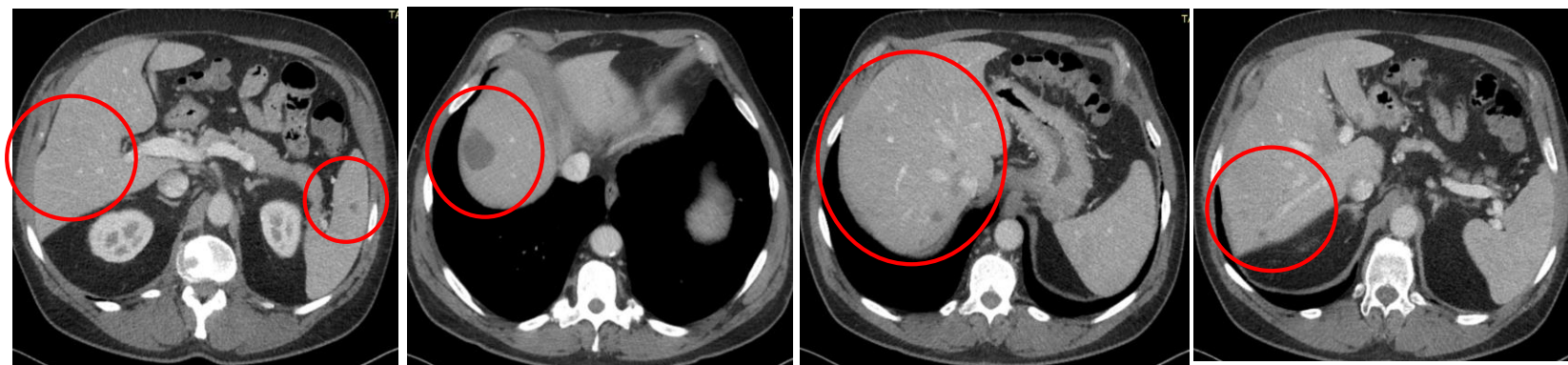
Patient #: 1122-2007 (Yervoy/Opdivo refractory melanoma) – ongoing PR

48

22nd Oct
2019
(Screenin
g)



9th March
2020



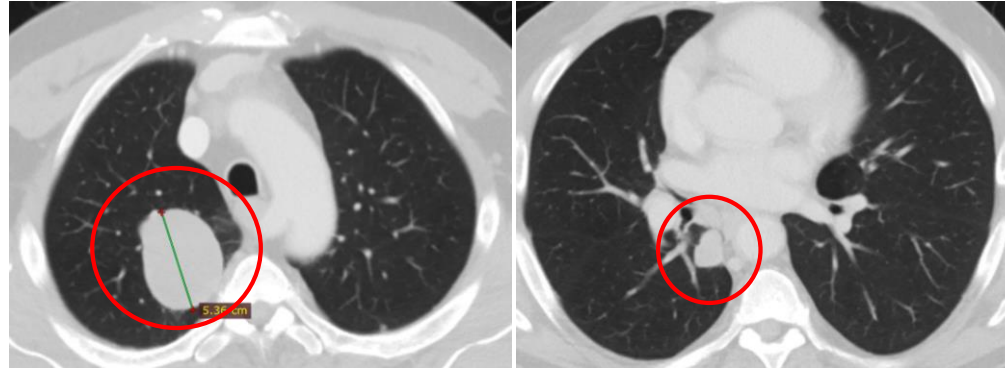
D43 liver biopsy tumor free

Reduction of injected & uninjected liver lesions

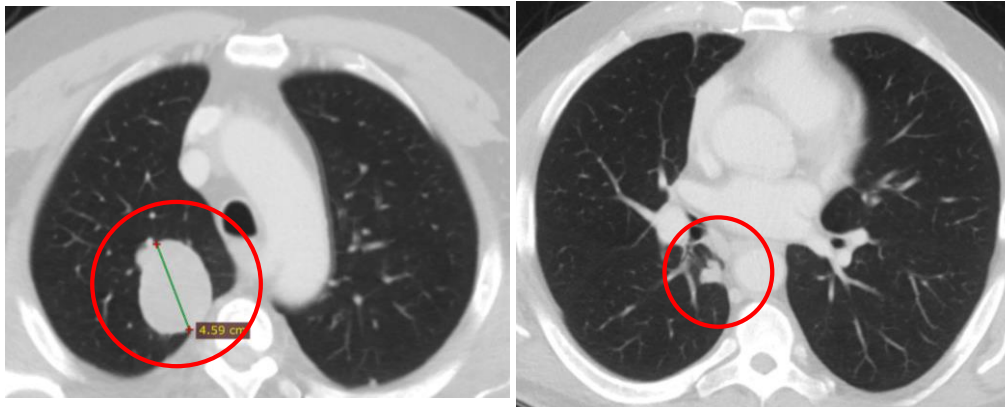
Patient #: 1122-2007 (Yervoy/Opdivo refractory melanoma) – ongoing PR

49

22nd Oct
2019
(Screening)



9th March
2020



Reduction of uninjected lung lesions

Patient #: 1119-2003 (Yervoy/Opdivo refractory melanoma) – ongoing PR

50

1st July 2019
(screening)



26th August

2019



22nd October 2019



5th November

2019



7th April 2020



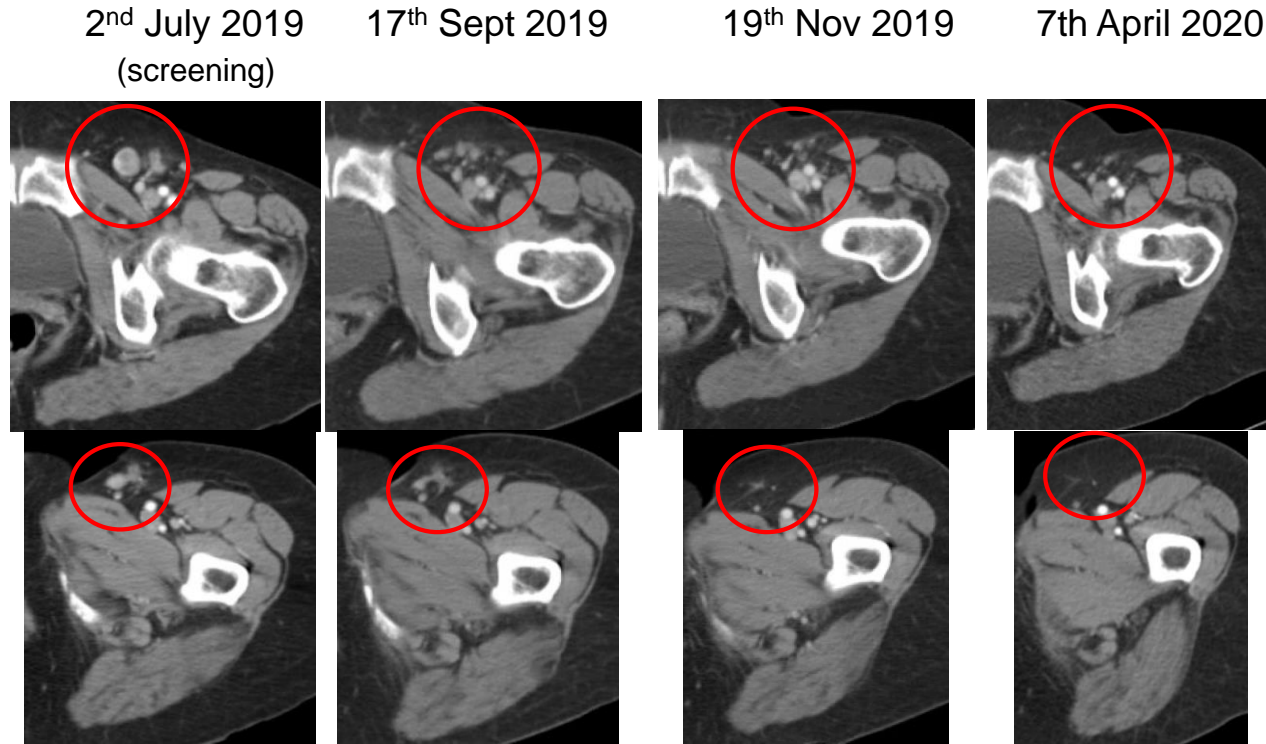
Biopsy
awaited to
confirm CR



- Disease in the foot, leg & nodes in the groin
- Initial progression in the leg/foot followed by response

Patient #: 1119-2003 (Yervoy/Opdivo refractory melanoma) – ongoing PR

51



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

52

10th June 2019

24th June 2019 (pre Opdivo)

2nd September 2019

16th March 2020

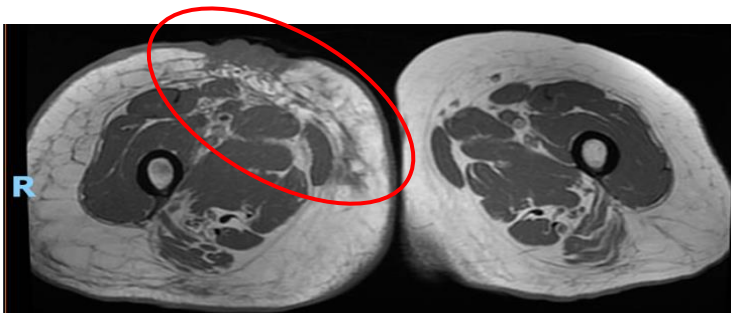


- Baseline disease in the thigh, groin & lungs
- Tumors in the thigh flattened after the first dose of RP1, i.e. prior to Opdivo & extensive oedema rapidly reduced

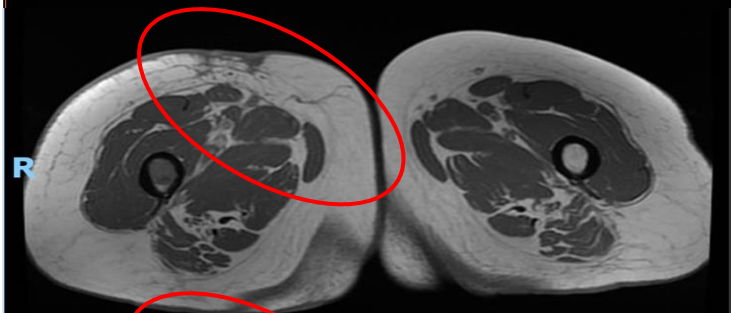
Patient #: 4403-1003 (Yervoy/Opdivo refractory melanoma) – ongoing PR

53

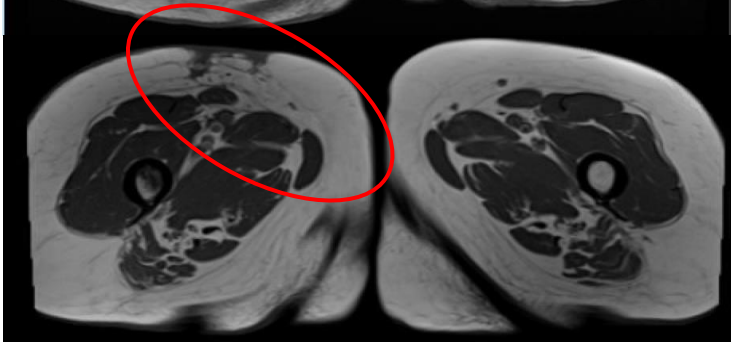
May 2019
(Baseline)



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

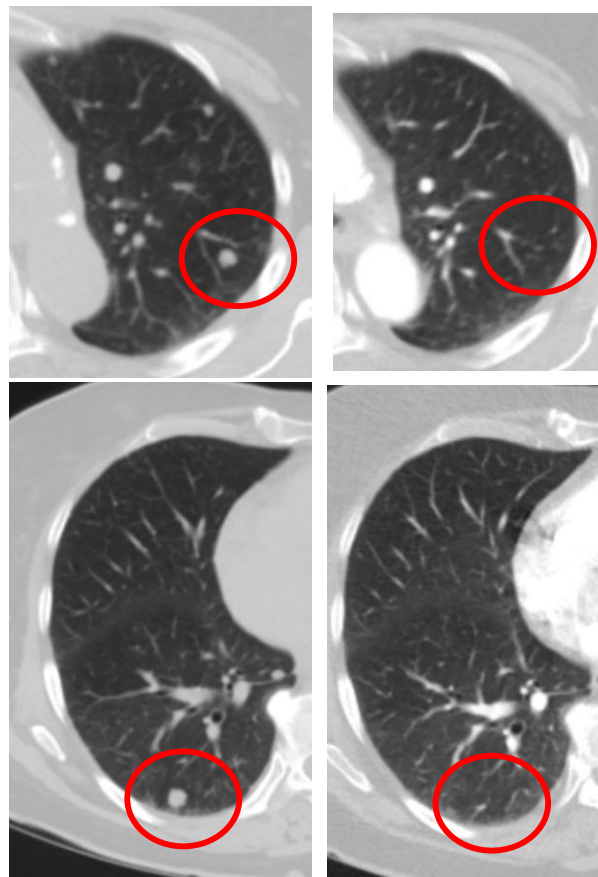
Patient #: 4403-1003 (Yervoy/Opdivo refractory melanoma) – ongoing PR

54

22nd May 2019 16th March 2020



22nd May 2019 16th March 2020



Reduction of
uninjected lung
lesions

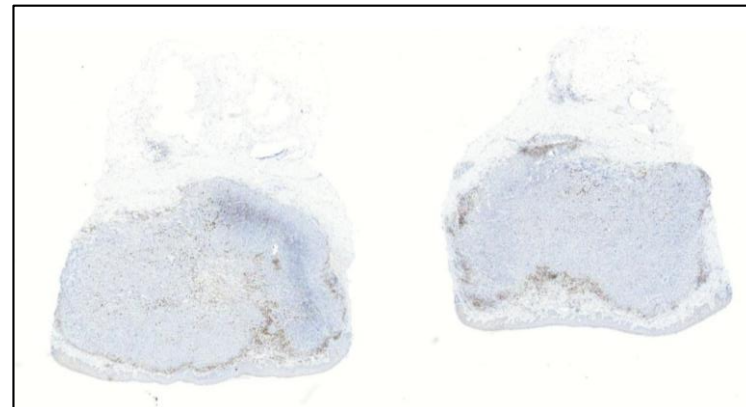
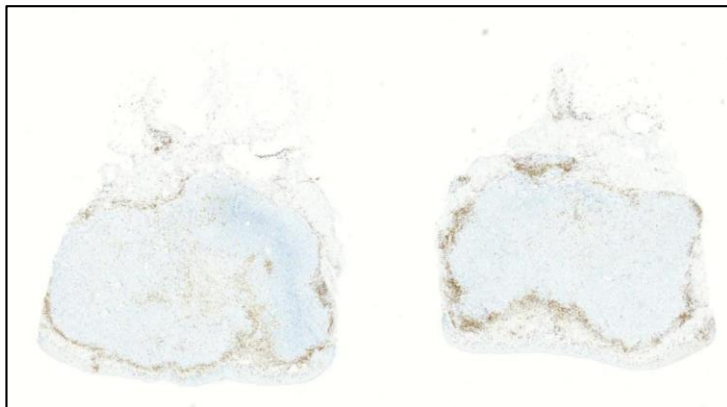
Patient #: 4403-1003: Reversal of T cell exclusion with RP1 combined with Opdivo

55

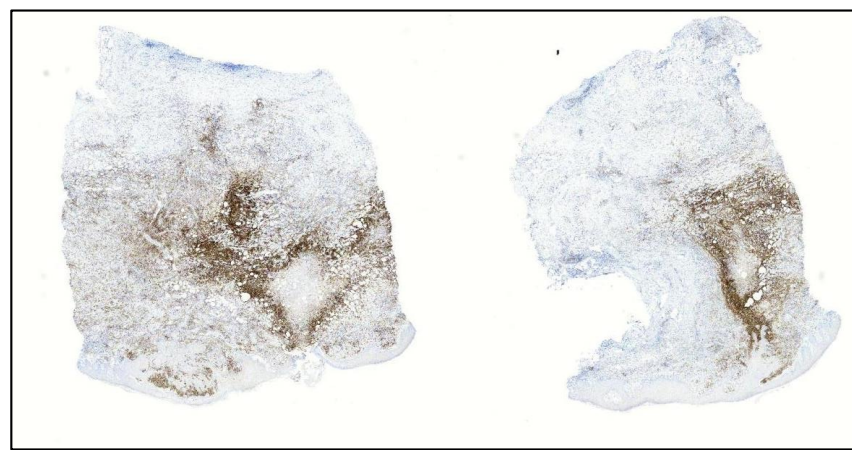
CD8

PD-L1

Baseline



Day 43
biopsy

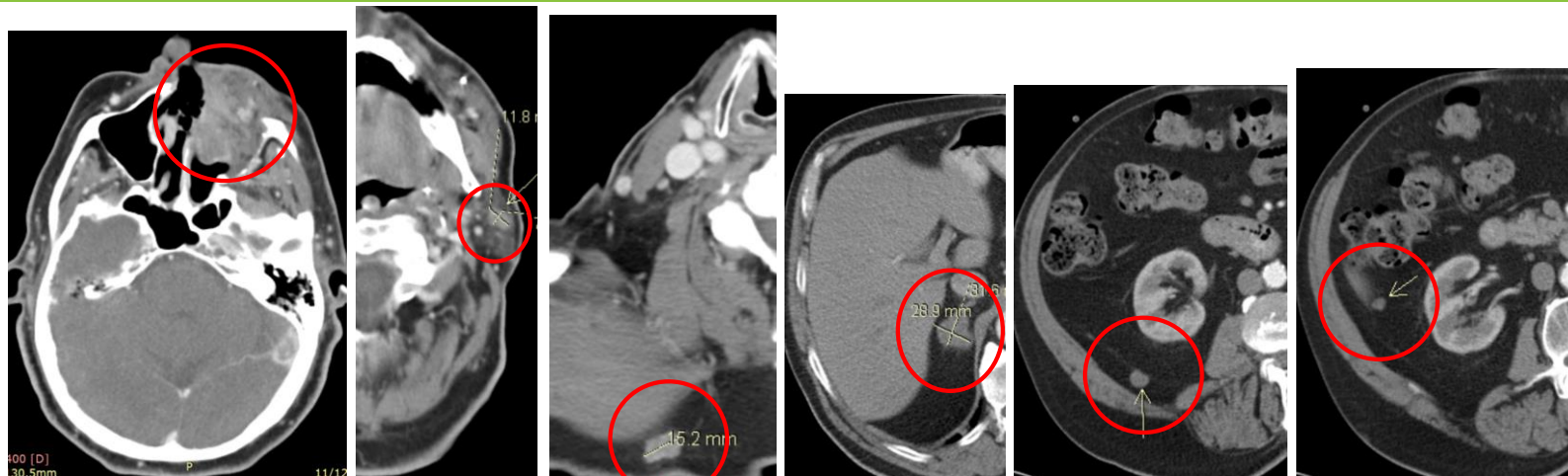


Mucosal melanoma patients

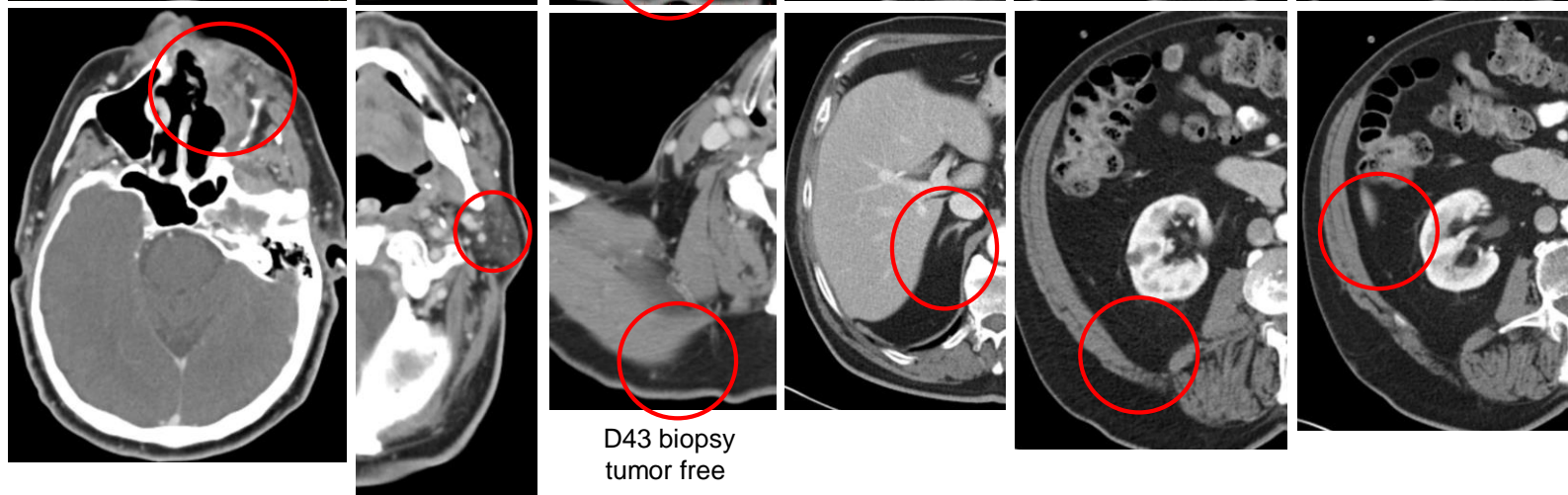
Patient #: 1119-2007 (mucosal melanoma) – ongoing PR

57

12th Nov
2019
(Screening)



12th
March
2020



Patient #: 4401-2002 (pembrolizumab refractory mucosal melanoma) – ongoing CR

58

20th Aug
2019
(Screenin
g)



15th Jan
2020



Excision biopsy
tumor free 1st
April 2020

Uveal melanoma patients

Patient #: 4403-1001 (Yervoy/Opdivo refractory uveal melanoma)

60

Baseline (2nd Jan 2019)



24th April 2019



Baseline disease included multiple c/sc deposits up to 4cm, 5-13mm lung & liver mets, multiple intra-abdominal up to 2cm.

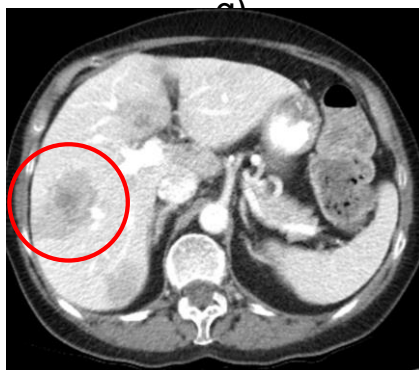
Initial response in numerous c/sc deposits, including uninjected (some biopsied showing no remaining residual tumor) and large scalp lesion. Other disease stable.

Treatment discontinued 20th Nov 2019 (new brain lesions).

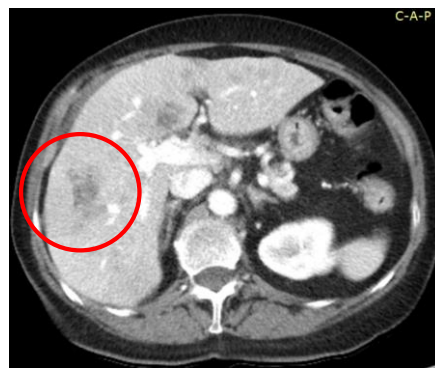
Patient #: 1112-2002 (Yervoy/Opdivo refractory uveal melanoma)

61

25th Sept
2019
(Screenin
g)



3rd April
2020



- Patient with extensive disease in the liver
- 27.3% reduction by RECIST (unidimensional), 61% reduction by WHO (bi-dimensional)
- Treatment ongoing

RP1 in other tumor types

Activity in a patient with angiosarcoma (ongoing PR)

63



6th November 2019



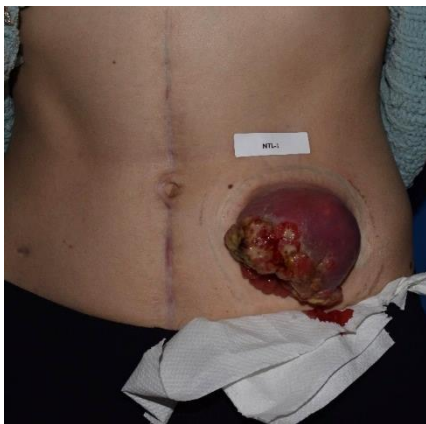
18th February 2020

- Patient withdrew from treatment due to Opdivo side effects

MSI-H colorectal cancer

64

- 22 year old female with MSI-H rectal cancer
- Prior neoadjuvant FOLFOXIRI
- Treated with RP1 combined with Opdivo
- Ongoing PR
- Biopsy “No tumour present - strips of dysplastic epithelium and inflammatory exudate only”



9th October 2019



20th November 2019



15th January 2020



25th March

2020

MSI-H colorectal cancer

65

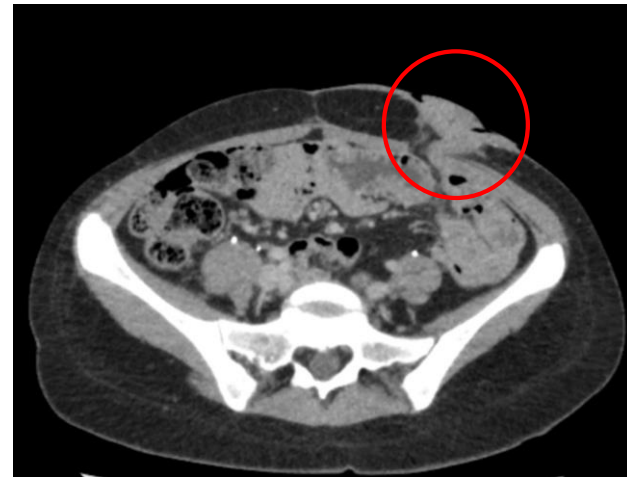
- Latest scan (March 2020) shows 87% reduction (including of uninjected abdominal disease)



4th Dec 2019 (C5)



29th Jan 2020 (C8)



25th March 2020 (C11)

Esophageal cancer

66

- Heavily pre-treated esophageal cancer (8 prior therapies)
- Lung lesions & lesions around the esophagus.
- Treated with RP1 combined with Opdivo
- Ongoing PR at 10 months



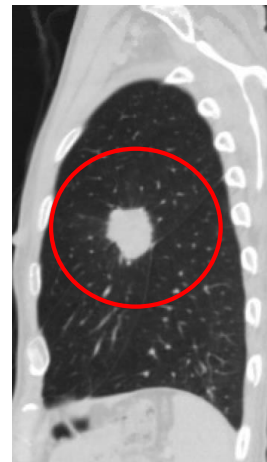
Baseline



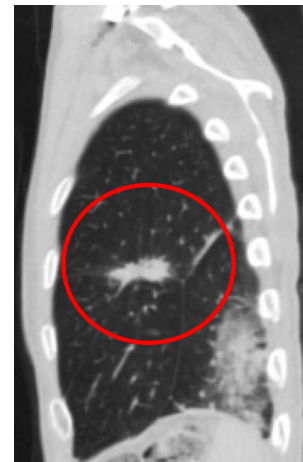
C5



C11



Baseline
C11



Esophageal cancer: CD8 T cell & PD-L1 staining

67

