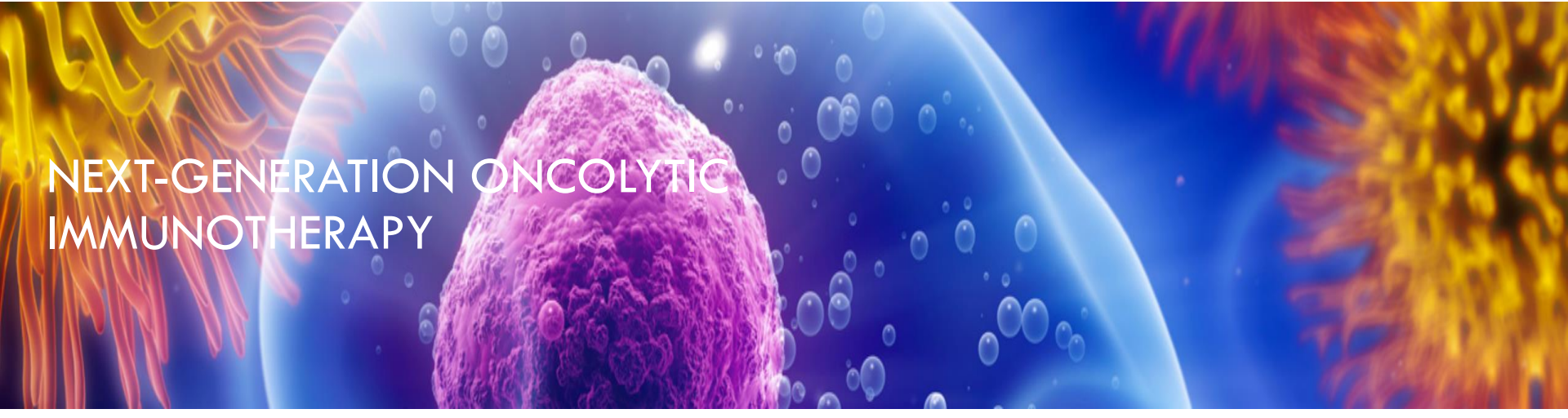
Replimune



Data Update
June 3rd 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 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.

Agenda

Introduction	Philip Astley-Sparke / Chief Executive Officer
Summary of Interim Results	Robert Coffin, Ph.D. / Founder & Head of R&D
CSCC Data Update	Kevin Harrington, Ph.D. / The Royal Marsden
Melanoma Data Update	Mark Middleton, Ph.D. / University of Oxford
Pipeline Update	Robert Coffin, Ph.D. / Founder & Head of R&D
Summary Remarks	Philip Astley-Sparke / Chief Executive Officer

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Dr. Kevin Harrington, The Royal Marsden Hospital

- Professor of Biological Cancer Therapies at The Institute of Cancer Research, London, and Consultant Clinical Oncologist at The Royal Marsden NHS Foundation Trust
- Leads the Targeted Therapy Team which focuses on two main areas: (i) the use of viruses as anti-cancer agents; and (ii) the development of new drugs that sensitize cancer cells to radiation.
- Specializes in treating patients with head and neck cancer, salivary gland and skin cancers.
- He has published more than 500 articles on cancer treatment and his work has been featured in newspaper and television reports.

Dr. Mark Middleton, The University of Oxford

- Professor of Experimental Cancer Medicine in the Department of Oncology, consultant Medical Oncologist at the Oxford Cancer and Haematology Centre and Head of the Department of Oncology at the University of Oxford.
- Research specializes on the development of new cancer drugs and on the treatment of melanoma and upper gastrointestinal tract cancers.
- Mark has overseen the development of internationally leading melanoma and upper GI clinical research groups and establishment of portfolios of early phase radiotherapy and haematooncology trials in Oxford.

Replimune

- 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)
    - Strong efficacy signal from single arm data in combination with Opdivo – data updated today
    - 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 today
- 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

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

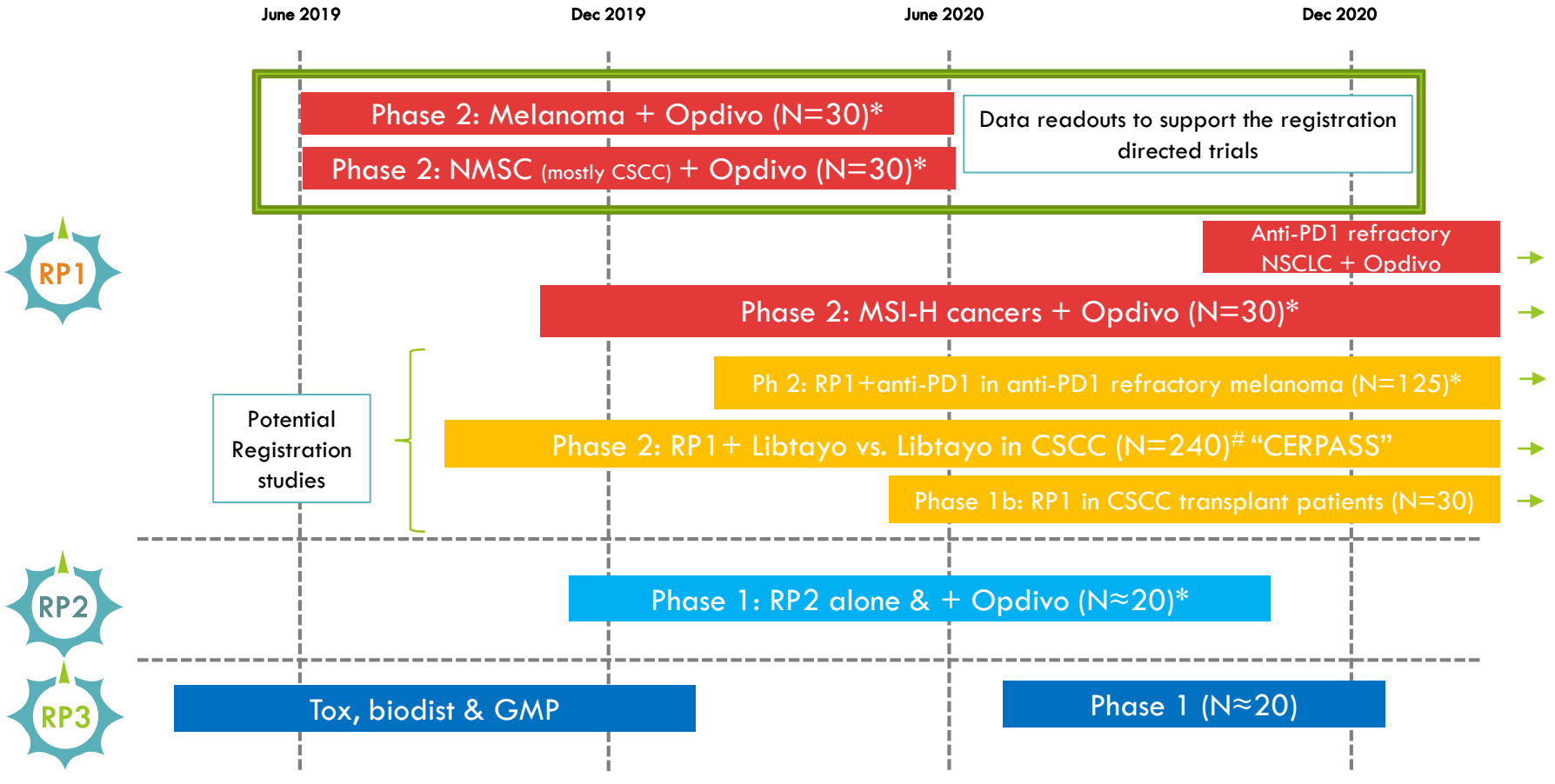
Focus on *clinically validated* pathways which function at the time & place of immune response initiation, but where systemic engagement is sub-optimal

- 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

Summary of today's data

Cutaneous squamous cell carcinoma data update

- Six of seven patients with follow up treated with RP1+Opdivo have ongoing PRs or CRs
- 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

Anti-PD1 refractory cutaneous melanoma data update

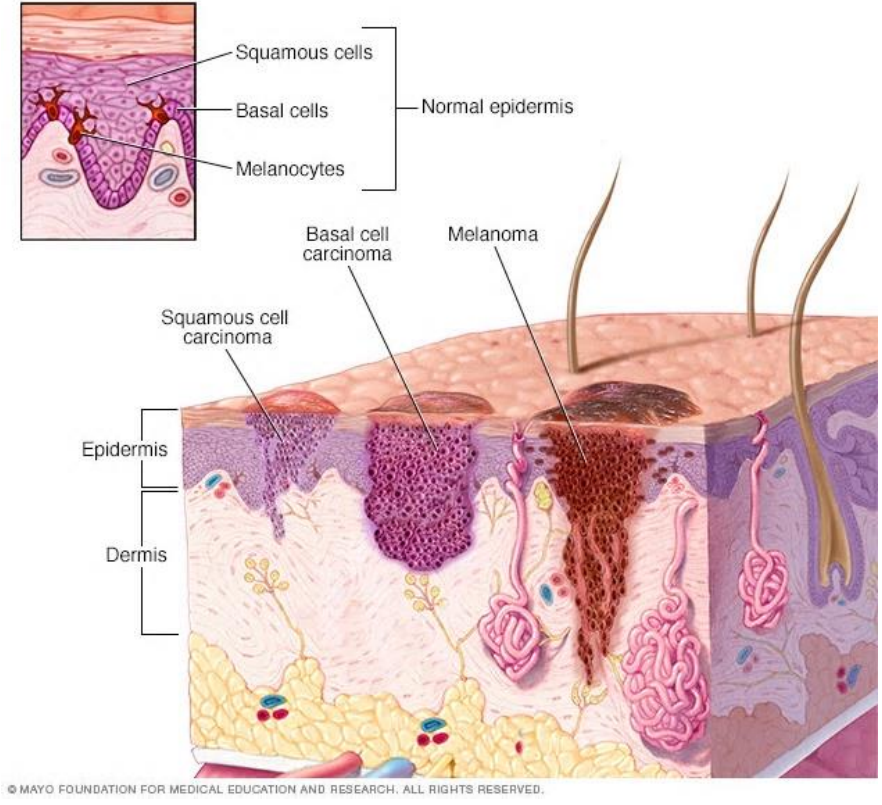
- 16 patients treated with RP1 in combination with Opdivo
  - 5 patients in response - 2 further patients remain on treatment with the opportunity for response
  - These responses (which include patients with extensive visceral disease) wouldn't be expected with a second line of anti-PD1; 4/5 had failed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

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

CSCC opportunity overview

Lead indication overview: CSCC

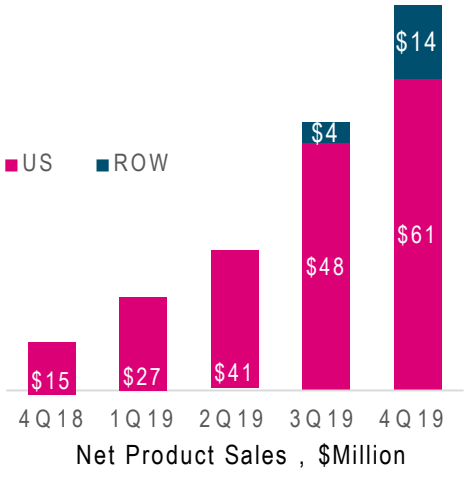
- The second most common skin cancer with ≈700,000 patients annually in the U.S.[1]
- Occurs when DNA damage from exposure to ultraviolet radiation or other agents triggers abnormal changes to squamous cells
- 10% have 'high risk' disease (recurs following initial surgery)
- Approximately 7,000-15,000 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]
- Only approved anti-PD-1 therapy: Libtayo (Regeneron)



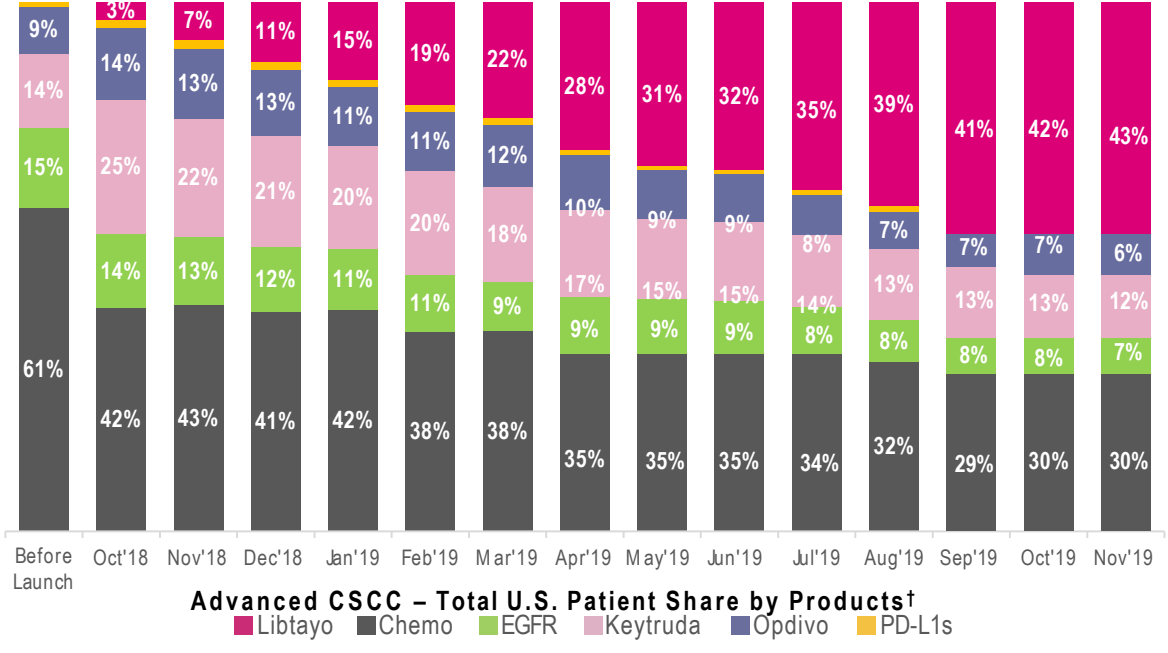
[1]Rogers et al JAMA Dermatol **10** 2015
[2]Clayman et al JCO **23** 2005
[3]Mansouri et al J Am Acad Dermatol **153** 2017
[4]Schmults et al JAMA Dermatol **149** 2013
[5]Motaparthi et al Adv Anat Pathol **24** 2017

Regeneron has paved the way in CSCC

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

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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	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%

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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

Additional clinical trials in CSCC

- 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 years[1]
  - 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

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

Current CSCC data

RP1 + Opdivo data summary in advanced CSCC

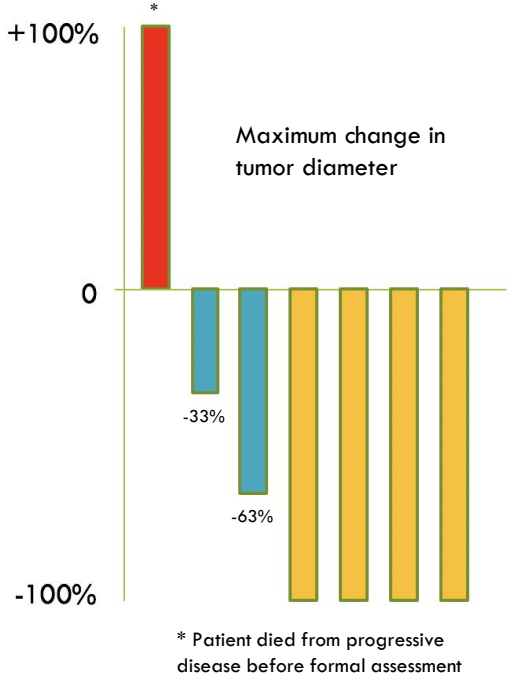
So far, nine patients have been treated with RP1 + Opdivo:

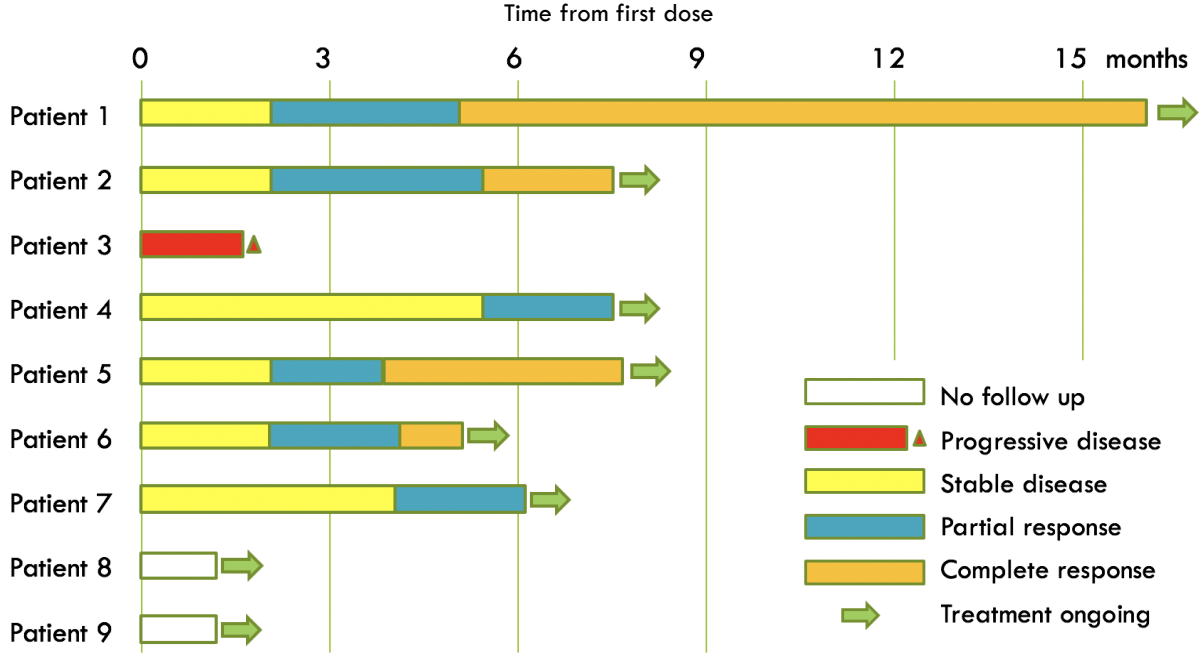
- 4 locally advanced, 5 metastatic, 56% had prior systemic therapy
- 6/7 patients with follow up in ongoing response
  - Patient 1: Ongoing CR
  - Patient 2: Ongoing CR (previously PR)
  - Patient 3: PD
  - Patient 4: Ongoing PR
  - Patient 5: Ongoing CR
  - Patient 6: Ongoing CR (new)
  - Patient 7: 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

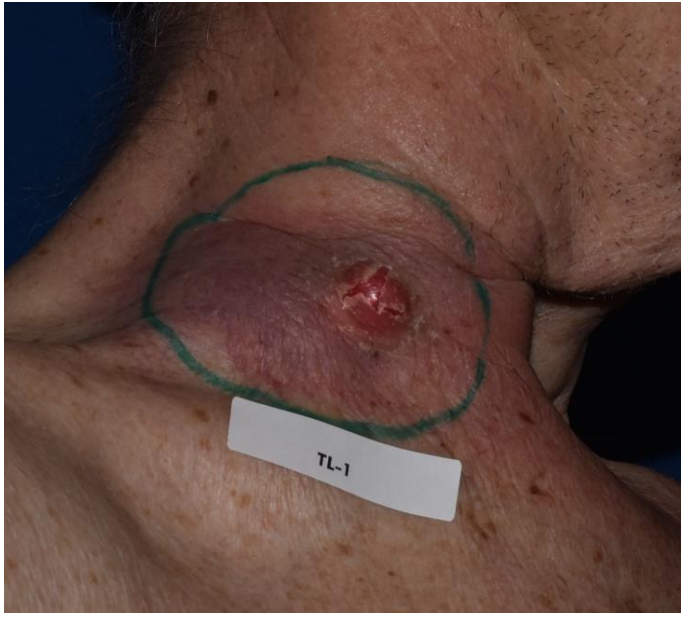




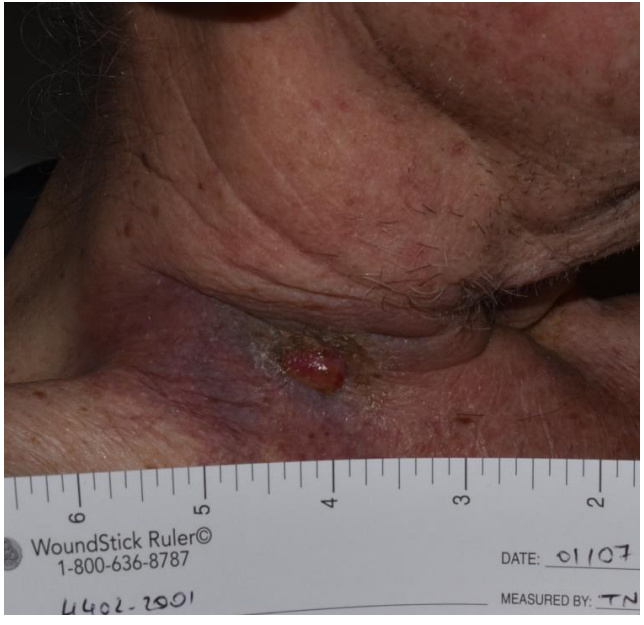
Example CSCC patients

Patient 2 (4402-2001): Ongoing CR

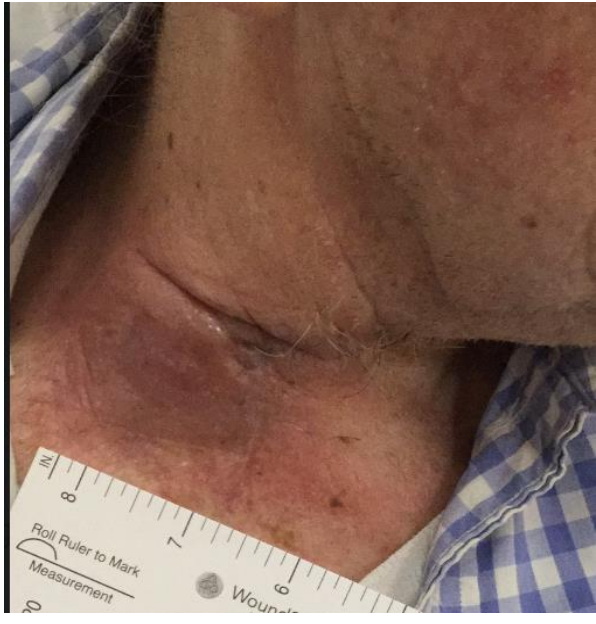
16th June 2019
(baseline)



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



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

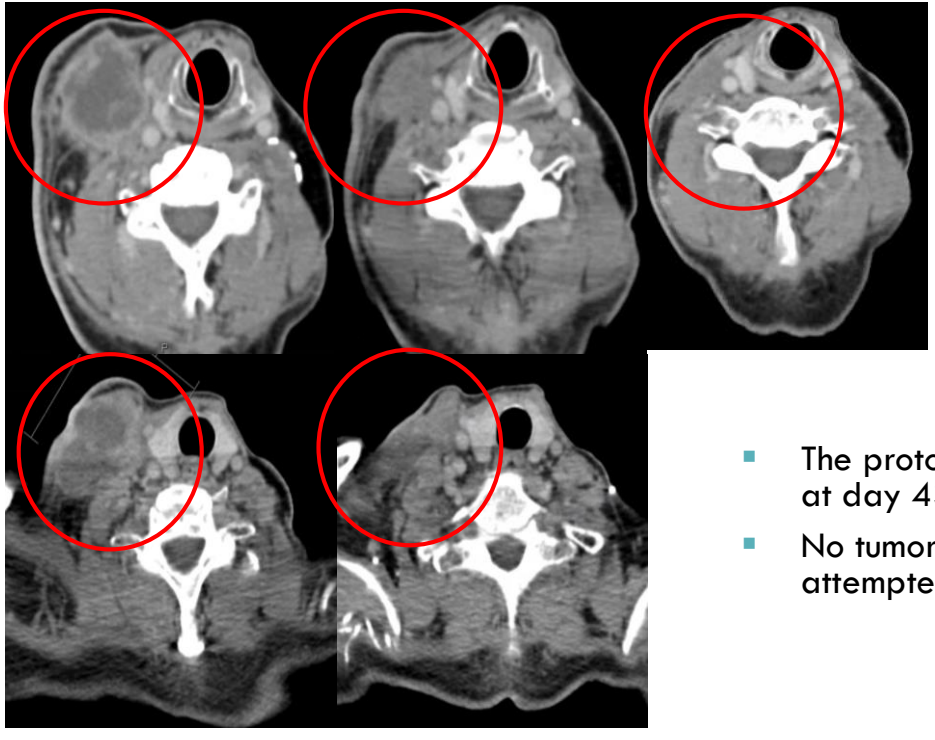


- Patient with recurrent CSCC of the neck (bilateral, right injected), retroperitoneal nodes & bone metastases (not injected)
- Previously treated with cisplatin-based chemoradiation & carboplatin/5-FU
- Both the large injected tumor & the smaller contralateral tumor in the neck reduced considerably 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

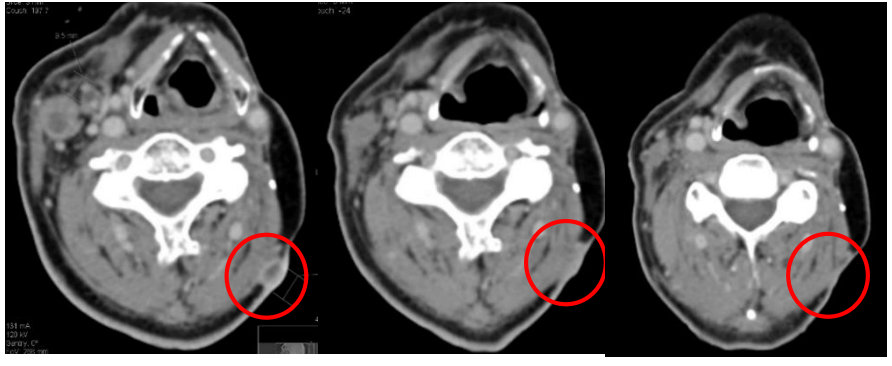
Right neck (injected)

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

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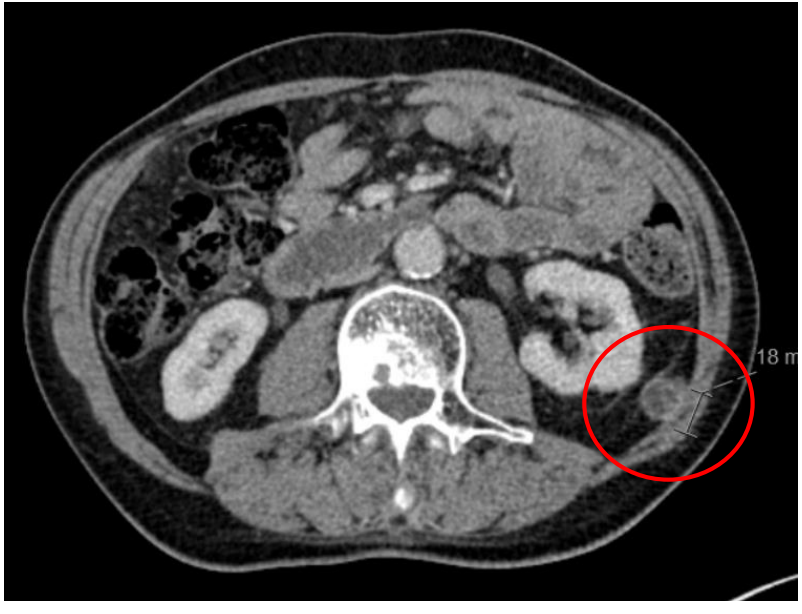
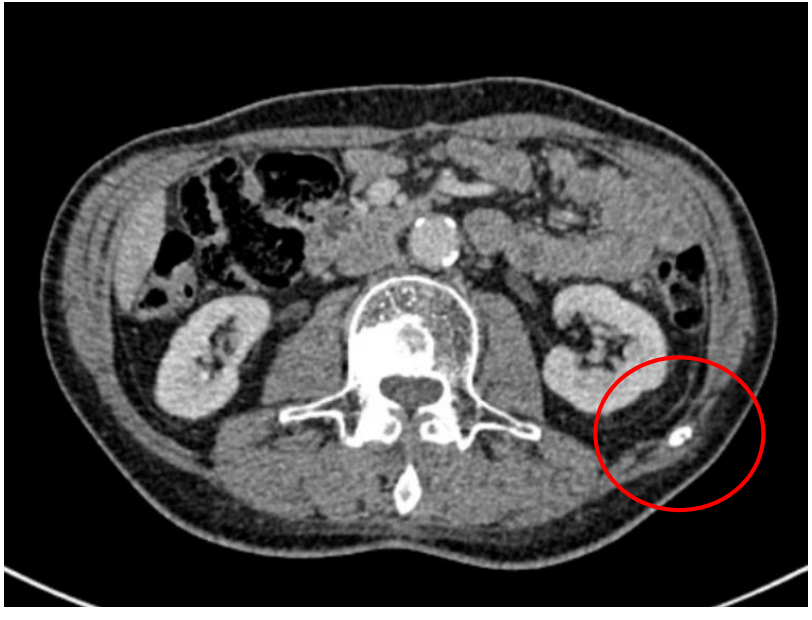
Patient 2 (4402-2001): Ongoing CR

Baseline

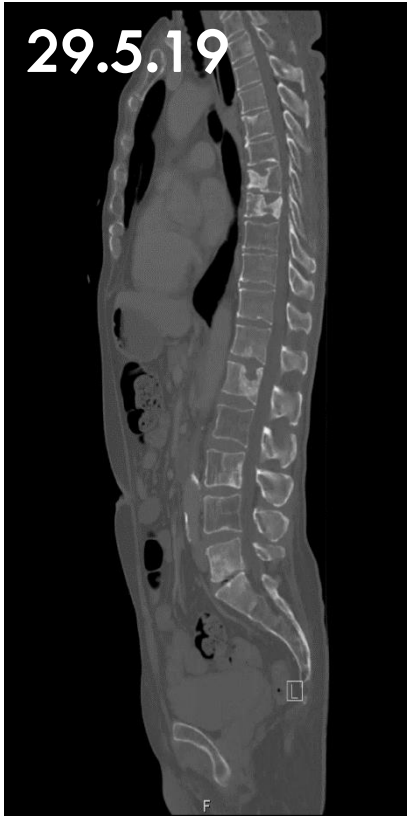


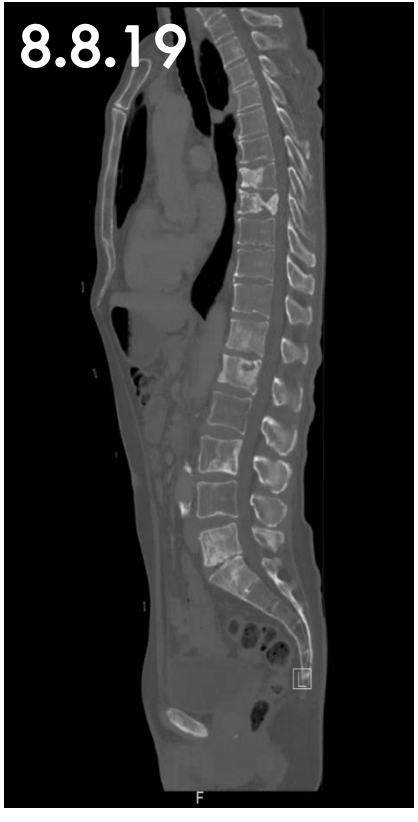
16 weeks

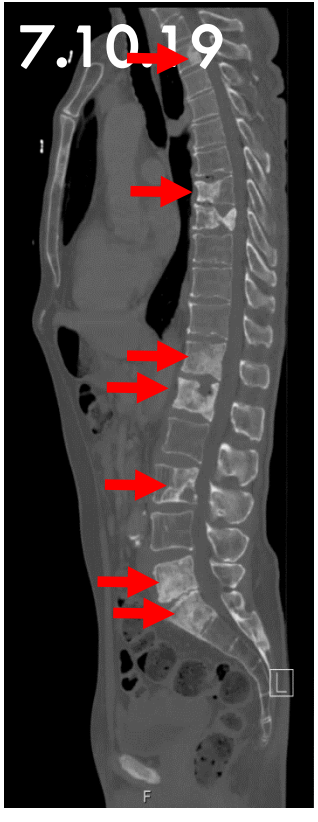


- The patient also had baseline retroperitoneal tumors which have completely resolved

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)

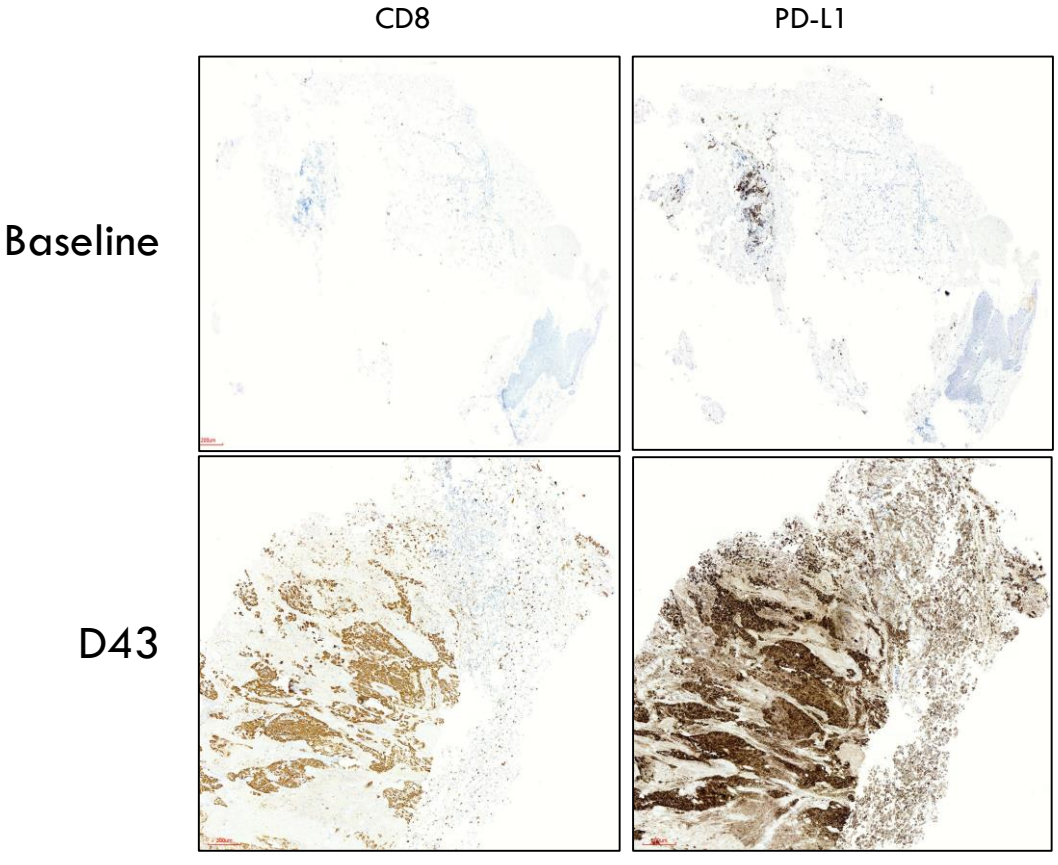
→ Indicates area of increased bony sclerosis, indicative of healing response of lytic metastases

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



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Patient 4 (4402-2004): Ongoing PR

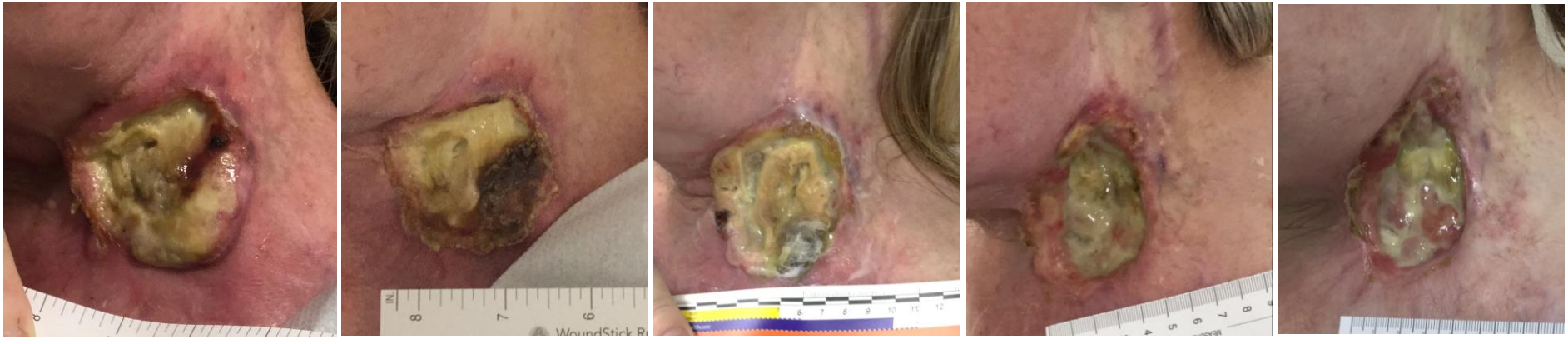
2nd Sept 2019 (pre-dosing)

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

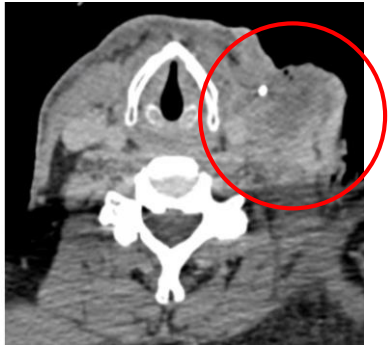
15th Oct

2nd Dec

13th Jan



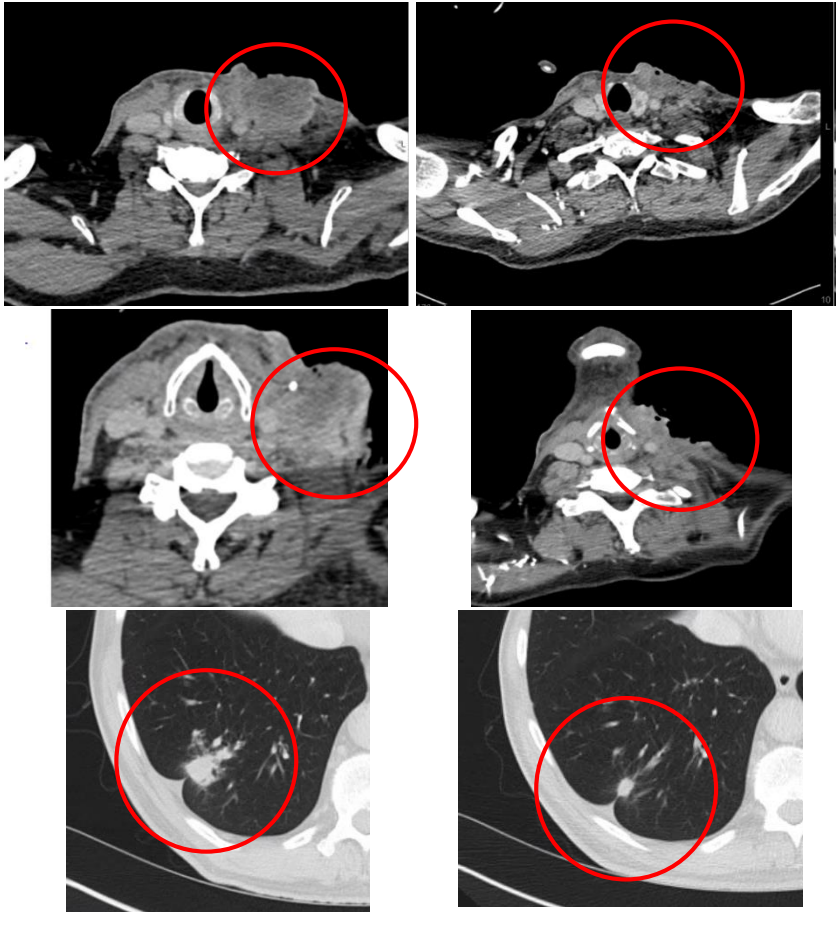
Baseline scan



- 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

28th August 2019 | 25th October 2019



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

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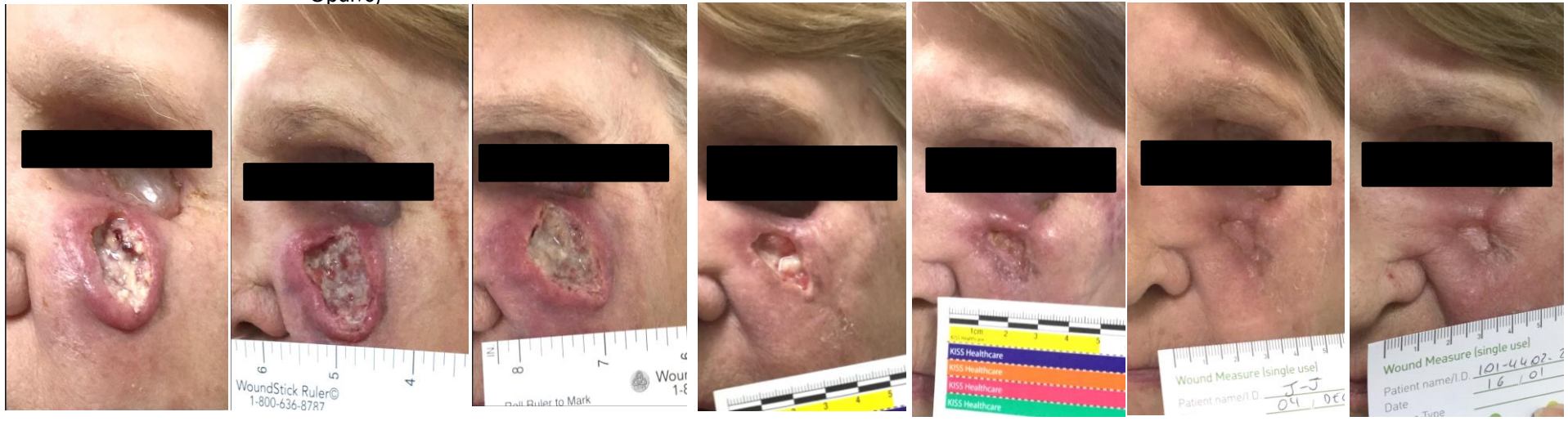
Patient 5 (4402-2005): Ongoing CR

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	16th Jan 2020



- 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

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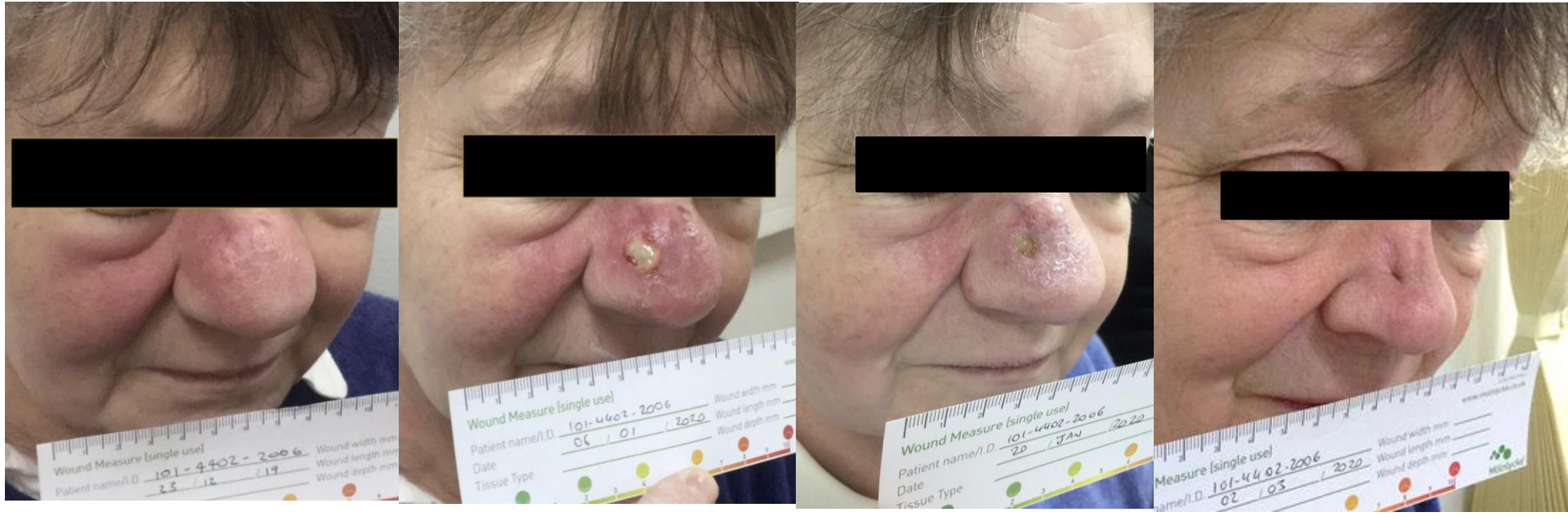
Patient 6 (4402-2006): Ongoing CR

23rd December 2019 (Baseline)	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

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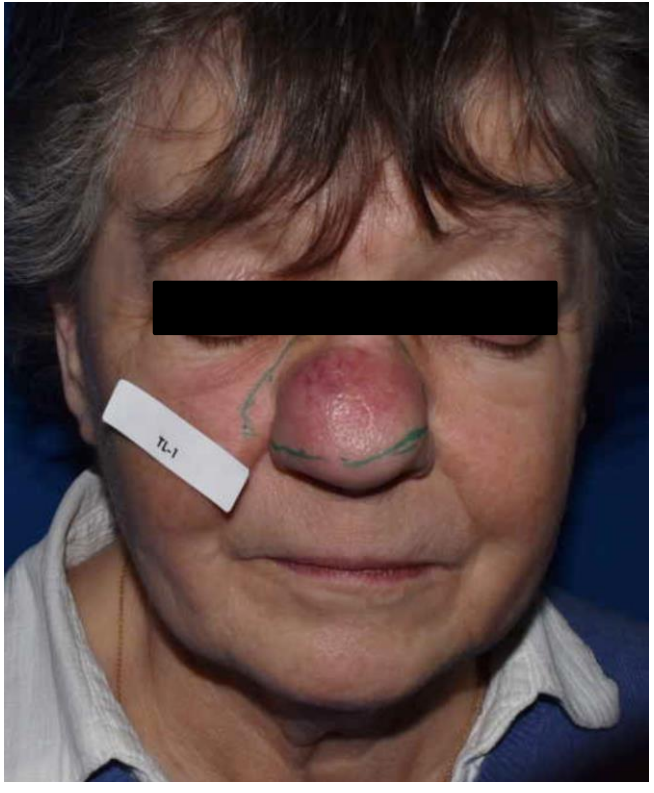
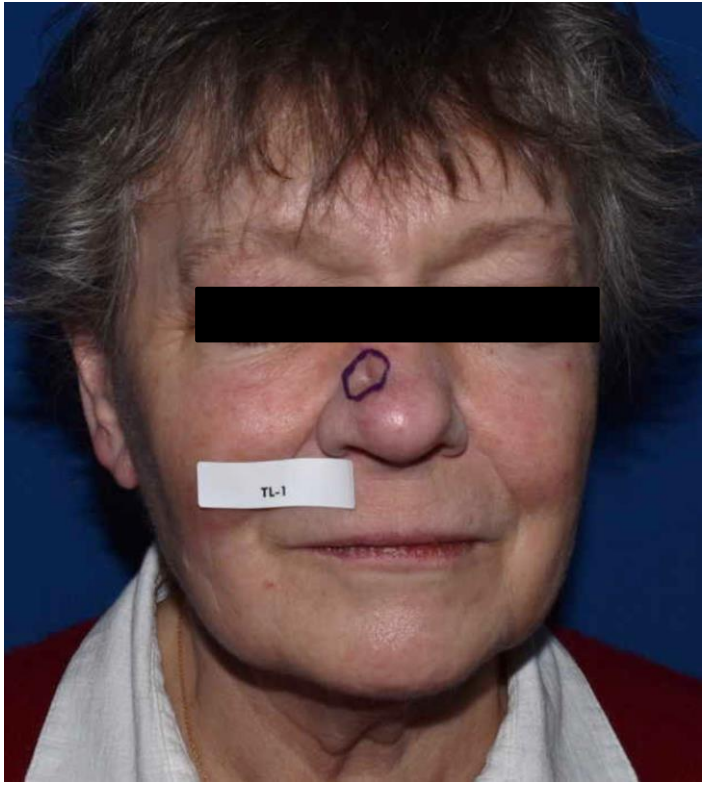
Patient 6 (4402-2006): Ongoing CR

Baseline



Day 57



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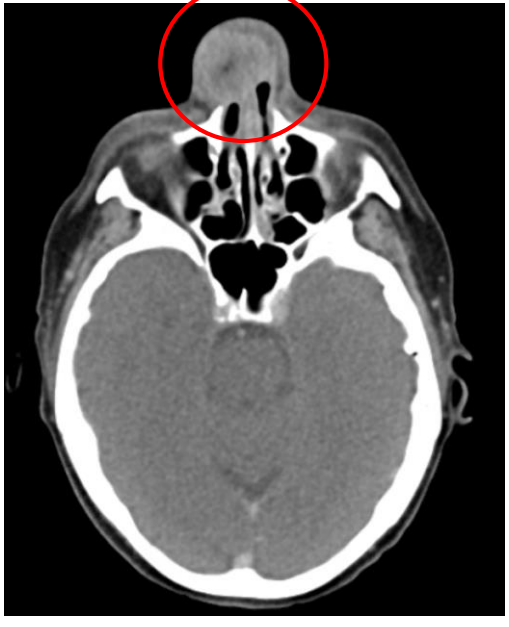
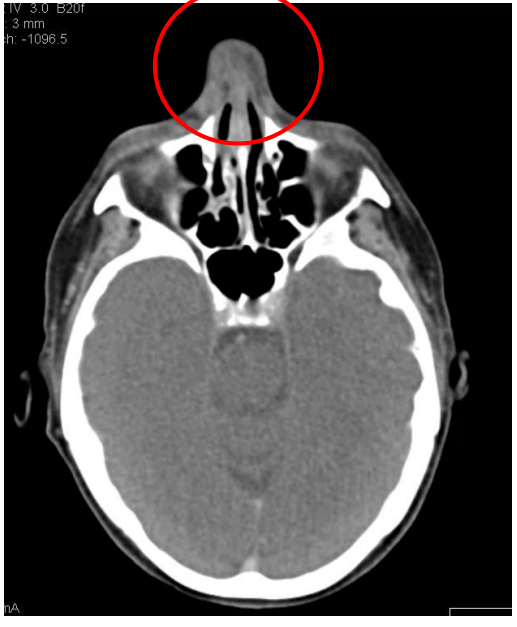
Patient 6 (4402-2006): Ongoing CR

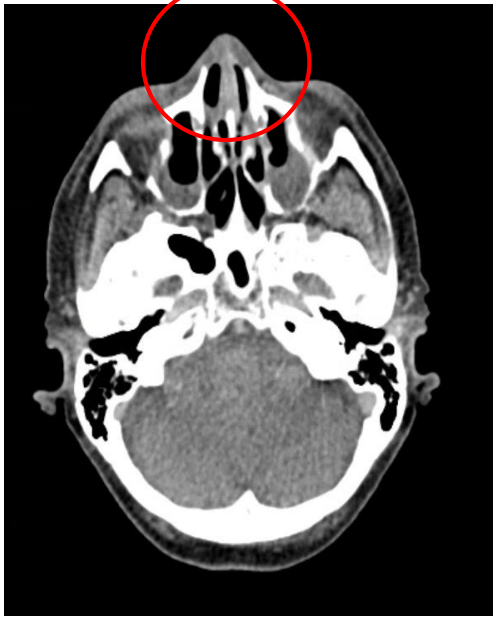
18th Dec 2019
(Screening)



2nd Feb 2020



14th April 2020*



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

- The alternative to study treatment was rhinectomy

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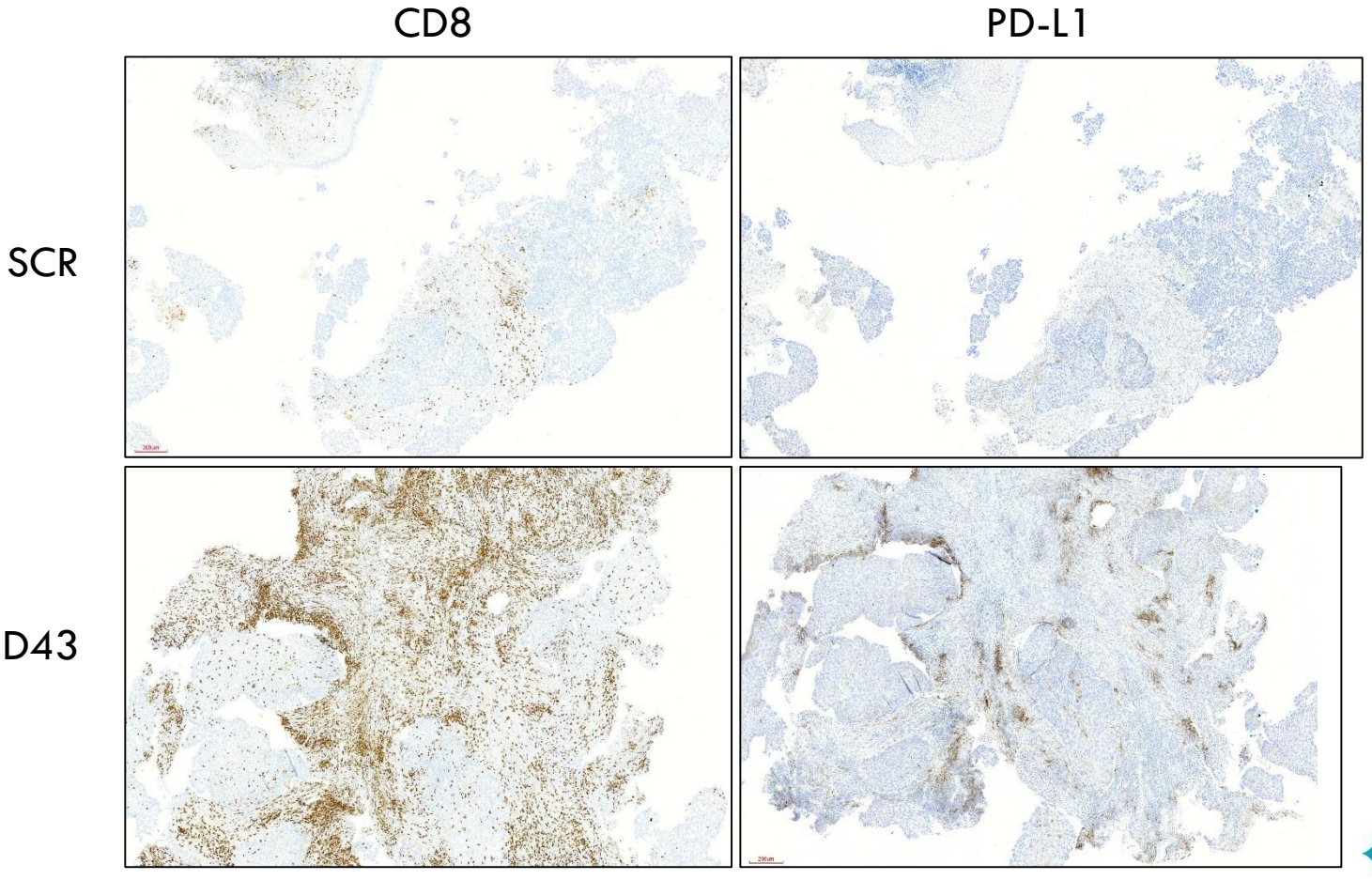
Patient 6 (4402-2006): Ongoing CR



Anti-PD-1 refractory melanoma opportunity overview

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; 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

Current melanoma data

Melanoma data summary

- 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 patients in this immature data set was:
  - Anti-PD1 refractory cutaneous melanoma (N=16 [8 having had prior anti-CTLA-4 and anti-PD1]): Nine patients showed initial clinical benefit**, seven ongoing, with five so far having met the formal definition of response***
  - Anti-PD1 naive cutaneous melanoma (N=8): Eight patients showed initial clinical benefit**, six ongoing, with four so far having met the formal definition of response
  - Mucosal melanoma (N=6): 3 patients showed initial clinical benefit**, two ongoing (one anti-PD1 naive, one having had prior anti-PD1), with both having met the formal definition of response***
  - Uveal melanoma (N=6): Five patients showed initial clinical benefit** (all anti-PD1 refractory), two ongoing, one having a 27.3% reduction by RECIST (uni-dimensional measurement)/61% reduction by WHO (bi-dimensional measurement)

*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

Melanoma patients treated with RP1+ Opdivo

	All	Cutaneous melanoma	Mucosal melanoma	Uveal melanoma
Number	36	24	6	6
Age: Range	28-95	28-95	40-78	44-85
Prior anti-PD1	25	16*	5	4
Prior single agent anti-PD1	9	7	1	1
Prior anti-PD1/anti-CTLA-4	16	9	4	3
Prior anti-PD1 %	69%	67%	83%	67%
Stage IIIc	2	2	0	0
Stage IV M1a	7	3	4	0
Stage IV M1b	11	10	1	0
Stage IV M1c	16	9	1	6
Stage IV M1b/c %	75%	79%	33%	100%

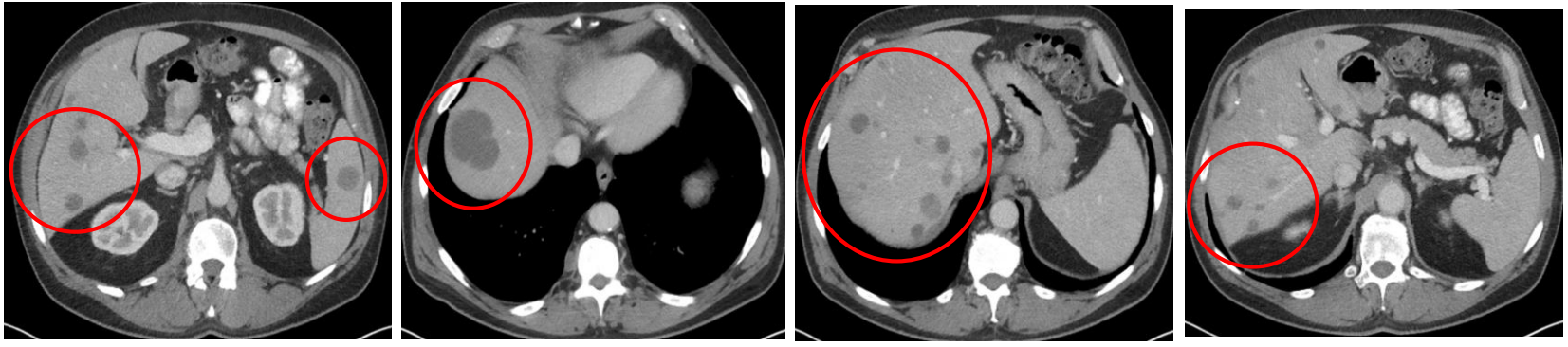
* 87.5% with Stage IV M1b/c (visceral) disease

Example melanoma patients

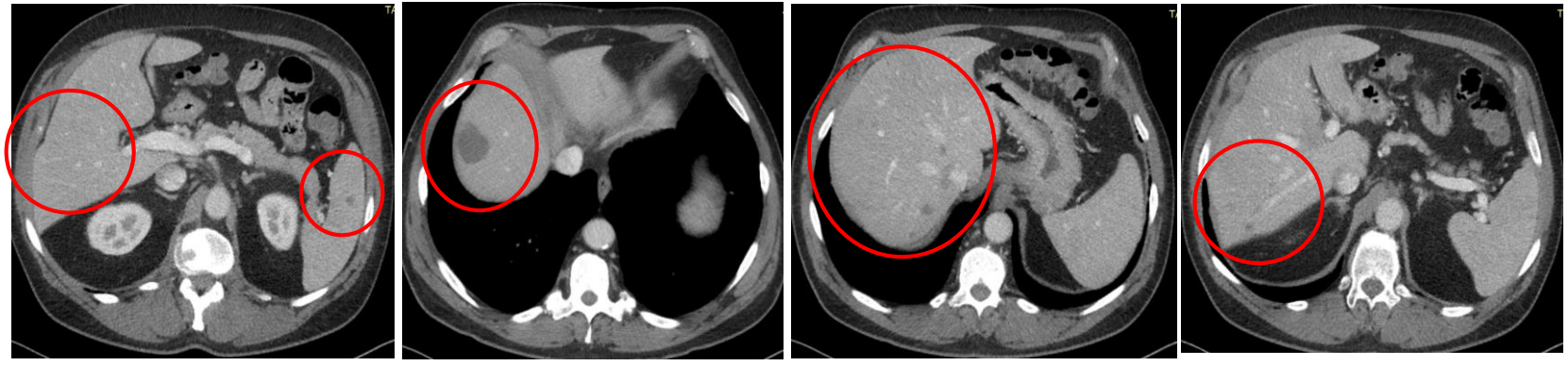
Anti-PD1 refractory cutaneous melanoma patients

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

22nd Oct 2019 (Screening)



9th March 2020



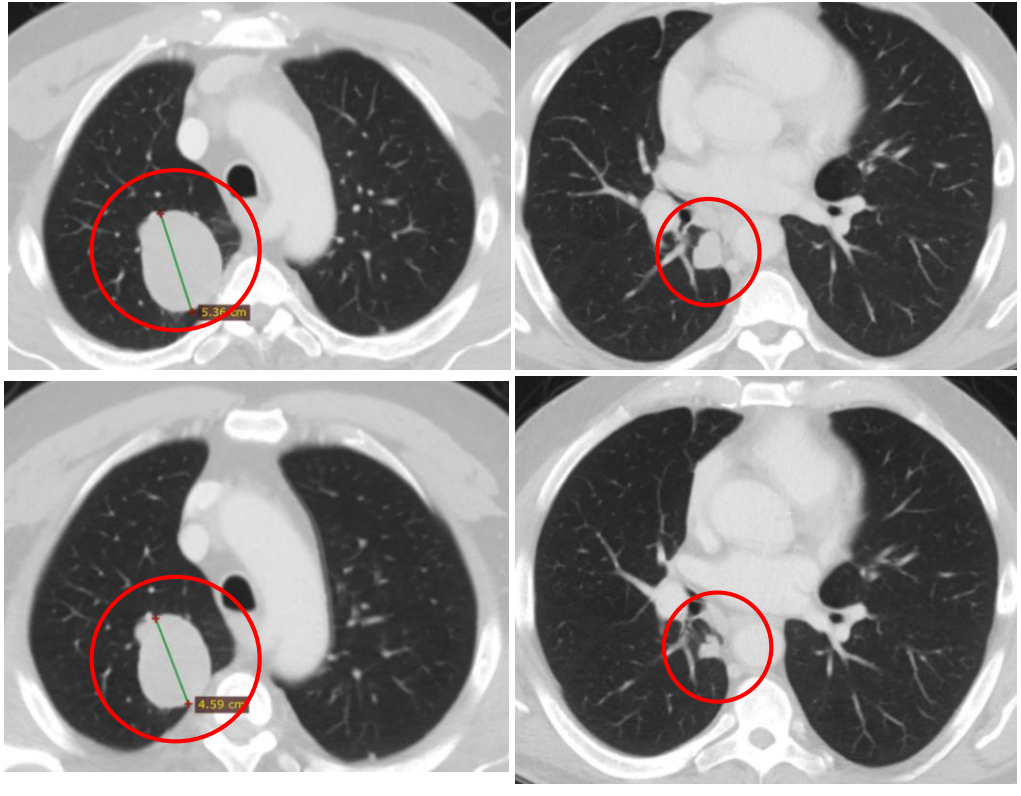
D43 liver biopsy tumor free

Reduction of injected & uninjected liver lesions

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

22nd Oct 2019 (Screening)

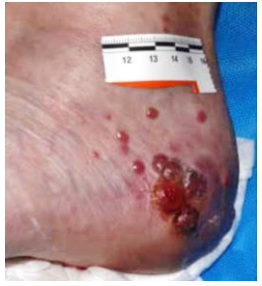
9th March 2020

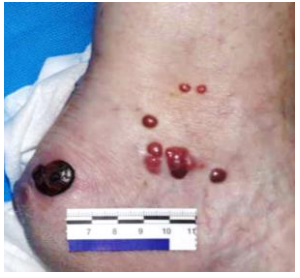


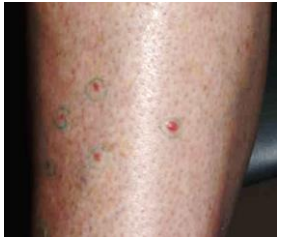
Reduction of uninjected lung lesions

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

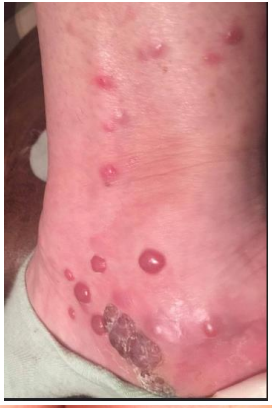
1st July 2019
(screening)

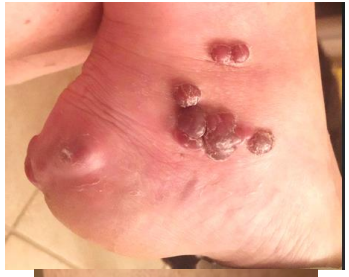


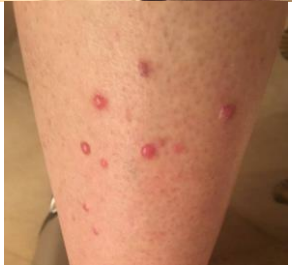




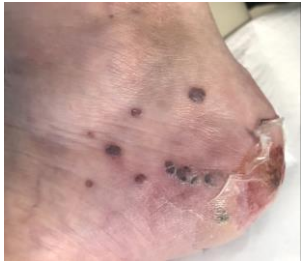
26th August 2019

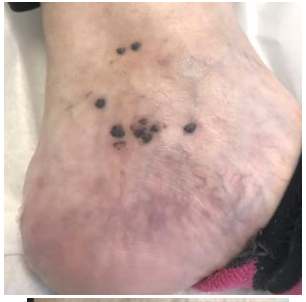


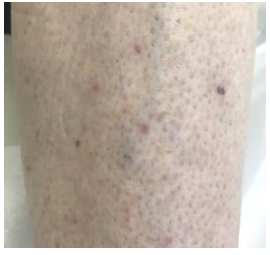




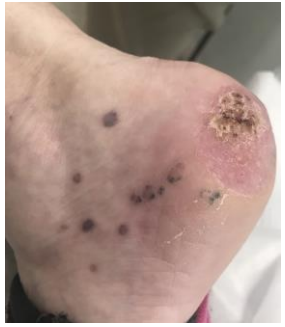
22nd October 2019

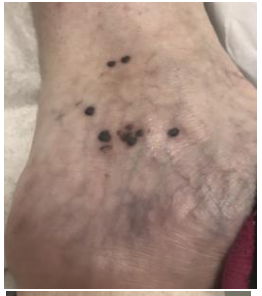


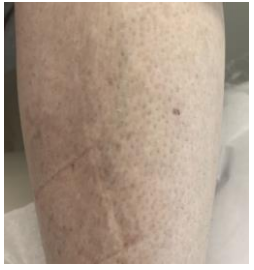




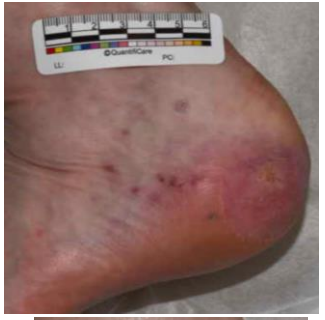
5th November 2019

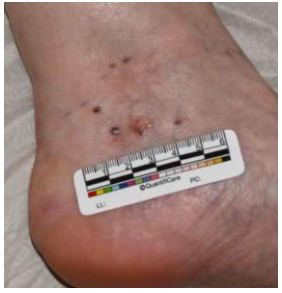






7th April 2020





Biopsy awaited to confirm CR

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

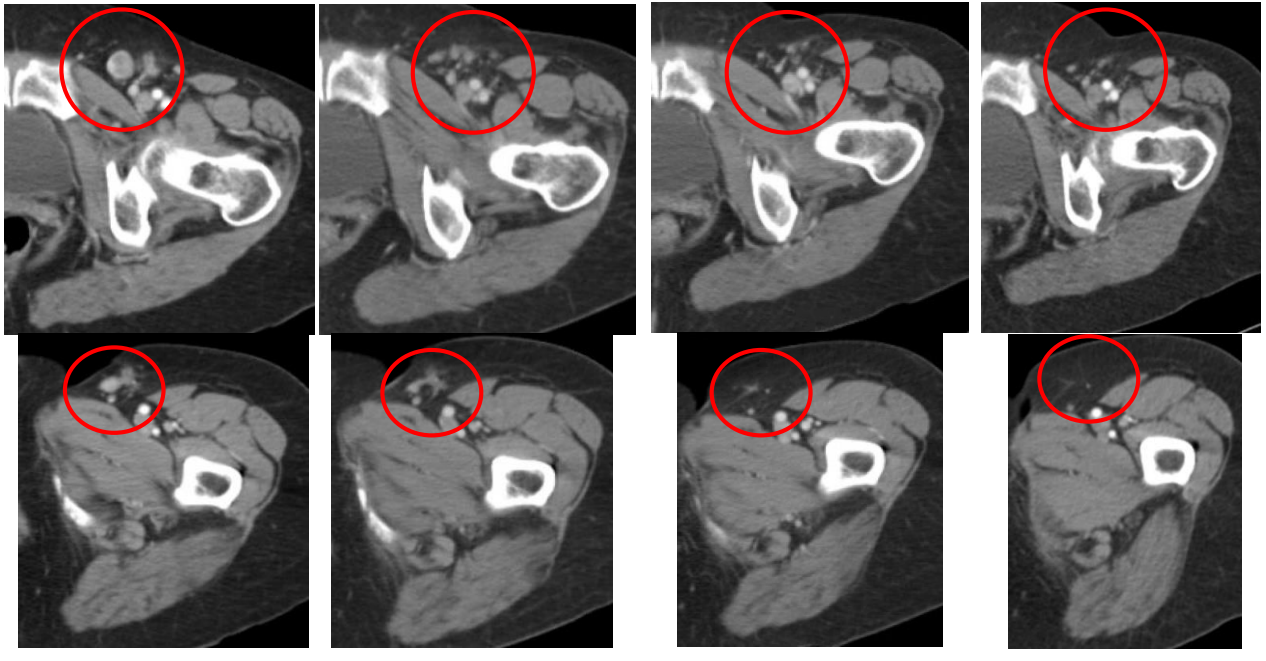
Patient #: 1119-2003 (Yervoy/Opdivo refractory melanoma) – ongoing PR

2nd July 2019 (screening)

17th Sept 2019

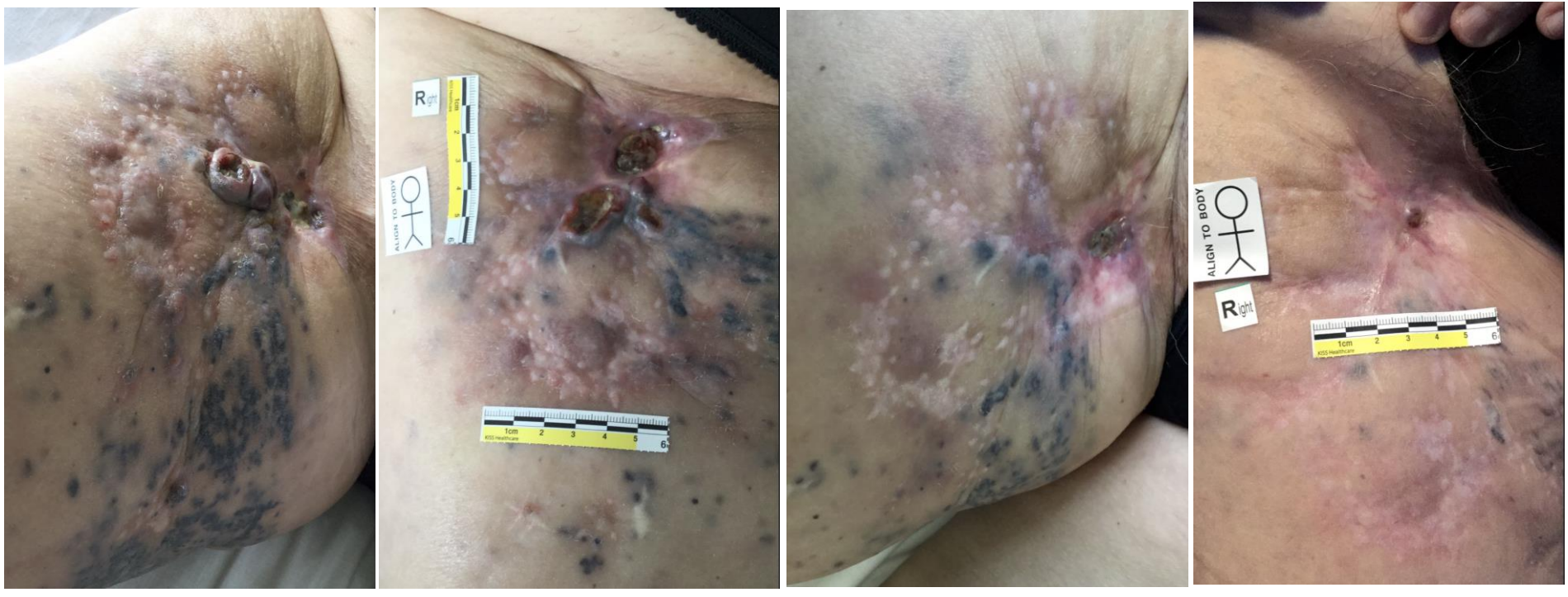
19th Nov 2019

7th April 2020



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

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



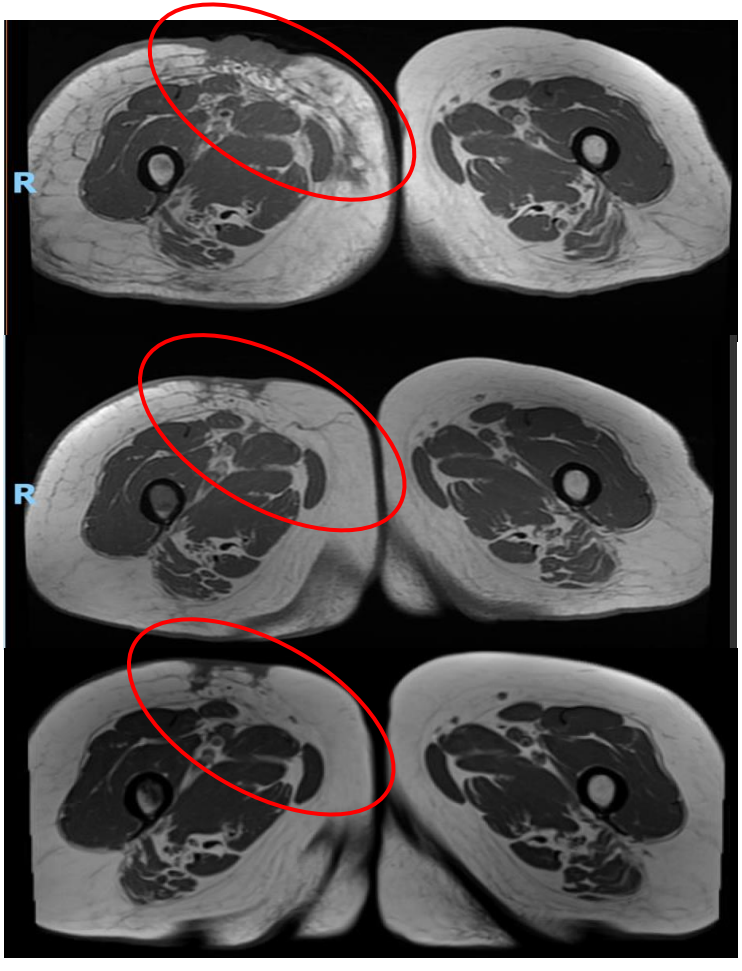
- Baseline disease in the thigh, groin & lungs
- Tumors in the thigh flattened after the first dose of RP1, i.e. prior to Opdivo & extensive oedema rapidly reduced

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

May 2019 (Baseline)

August 2019

December 2019

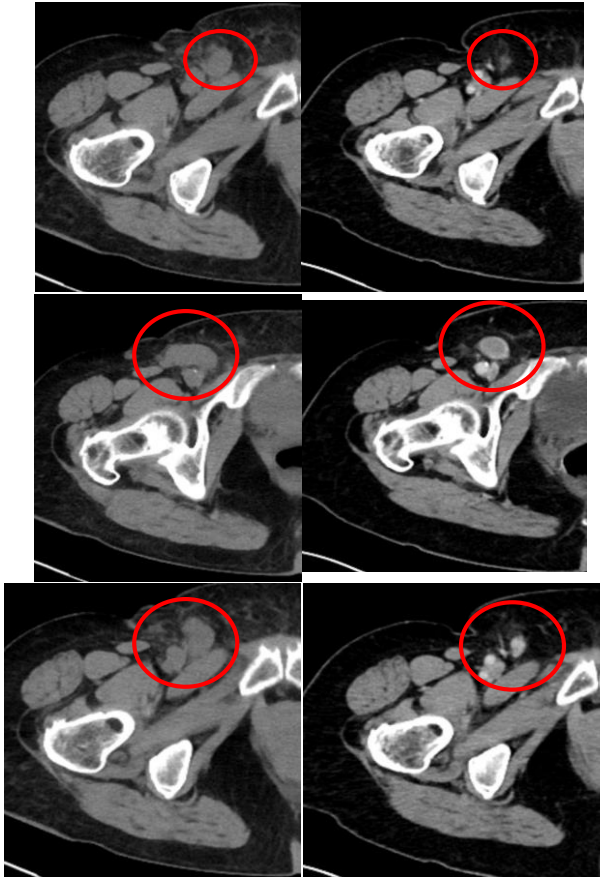


- Patient quality of life has also greatly improved, from being essentially immobile to being fully mobile
- Patient remains on treatment at 10 months

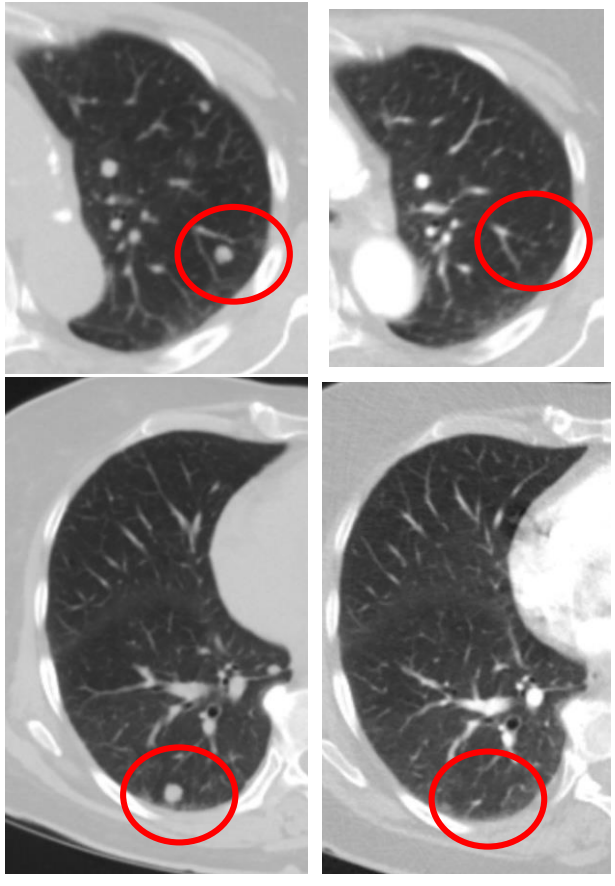
Replimune

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

22nd May 2019 16th March 2020



22nd May 2019 16th March 2020



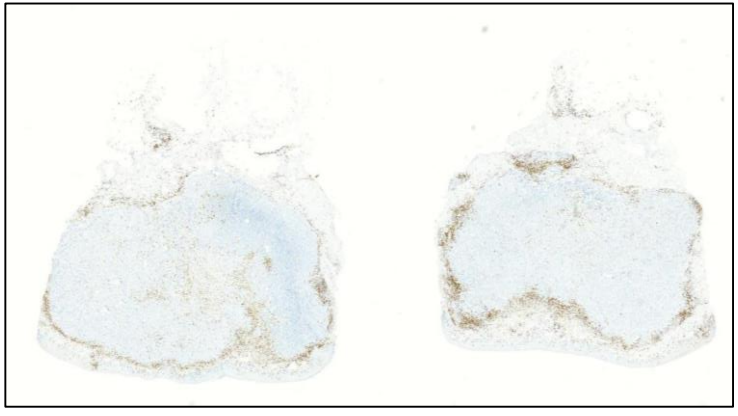
Reduction of uninjected lung lesions

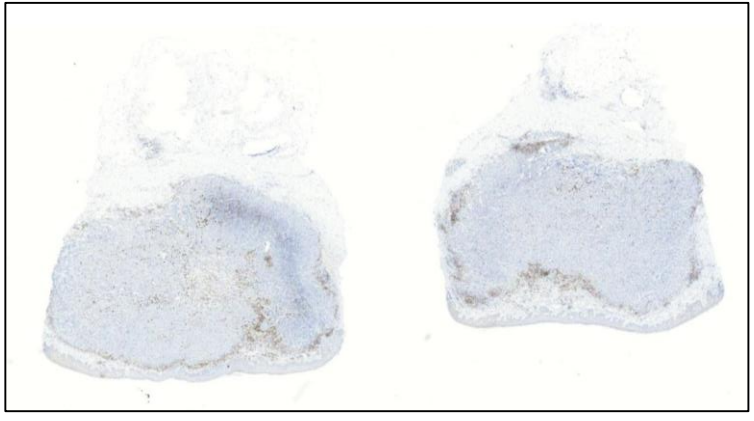
Patient #: 4403-1003: Reversal of T cell exclusion with RP1 combined with Opdivo

CD8

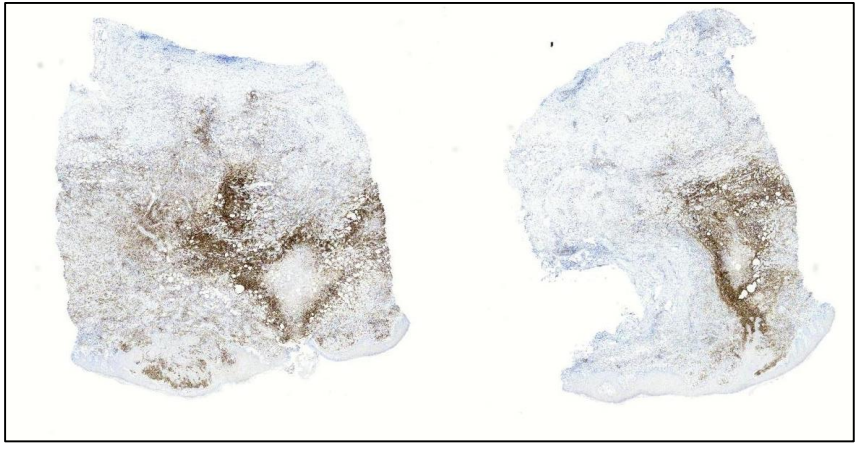
PD-L1

Baseline





Day 43 biopsy

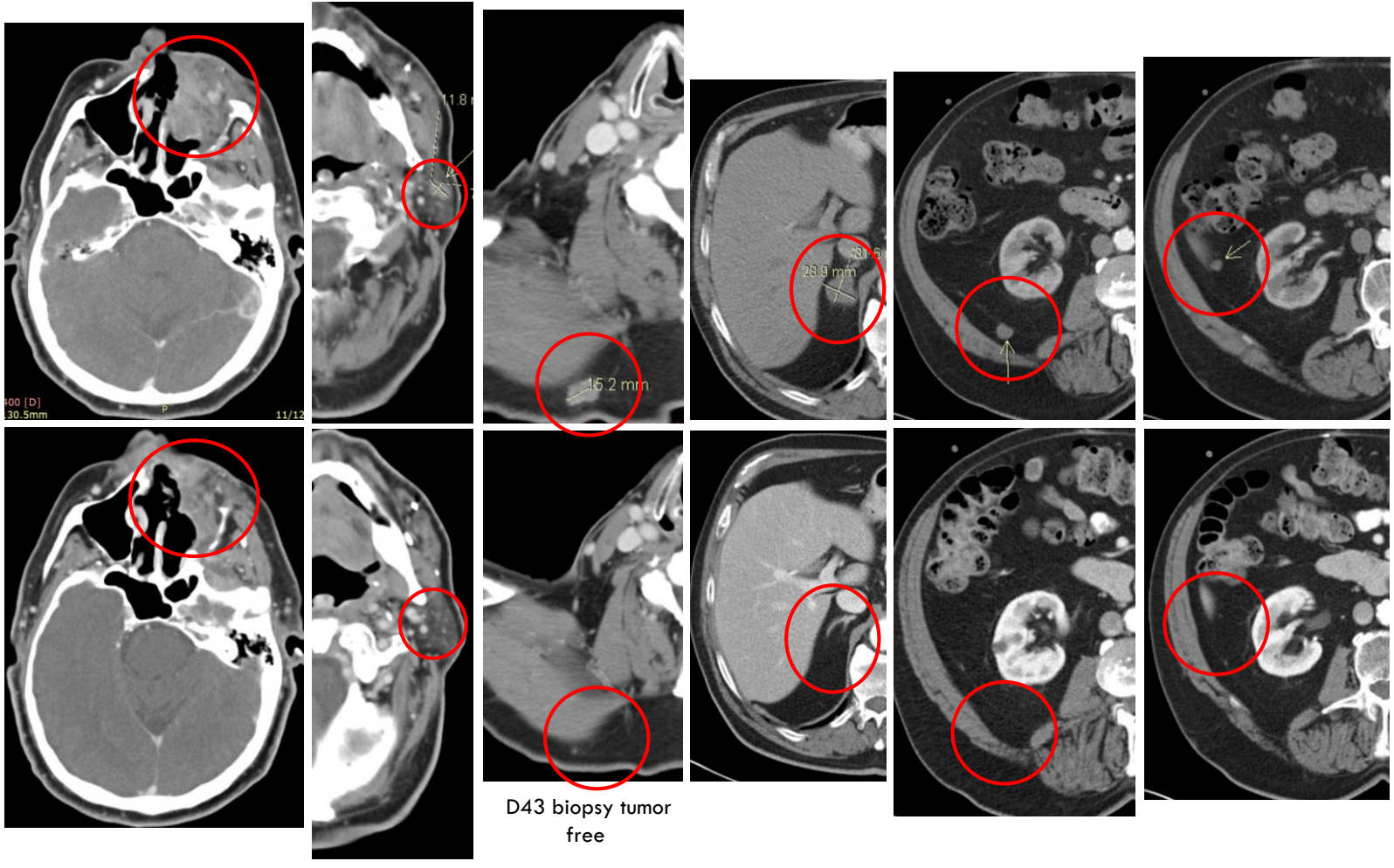


Mucosal melanoma patients

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

12th Nov 2019 (Screening)

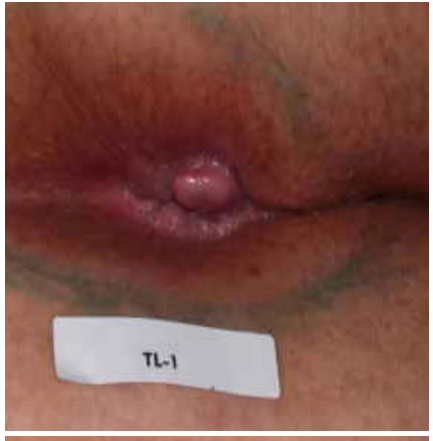
12th March 2020



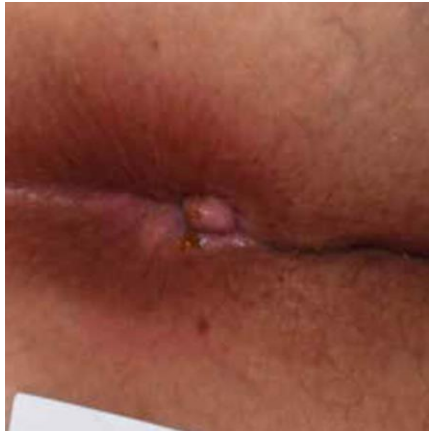
D43 biopsy tumor free

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

20th Aug 2019 (Screening)



15th Jan 2020

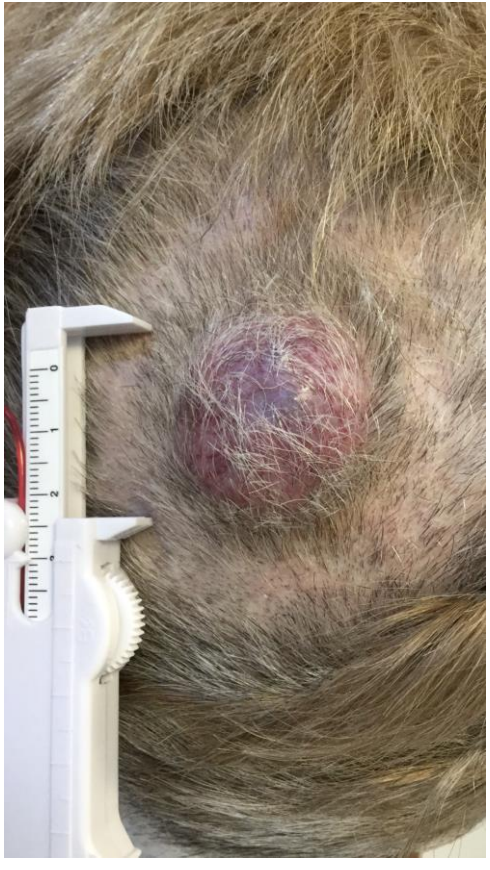


Excision biopsy tumor free 1st April 2020

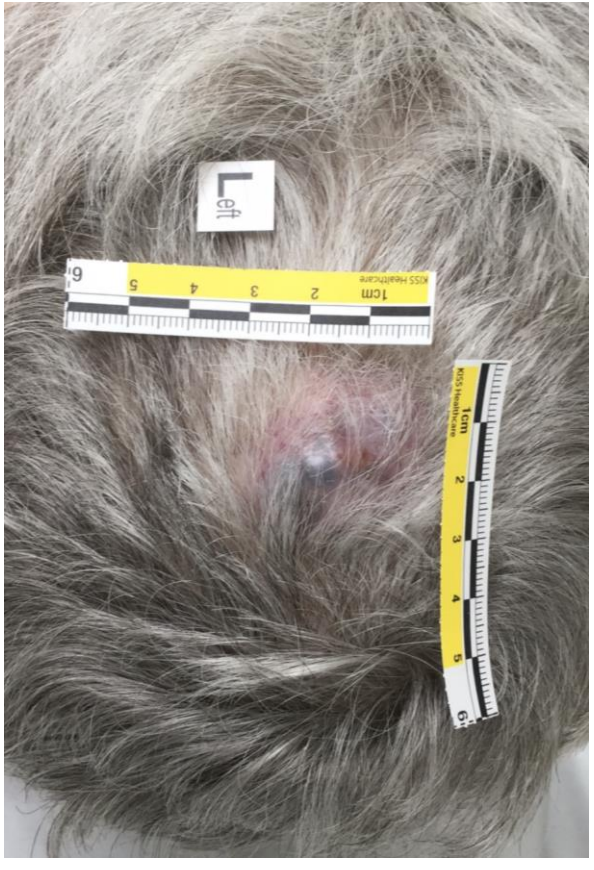
Uveal melanoma patients

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

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.

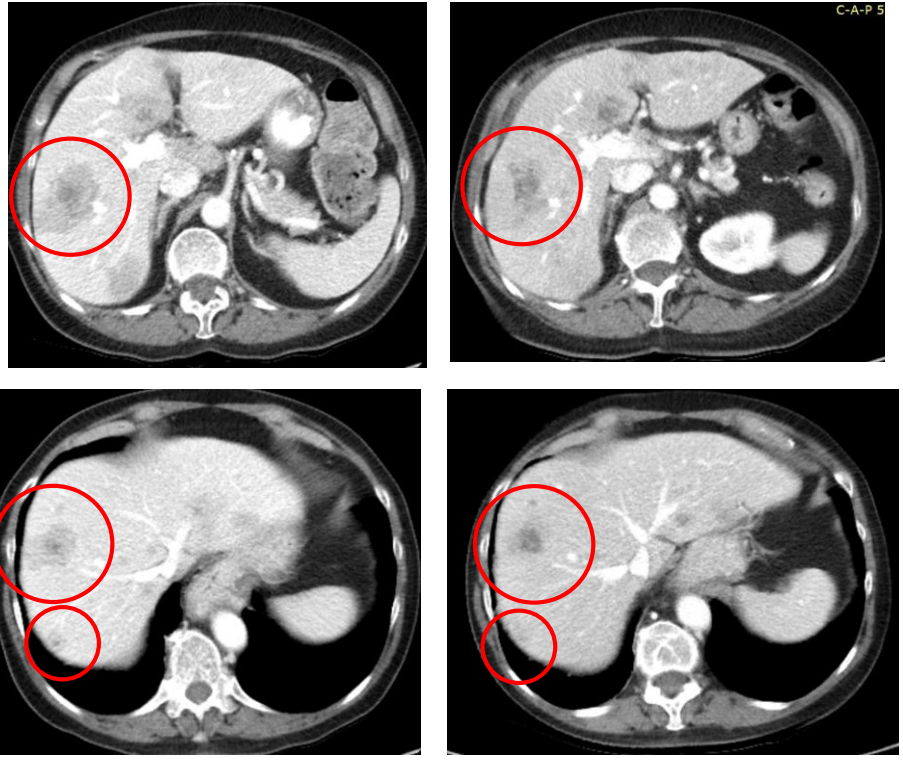
Initial response in numerous c/sc deposits, including uninjected (some biopsied showing no remaining residual tumor) and large scalp lesion. Other disease stable.

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

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

25th Sept 2019 (Screening)

3rd April 2020



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

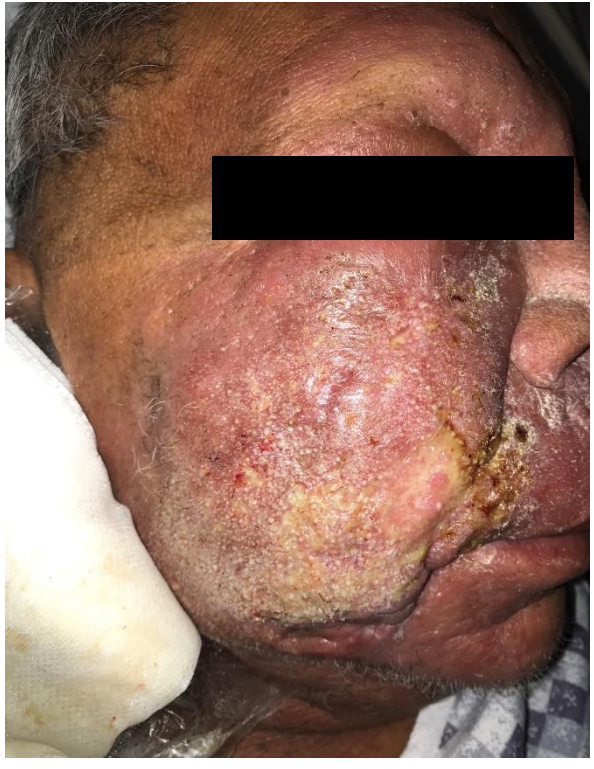
Safety of RP1 combined with Opdivo in patients with skin cancers

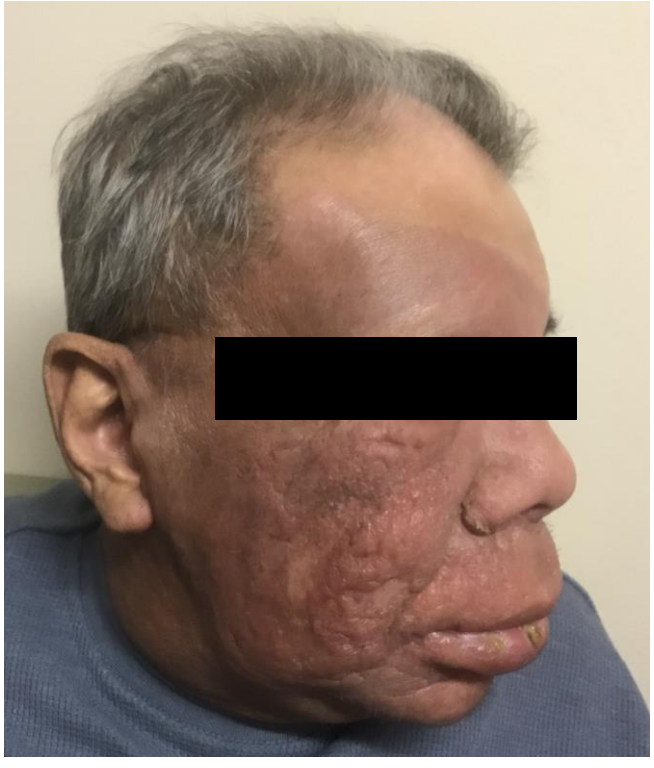
Treatment related treatment emergent adverse events (TEAEs) N=41				
Preferred term	Grade 1-2 (>15%) # (%)	Grade 3 (all) # (%)	Grade 4 (all) # (%)	Grade 5 (all) # (%)
Pyrexia	17 (41.5)	1 (2.4)	0	0
Chills	16 (39.0)	0	0	0
Influenza like symptoms	11 (26.8)	0	0	0
Fatigue	8 (19.5)	5 (12.2)	0	0
Decreased appetite		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

RP1 in other tumor types

Activity in a patient with angiosarcoma (ongoing PR)





- Patient withdrew from treatment due to Opdivo side effects

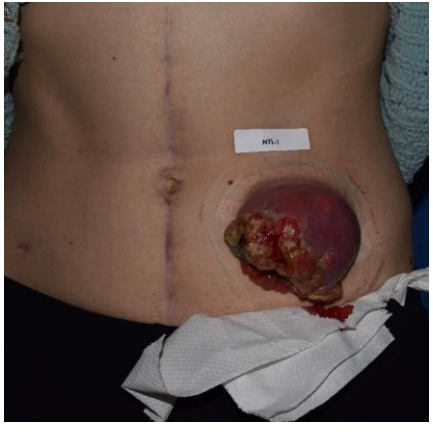
6th November 2019

18th February 2020

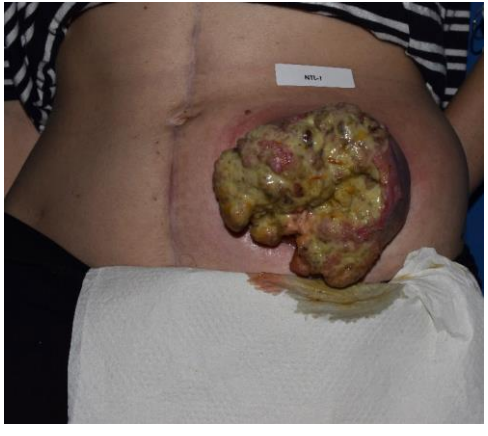
Replimune

MSI-H colorectal cancer

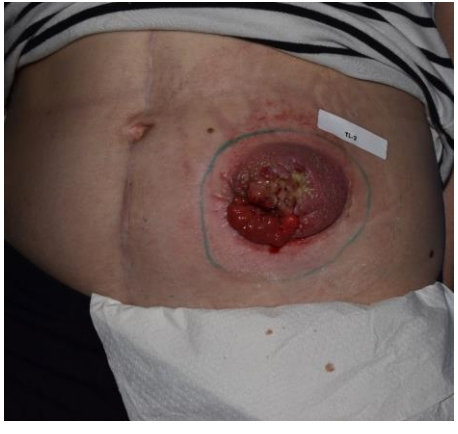
- 22 year old female with MSI-H rectal cancer
- Prior neoadjuvant FOLFOXIRI
- Treated with RP1 combined with Opdivo
- Ongoing PR
- Biopsy “No tumour present - strips of dysplastic epithelium and inflammatory exudate only”



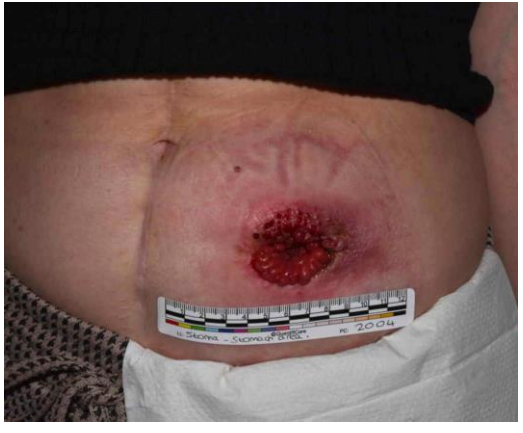
9th October 2019



20th November 2019



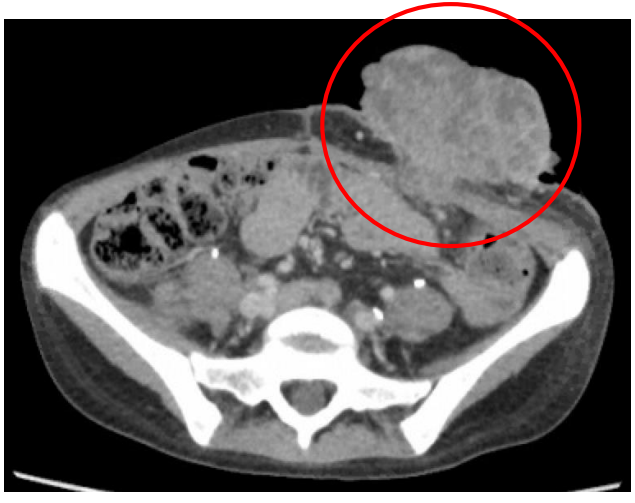
15th January 2020



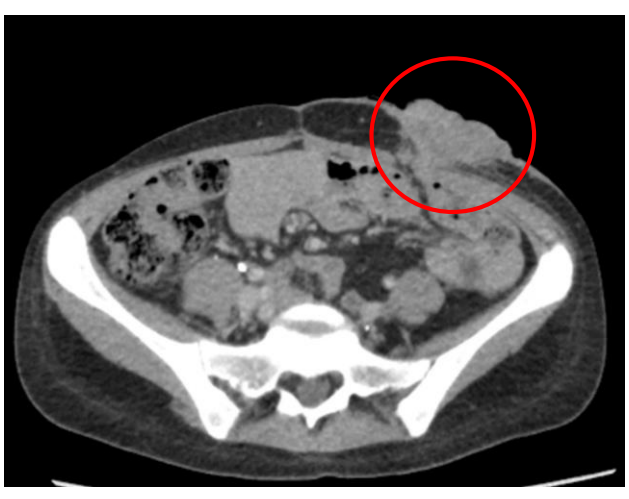
25th March 2020

MSI-H colorectal cancer

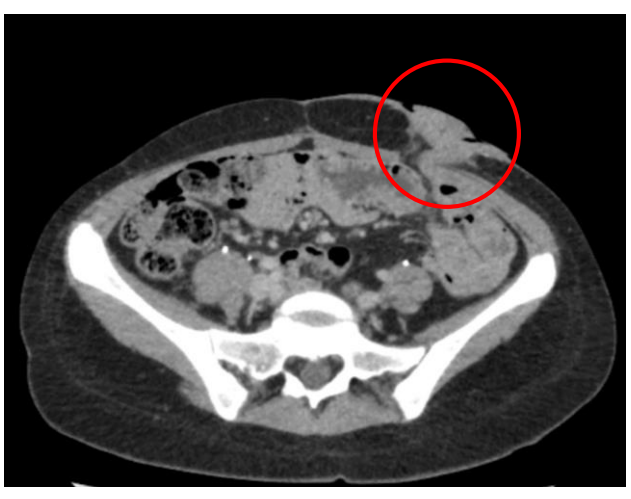
- Latest scan (March 2020) shows 87% reduction (including of uninjected abdominal disease)



4th Dec 2019 (C5)



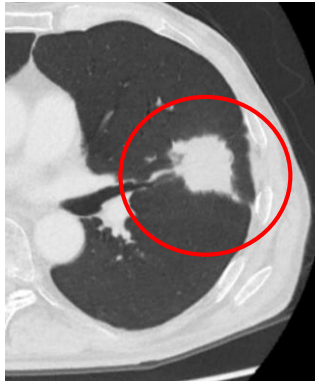
29th Jan 2020 (C8)



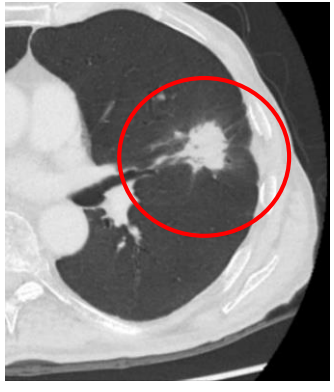
25th March 2020 (C11)

Esophageal cancer

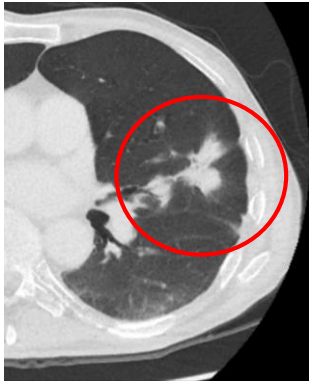
- Heavily pre-treated esophageal cancer (8 prior therapies)
- Lung lesions & lesions around the esophagus.
- Treated with RP1 combined with Opdivo
- Ongoing PR at 10 months



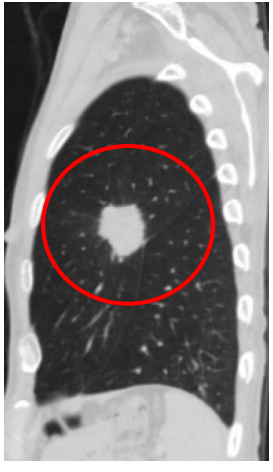
Baseline



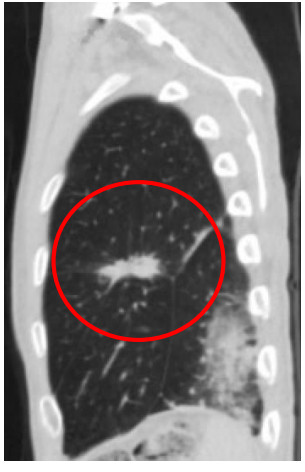
C5



C11

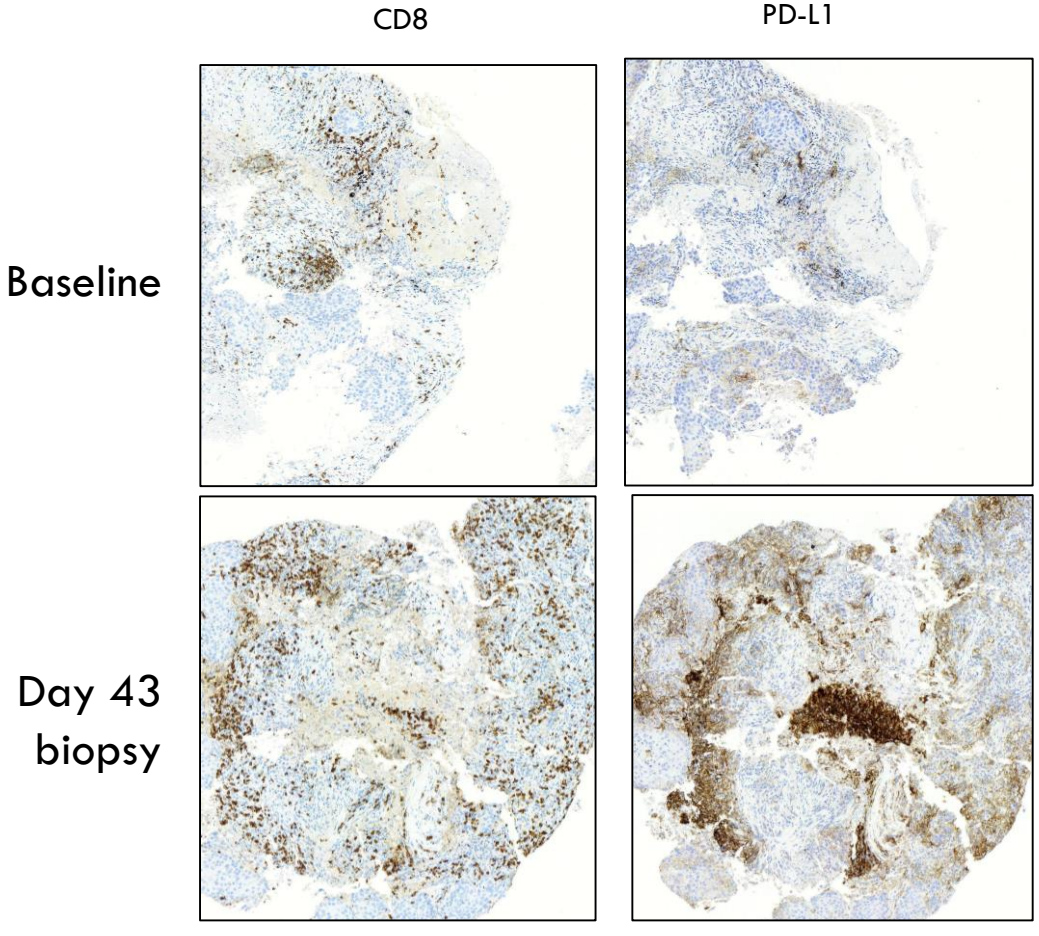


Baseline



C11

Esophageal cancer: CD8 T cell & PD-L1 staining



Replimune

New cohort in anti-PD1 refractory NSCLC & termination of bladder cohort

- Due to the changing competitive landscape in bladder cancer Replimune has elected to direct resources to a new high-value target & terminate the enrollment of the bladder cancer cohort

- 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

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Beyond immune responsive tumor types:

RP2 & RP3

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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
- 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
    - 4-1BBL: Promotes the expansion of cellular & memory immune responses
    - Phase 1 trial alone & combined with anti-PD1 expected to initiate this year

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Conclusions from today's data: *"Building the Second Cornerstone of IO"*

- 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*

- 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.

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