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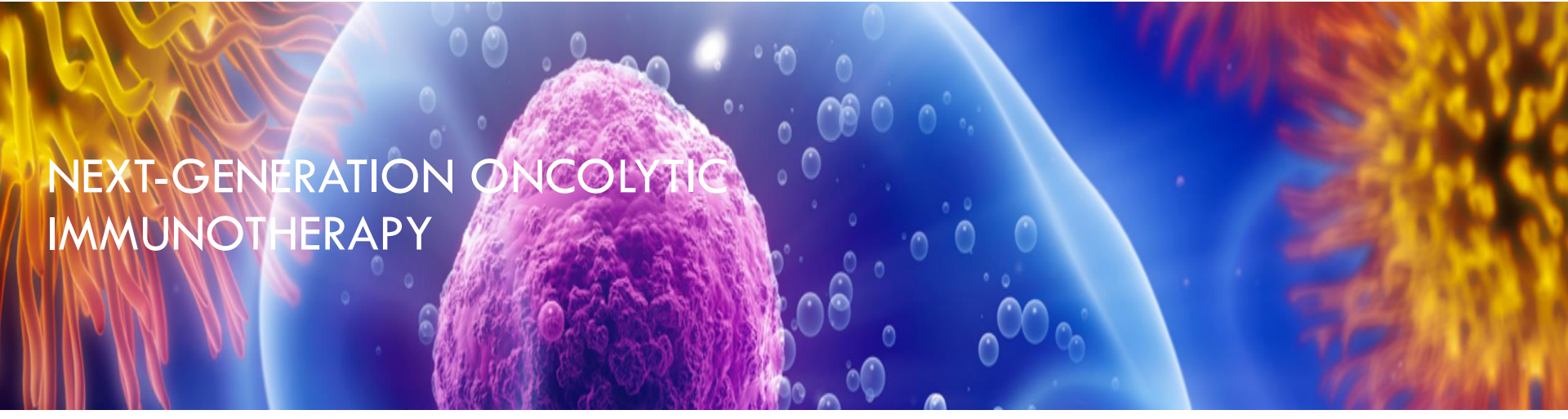

June 3rd 2021 Data Update

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 Data to be Presented	Robert Coffin, Ph.D. / Founder & Head of R&D
Melanoma & NMSC Data Updates	Mark Middleton, Ph.D. / University of Oxford
RP2 Data Update	Mark Middleton, Ph.D. / University of Oxford
Beyond skin cancers – what's next?	Robert Coffin, Ph.D. / Founder & Head of R&D
Summary Remarks	Philip Astley-Sparke / Chief Executive Officer

Proprietary 'Immulytic' oncolytic immuno-gene therapy platform

- Intended to maximally activate a systemic immune response against a patient's cancer
- Intended to establish Replimune's products as the second cornerstone of immuno-oncology

High rate of COMPLETE RESPONSE in patients treated with RP1 (vusolimogene oderparepvec) combined with Opdivo® (nivolumab)

- Registration directed development supported by compelling efficacy & safety profile
  - CERPASS study in advanced cutaneous squamous cell carcinoma (CSCC) of RP1 combined with Libtayo® (cemiplimab) enrolling
  - IGNYTE study of RP1 combined with Opdivo® in anti-PD1 failed cutaneous melanoma enrolling
- Dosing underway in 30 patient anti-PD1 failed non-small cell lung cancer cohort

Next generation product candidates optimized for superior immune stimulation, intended to treat immunologically 'cold' tumors

- RP2 – single agent activity demonstrated in heavily pre-treated immune insensitive tumor types; initial data combined with Opdivo® being presented today
- RP3 – single agent dosing in high dose cohort commencing

Company positioned for long term growth to support a new pillar in oncology treatment

- Commercial scale manufacturing facility operational; first GMP batches filled
- CCO hired; Commercial planning activities underway
- Well capitalized to deliver; cash ~$476m as of March 31st

Replimune's best in class platform

1. Optimized to infect, replicate in, and kill tumor cells – intended to maximize tumor destruction & immunogenic cell death (immunogenic 'Signal 1')
   - Potent clinical HSV strain selected from comprehensive screen for anti-cancer lytic activity
   - Modifications for selective replication in tumors sparing healthy tissue (ICP34.5 deleted for selectivity, US11 upregulated)
   - Fusogeneic protein (GALV-GP R-) increases killing & immunogenic cell death 10-100 fold
2. Further armed with immune activating transgenes intended to maximize T cell co-stimulation ('Signal 2') & systemic immune activation (including through induction of inflammatory cytokines: 'Signal 3')

	Programs:	RP1	RP2	RP3
RH018A viral strain	Optimized tumor infectivity and lytic activity, engineered for selective replication	✓	✓	✓
GALV-GP R-	Increased tumor killing & immunogenic cell death	✓	✓	✓
GM-CSF	DC expansion & maturation	✓	✓	
Anti-CTLA-4	APC/T-cell feedback loop blocking		✓	✓
CD40L	APC maturation, T-cell co-stimulation, inflammatory cytokine release (IFN-γ)			✓
4-1BBL	T-cell co-stimulation, NK-cell ADCC, APC maturation, inflammatory cytokines release (IL-2, IL-8, IL-12, IFN-γ)			✓

Replimune's fusion-enhanced backbone virus described in Thomas et al *JITC* 2019 (7)

Practical and comprehensive activation of a tumor specific immune response

Our platform offers ***significant potential advantages compared to competing approaches,*** including cell-based therapies and personalized cancer vaccines

	Replimune's Immulytic platform	Cell-based therapy (including TILs)	Personalized cancer vaccines
"Off the shelf" – no patient-specific manufacturing	✓	✗	✗
Commercially attractive COGS	✓	✗	✗
Efficacy from different immune modalities – both innate & adaptive immunity stimulated	✓	✗	✗
Attractive safety profile, with limited high-grade side effects	✓	✗	✓
Applicable to nearly all patients with solid tumors – not limited by surface markers or mutations	✓	✗	✗

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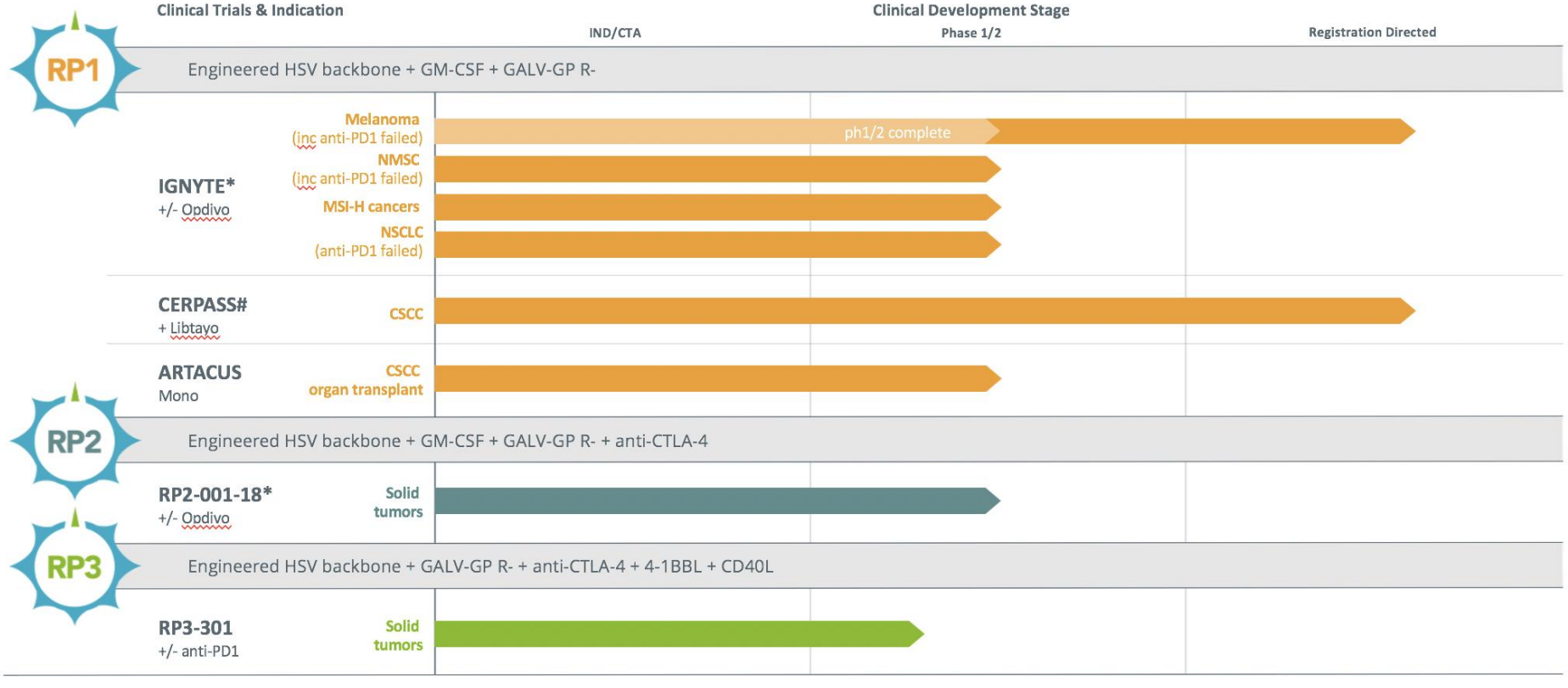
Replimune's pipeline



* Under a clinical trial collaboration & supply agreement with BMS for the supply of Opdivo – full commercial rights retained by Replimune
# Under a clinical trial collaboration agreement with Regeneron; 50:50 sharing of clinical trial costs – full commercial rights retained by Replimune

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Summary of IGNYTE (RP1+Opdivo) skin cancer data

- CSCC (N=15; enrollment ongoing)
  - Complete responses continue to accumulate with a current CR rate of 46.6%[+] & ORR of 60%
    - SITC 45% & 72.7% respectively; A number of patients with particularly high tumor burden were recently enrolled who rapidly progressed
    - 7[+]/9 responses are CRs (one of the dual primary endpoints for the CERPASS study; 5/8 at SITC)
  - Durability of response continues to be demonstrated with responses ongoing out to >600 days
- Melanoma (N=30; fully enrolled)
  - Responses continue to be durable
  - The ORR for anti-PD1 naïve melanoma is now 62.5% (50% at SITC)
  - The ORR for anti-PD1 failed cutaneous melanoma remains at 31.25%
- Other NMSC (N=11; enrollment ongoing)
  - Further activity demonstrated in other non-melanoma skin cancers (Merkel cell, basal cell carcinoma & angiosarcoma)
- Re-initiation of RP1 (2nd treatment course) has been well tolerated, with clinical activity seen
- Data continues to highlight that RP1 combined with Opdivo is well tolerated & drives deep & durable responses in skin cancer

Data continues to support the current registration-directed clinical trials with RP1 combined with Opdivo or Libtayo in anti-PD1 failed cutaneous melanoma & CSCC

[+]One additional patient is currently awaiting formal per protocol confirmation of CR by biopsy

Summary of single agent RP2 data

- N=9; fully enrolled
  - Update on the three patients with RECIST responses reported at SITC (October 2020)
    - Mucoepidermoid cancer: Ongoing CR at 15 months (SITC 8 months)
    - Esophageal cancer: Ongoing PR at 18 months (SITC 11 months); PET scan showed no evidence of metabolic disease on 7th May 2021
    - Uveal melanoma with liver metastases; progressed at 15 months
  - The MSS CRC patient with a mixed response in liver lesions progressed at 6 months
  - Activity shown in all patients where injections were made into the liver (3/3) including 2/3 RECIST responses

Summary of RP2 combined with Opdivo data

- 27 patients of the planned 30 patients have been enrolled
  - Includes cutaneous melanoma, sarcomas, chordoma, uveal melanoma, NPC, SCCHN, salivary gland cancers
- RP2 combined with Opdivo has been well tolerated, with no new safety signals
- 14 of the 27 patients have either responded or still have the opportunity for response
- As for RP2 monotherapy, activity is being observed in patients with hard-to-treat anti-PD1 failed cancers, including with liver metastases
- Six ongoing PRs so far (1x uveal melanoma, 4x cutaneous melanoma, 1x SCCHN – all pts having had prior anti-PD1)
  - Continued demonstration of activity in anti-PD1 failed melanoma (i.e. following from that also seen with RP1+Opdivo)
  - Continued demonstration of activity in uveal melanoma (i.e. as was also seen with RP2 monotherapy)

Data continues to support that RP2 has promising clinical activity in hard to treat anti-PD1 failed tumor types

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.

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IGNYTE skin cancer cohorts key eligibility criteria & treatment regimen

Key eligibility criteria

- Melanoma
  - Stage IIIb-IV melanoma for whom PD1 directed therapy is indicated or who have failed PD1/PD-L1 directed therapy, or have exhausted, become intolerant to, or refuse, currently available therapies for melanoma
- NMSC
  - Locally advanced or metastatic NMSC that is not treatable with surgery for whom PD1/PD-L1 directed therapy is indicated or who have exhausted or become intolerant to, or refuse, available therapies

Treatment regimen

- Up to 10mL (depending on tumor diameter) of RP1 given Q2Wx8 as a first dose of $1x10^6$ pfu/mL followed by subsequent doses of $1x10^7$ pfu/mL with Opdivo given according to the standard dosing regimen from the second dose for up to 2 years
- RP1 is directly injected into superficial or nodal tumors, or imaging guided injection used for injection into deeper tumors, including in visceral organs
- Since January 2021 a second course of up to 8 doses of RP1 has been allowed if protocol specified criteria are met (patient has remaining or recurrent disease during the nivolumab treatment period & for whom the investigator believes may benefit from further RP1 treatment)

Updated safety data for IGNYTE skin cancer patients treated with RP1 combined with Opdivo

Updated treatment related TEAEs for patients treated with RP1 combined with Opdivo in patients with skin cancer

Preferred term	Grade 1-2 (>10%) # (%)	Grade 3 (all) # (%)	Grade 4/5
	N=69		
Pyrexia	23 (33.3)	1 (1.4)	
Chills	21 (30.4)	0	
Fatigue	20 (29.0)	5 (7.2)	
Pruritus	18 (26.1)	0	
Influenza like illness	17 (24.6)	0	
Nausea	15 (21.7)	0	
Rash	8 (11.6)	0	
Vomiting	8 (11.6)	0	
Decreased appetite	7 (10.1)	1 (1.4)	
Diarrhoea	7 (10.1)	1 (1.4)	
Headache	7 (10.1)	0	
Myalgia	7 (10.1)	0	
Tumour pain	7 (10.1)	0	
Alanine aminotransferase increased		2 (2.9)	
Aspartate aminotransferase increased		2 (2.9)	
Hypotension		2 (2.9)	One Grade 4 dyspnoea & one Grade 5 immune mediated myocarditis, both Opdivo-related & in the same patient
Lipase increased		2 (2.9)	
Rash maculo-papular		2 (2.9)	
Blood alkaline phosphatase increased		1 (1.4)	
Blood bilirubin increased		1 (1.4)	
Dehydration		1 (1.4)	
Dyspnoea		1 (1.4)	
Eczema		1 (1.4)	
Hyponatraemia		1 (1.4)	
Hypovolaemic shock		1 (1.4)	
Immune-mediated hepatitis		1 (1.4)	
Immune-mediated myocarditis		1 (1.4)	
Injection site necrosis		1 (1.4)	
Localised oedema		1 (1.4)	
Lymph node pain		1 (1.4)	
Oedema		1 (1.4)	
Oral candidiasis		1 (1.4)	
Seroconversion test positive		1 (1.4)	
Uveitis		1 (1.4)	
Vertigo		1 (1.4)	
Total	59 (85.5)	19 (27.5)	

- RP1 combined with Opdivo continues to be generally well tolerated, with no new safety signals identified
- Injection into visceral organs has also been well tolerated, with in general only procedure related AEs seen, which are of similar severity & frequency as seen for image-guided biopsy

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Updated efficacy data for IGNYTE NMSC patients treated with RP1 combined with Opdivo

NMSC response table with changes since SITC 2020

	CSCC October	CSCC now	BCC October	BCC now	MCC October	MCC now	Angiosarcoma Oct	Angio now
# of patients	11	15[a]	3	4	1	4	3	5
Best overall response n (%)								
CR	5 (45.5)	7 (46.6)	0	0	0	0	0	0
PR	3 (27.3)	2[b] (13.2)	0	1 (25)	0	3[c] (75)	2 (66.7)	3[c] (60)
SD	1 (9.1)	1 (6.7)	2 (66.7)	2 (50)	0	0	1 (33.3)	1 (20)
PD	2 (18.2)	4 (26.7)	1 (33.3)	1 (25)	1 (100)	1(25)	0	1[d] (20)
OR	8 (72.7)	9 (60)	0	1 (25)	0	3 (75)	2 (66.7)	3 (60)
CR+PR+SD	9 (81.8)	10 (66.7)	2 (67.7)	3 (75)	0	3 (75)	3 (100)	4 (80)

[a] One patient died before the first response assessment [b] One PR patient is awaiting formal per protocol confirmation of CR by biopsy [c] One PR not yet confirmed [d] Treatment continuing post initial PD

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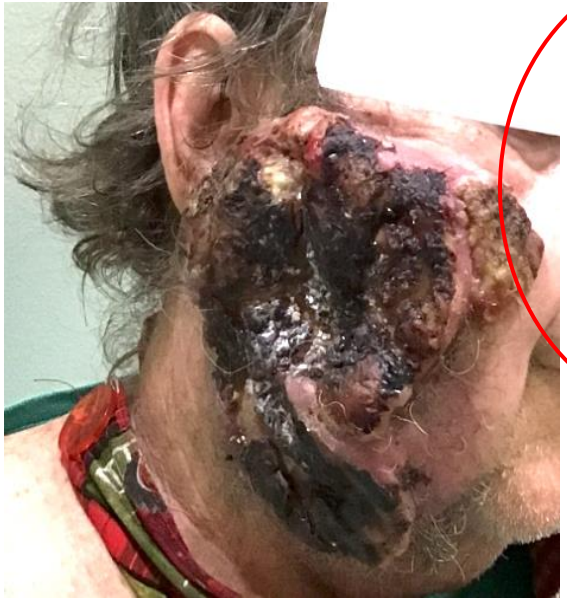
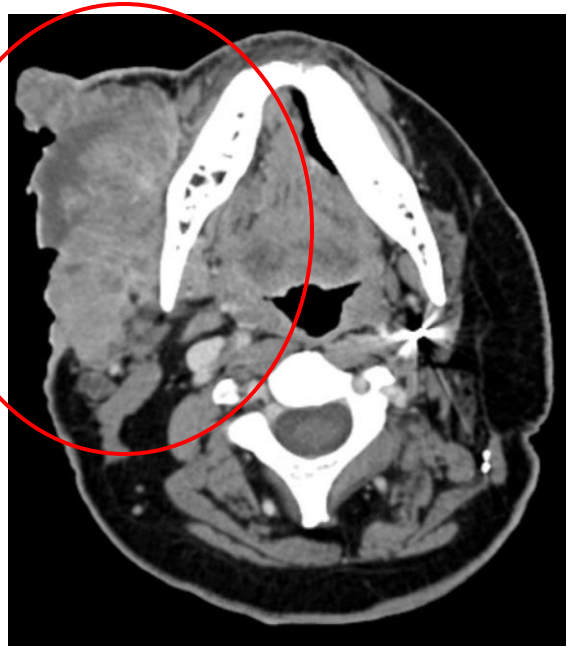
CSCC patients who rapidly progressed

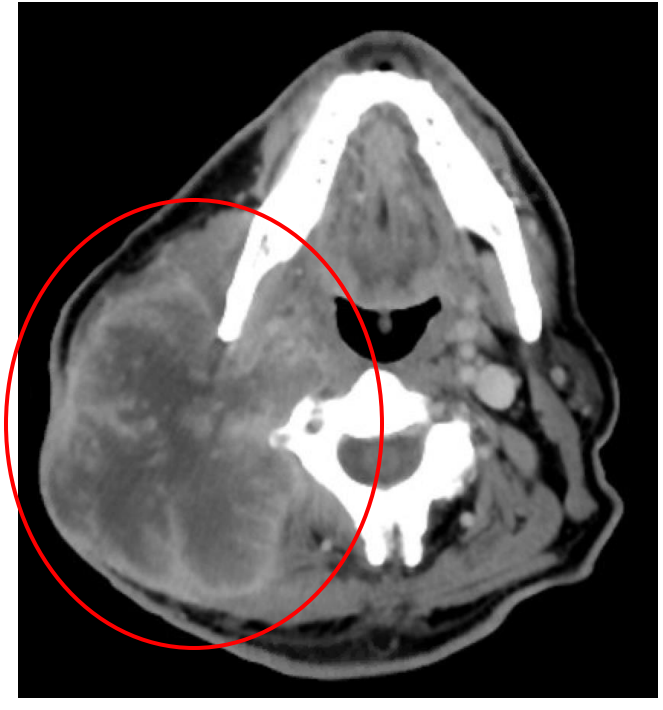
- Four new CSCC patients who were recently enrolled who had unusually high tumor burden, and went off study very rapidly due to PD at 1-2 months

Patient 1104-2002

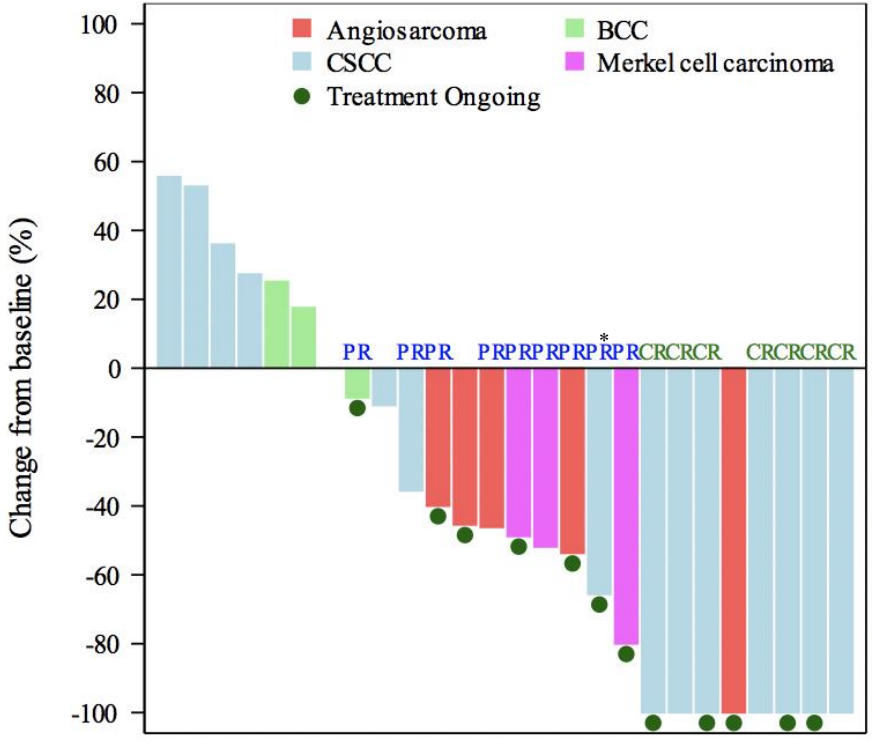




Patient 1112-2007



Maximum percent tumor reduction - NMSC



* Awaiting formal per protocol confirmation of CR by biopsy

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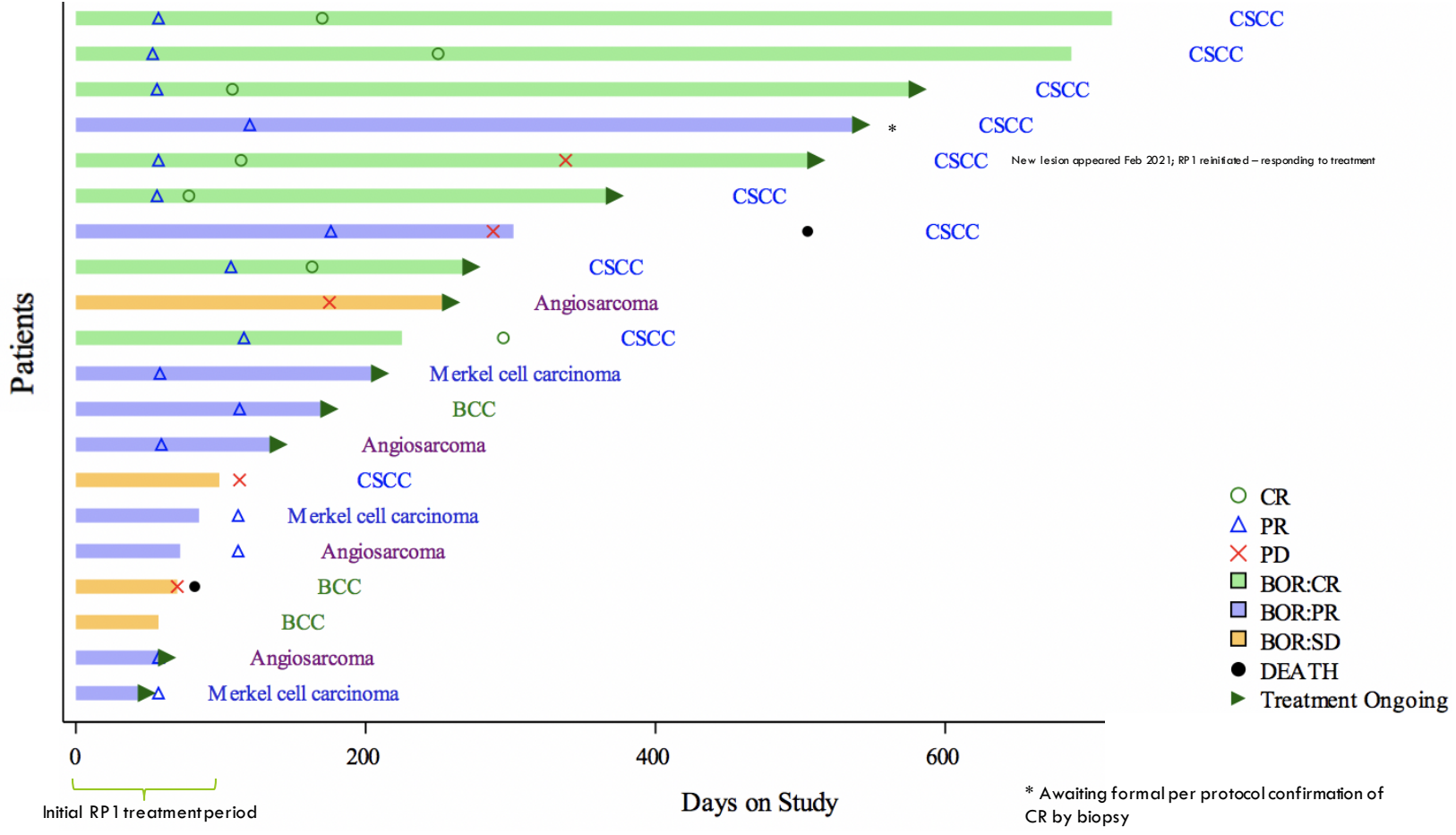
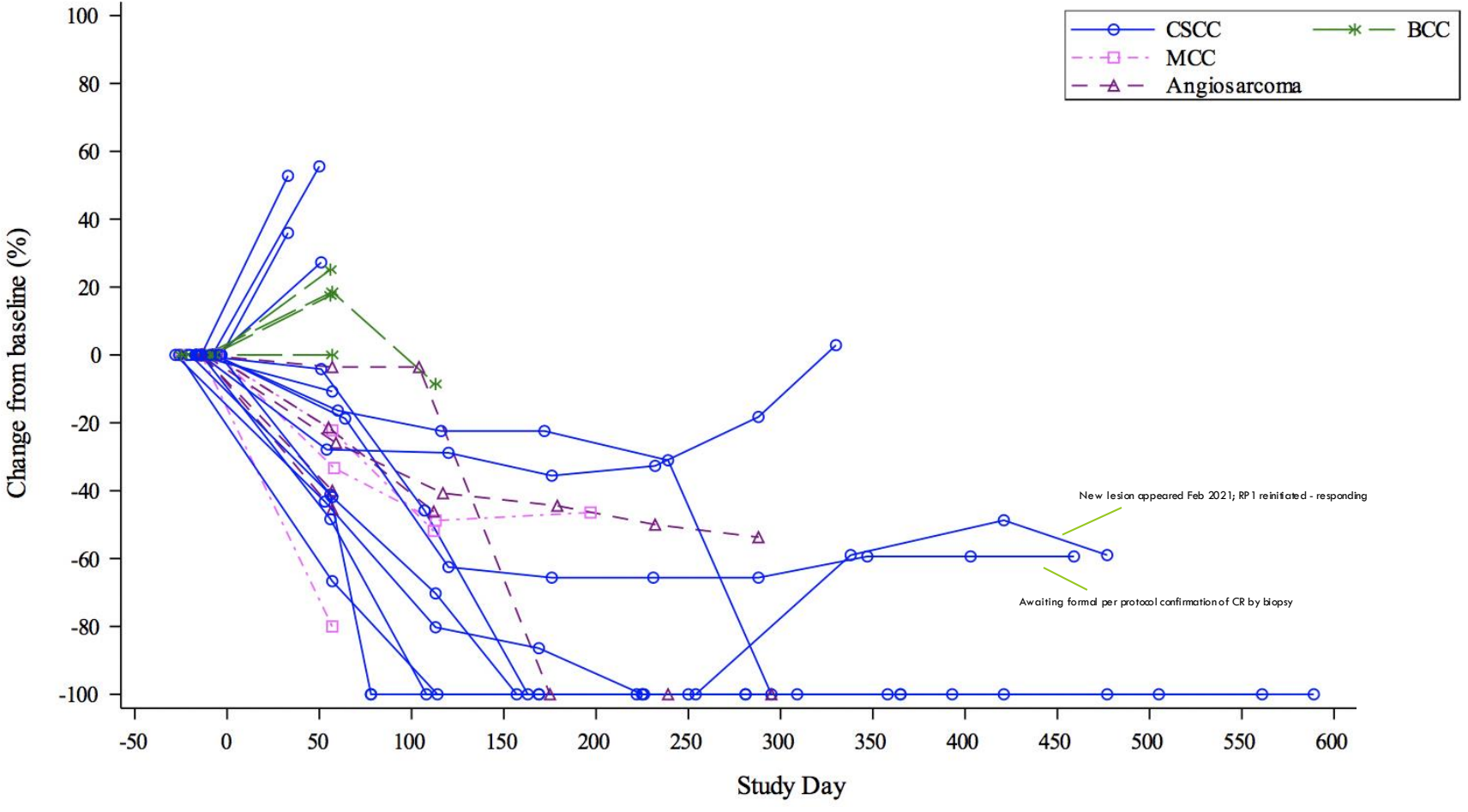
Duration of best response - NMSC

Patients with a best response of at least stable disease



* Awaiting formal per protocol confirmation of CR by biopsy

Change in sum of tumor diameters from baseline - NMSC

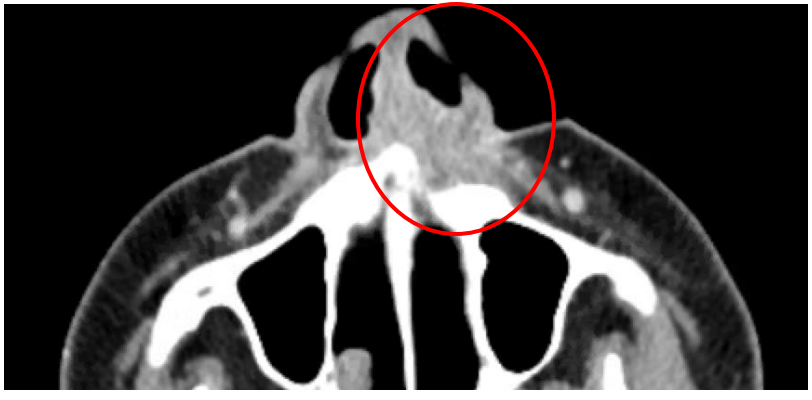


RP1 combined with Opdivo individual NMSC patient updates since October

Patient 1022-2018 (CSCC) - New CR

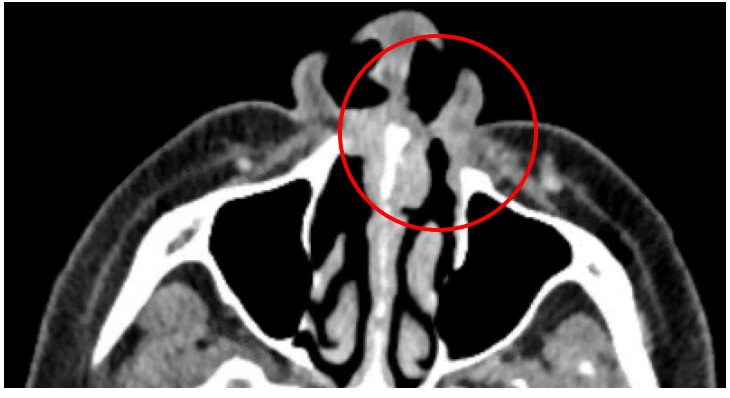
Baseline 26th June 2020

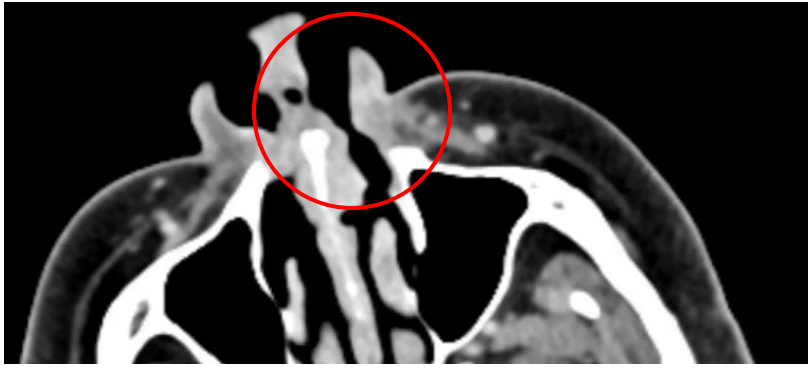
(2.4x2.1cm tumor eroding through the maxilla & extending into the incisive foramen)



6 Months

11th Dec 2020 (PR)





8 Months

12th Feb 2021 (CR)

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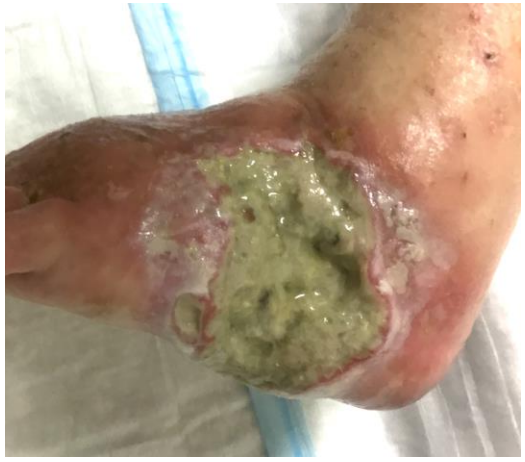
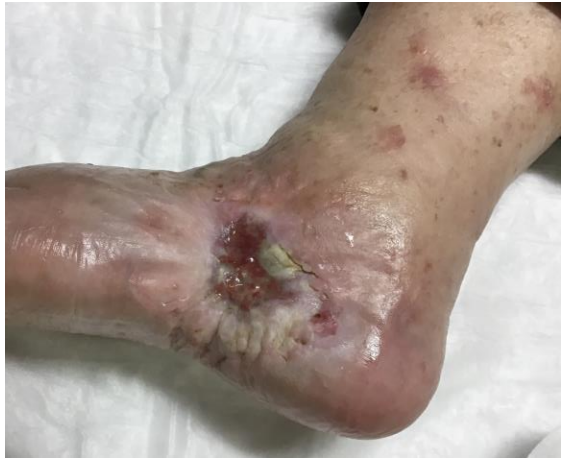
Patient 1122-2014 (CSCC) – PR converted to CR

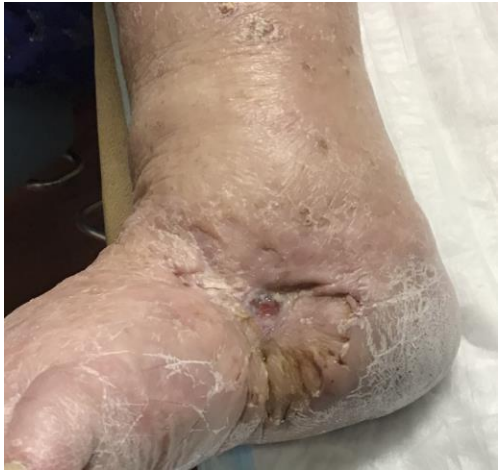
22nd May 2020

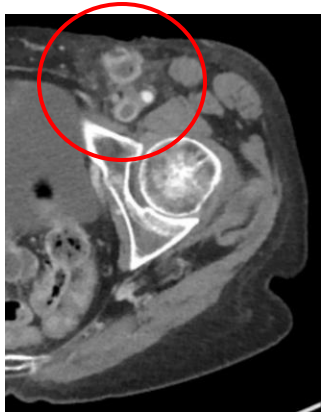


12th October 2020 (PR)

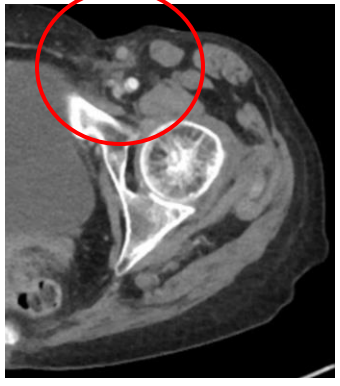


12th Feb 2021 (CR)

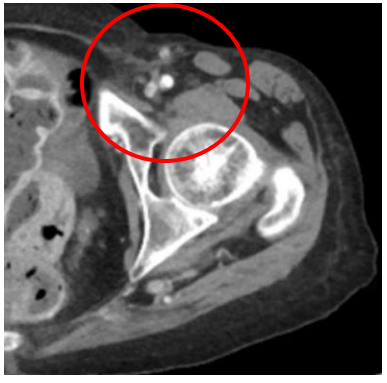




Screening



17th Aug 2020



18th Dec 2020

Patient had groin nodes which were initially injected & responded, before the foot was also injected following improvement

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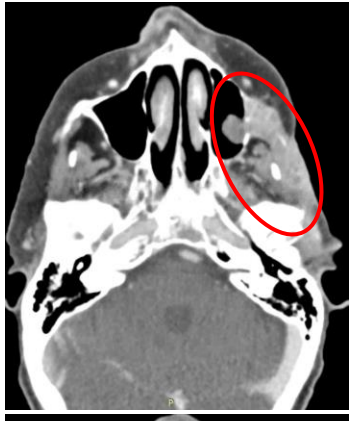
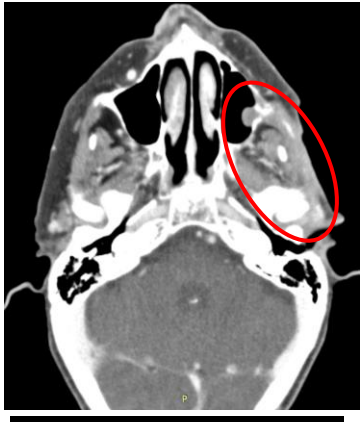
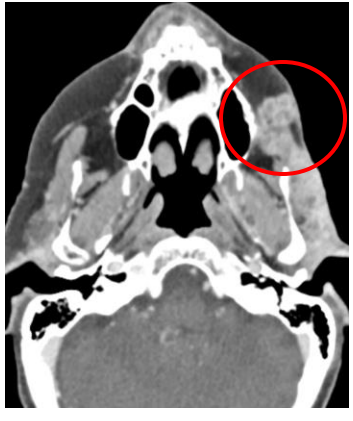
Patient 1122-2021 (BCC) - New PR (biopsy being scheduled for CR)

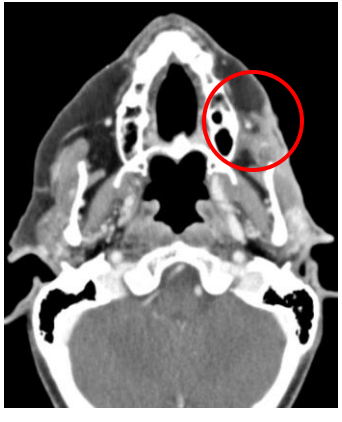
21st October 2020

22nd Feb 2021 (PR)









Baseline

7.0x2.1cm tumor around the left zygoma extending into the masticator space, lateral orbit & parotid gland with destruction of the left zygoma & maxillary sinus wall

Failed prior vismodegib

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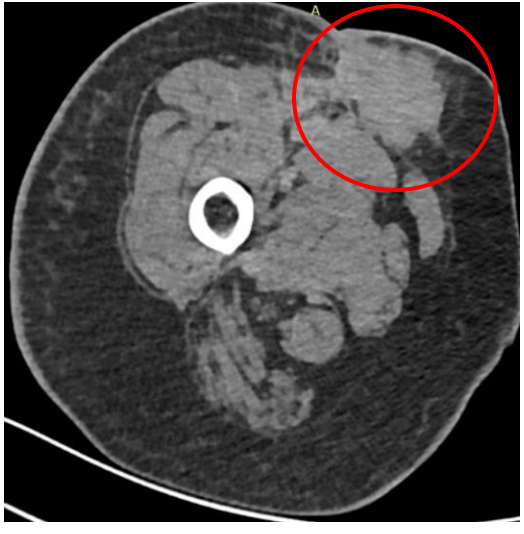
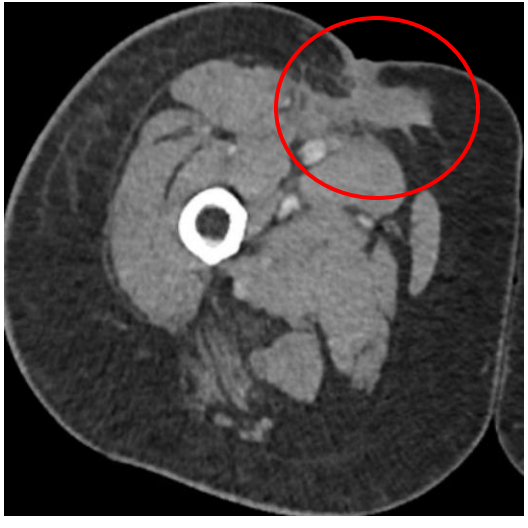
Patient 1119-2009 (MCC) - New PR (to be biopsied for CR)

9th Sept 2020

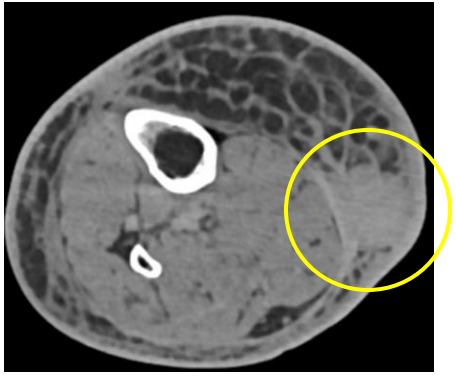
29th March 2021 (PR)

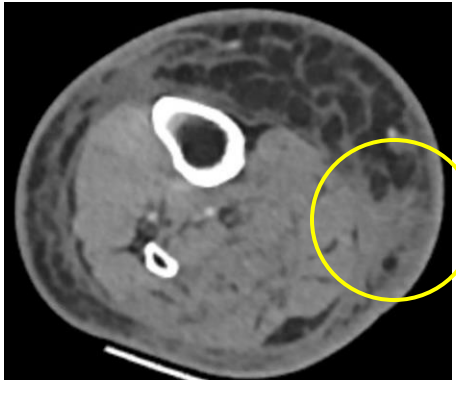




<u>Baseline</u>

Thigh mass: 5.1x3.7cm (shown: only lesion injected)
Popliteal mass: 3.2x2.7cm
Anterior right thigh mass: 1.3cm
Left calf mass: 3.3x2.5cm (shown)
Subcutaneous nodule: 1cm





Injected

Not injected

Updated efficacy data for IGNYTE melanoma patients treated with RP1 combined with Opdivo

Melanoma patients treated with RP1+ Opdivo - Demographics

	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%	75%
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% of anti-PD1 failed patients had Stage IV M1b/c (visceral) disease

Melanoma response table with changes since October

	Cutaneous: Anti-PD1 naïve October	Cutaneous: Anti-PD1 naïve now	Cutaneous: PD1-failed October	Cutaneous: PD1-failed now	Mucosal: Anti-PD1 naïve October	Mucosal: Anti-PD1 naïve now	Mucosal: PD1 failed October & now	Uveal: Anti-PD1 naïve October & now	Uveal: PD1 failed October & now
# of pts	8	8	16	16	1	1	5	3	3
Best overall response n (%)									
CR	2 (25.0)	3 (37.5)	1 (6.3)	1 (6.3)	0	1 (100)	1 (20.0)	0	0
PR	2 (25.0)	2[a] (25)	4 (25.0)	4[a] (25.0)	1 (100.0)	0	0	0	0
SD	4 (50.0)	2 (25)	2 (12.5)	2[b] (12.5)	0	0	0	1 (33.3)	3 (100.0)
PD	0	1 (12.5)	8 (50.0)	8 (50.0)	0	0	4 (80.0)	2 (66.7)	0
ORR	4 (50.0)	5 (62.5)	5 (31.3)	5 (31.3)	1 (100.0)	1 (100)	1 (20.0)	0	0
CR+PR+SD	8 (100.0)	7 (87.5)	7 (43.8)	7 (43.8)	1 (100.0)	1 (100)	1 (20.0)	1 (33.3)	3 (100.0)

[a] One anti-PD1 naïve PR patient is being treated with re-initiated RP1 with the aim of converting to CR; One anti-PD1 failed PR patient is a CR by PET scan (no metabolic activity seen) & PET scans are being scheduled for two others suspected to be NED at 18 and 23 months

[b] One SD patient has the potential for response following ongoing RP1 re-initiation; The second SD patient is a surgical CR (residual tumor removed at 4 months, ongoing at 18 months)

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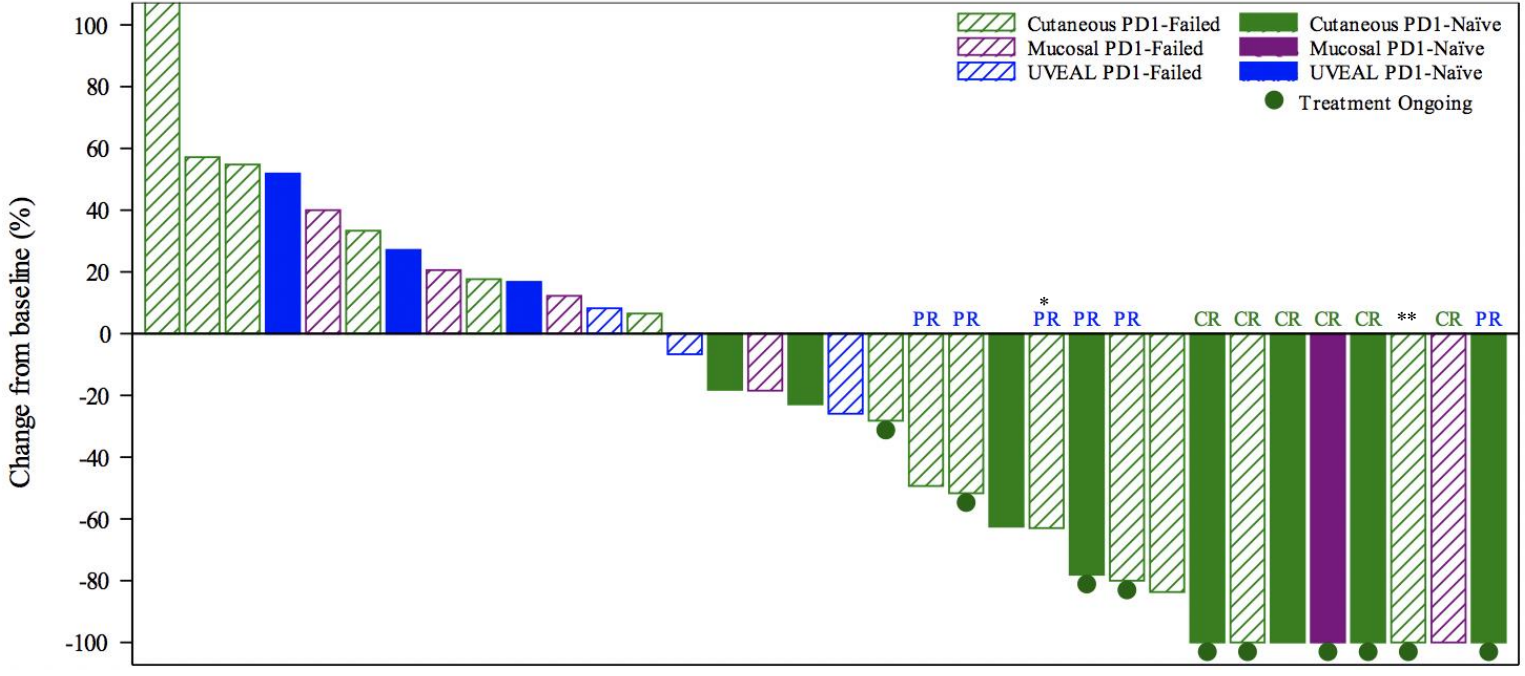
Maximum percent tumor reduction - Melanoma

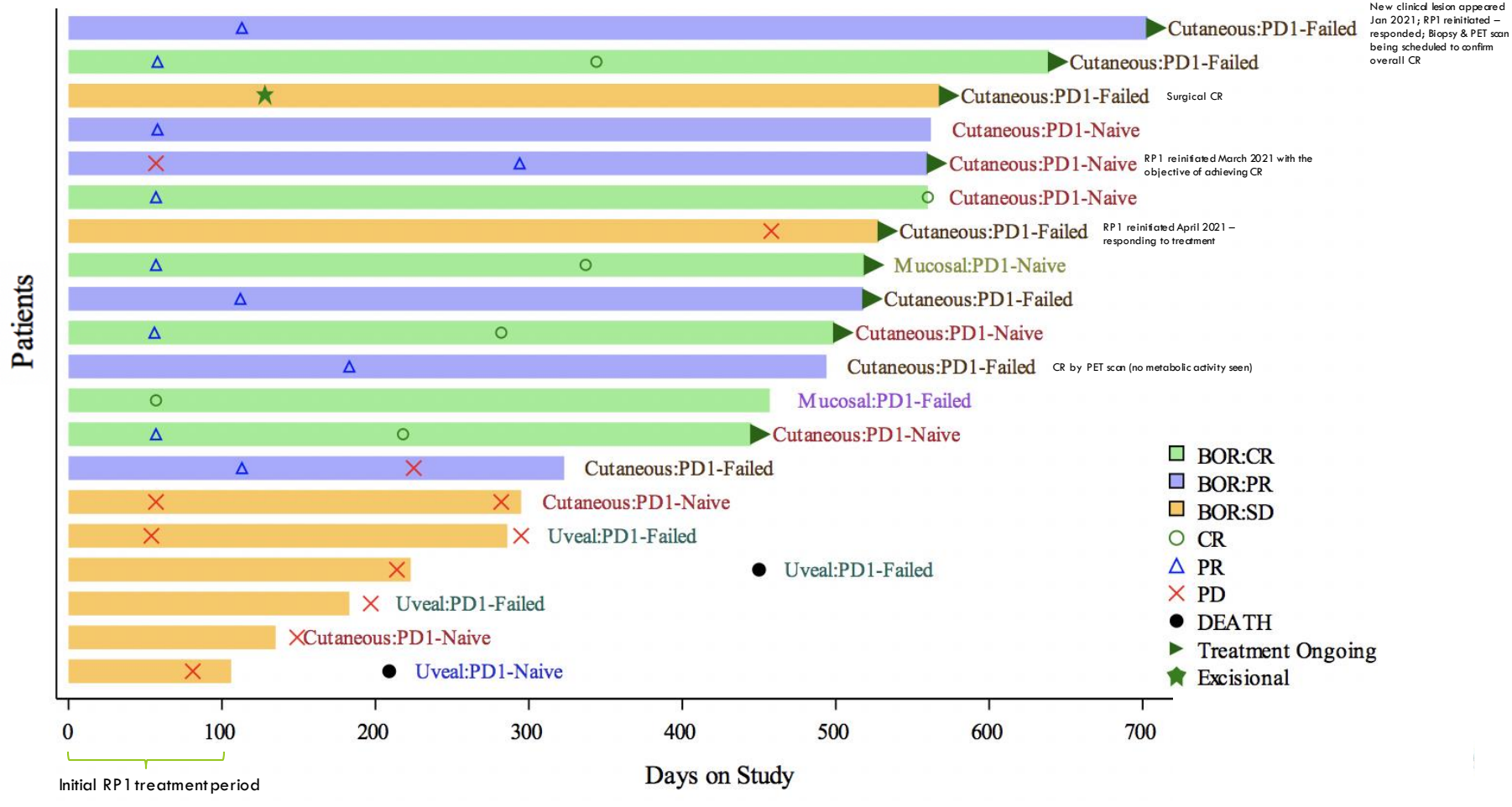


* CR by PET scan (no metabolic activity seen)

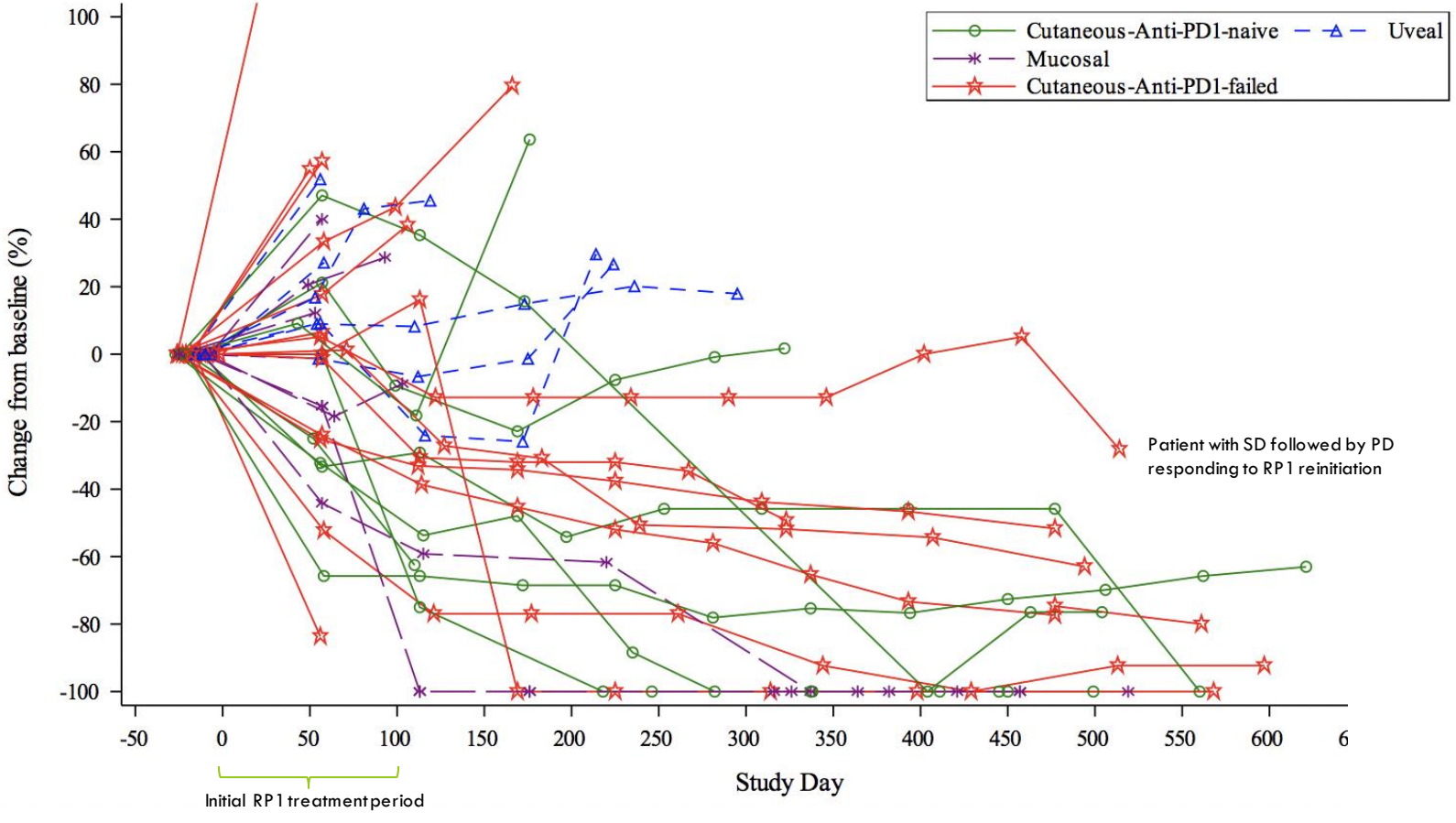
** Surgical CR

Duration of best response - Melanoma

Patients with a best response of at least stable disease



Change in sum of tumor diameters from baseline - Melanoma



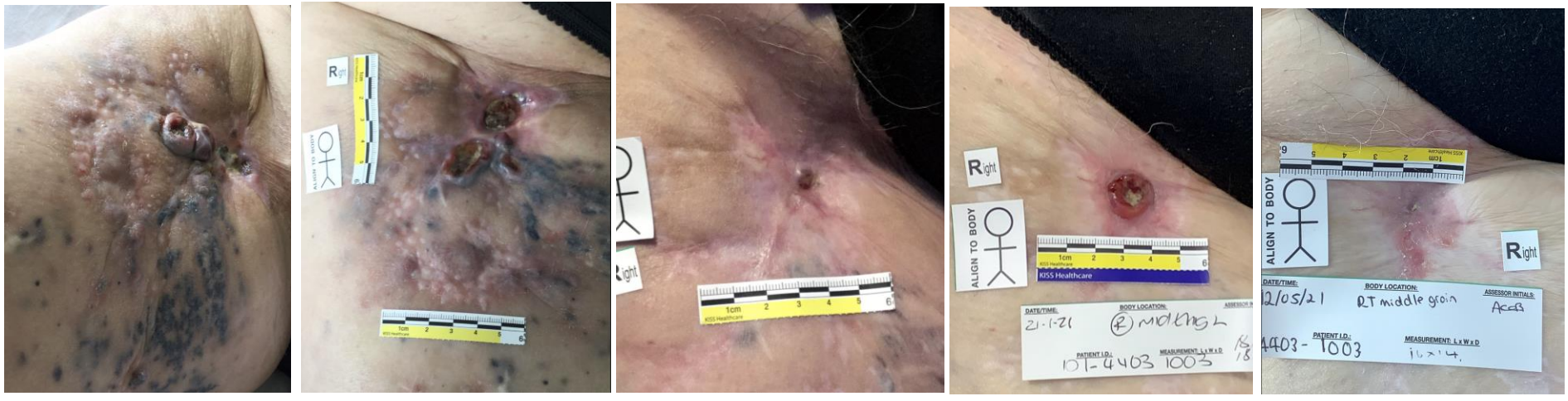
RP1 dosing re-initiation: Evidence of safety & clinical activity

In addition of demonstrating the safety & potential benefit of RP1 treatment re-initiation, this data also further demonstrates RP1 has activity beyond that of Opdivo; Patients completed dosing with RP1, relapsed while still being treated with single agent Opdivo, then further responded when RP1 was re-initiated

Re-initiation of RP1 post relapse shows efficacy in anti-PD1/anti-CTLA-4 failed melanoma – patient 4403-1003

Initial response to therapy (PR) | Relapse & response to re-initiation

Baseline	2 weeks	9 months	19 months	21 months
10th June 2019	24th June 2019	16th March 2020	18th Jan 2021	12th May 2021



- PR at 3 months, relapsed in the thigh only at 19 months when on continued Opdivo (other disease sites in the lung & groin [which continue in response])
- Re-initiated therapy at 20 months (17th Feb 2021) – responded to further RP1 injections – PET scan planned to assess for overall CR

Phase 1 data for patients with solid tumors having failed standard of care treated with RP2 monotherapy (updated data) or with RP2 combined with Opdivo (new data)

RP2 Phase 1 clinical trial key eligibility criteria & treatment regimen

Key eligibility criteria

- Patients with histologically confirmed advanced or metastatic non-neurological solid tumors, who have progressed on standard therapy or cannot tolerate standard therapy, or for which there is no standard therapy preferred to enrollment in a clinical trial

Treatment regimen

- RP2: Up to 10mL (depending on tumor diameter) of RP2 given Q2Wx8 as a first dose of $1x10^6$ pfu/mL followed by subsequent doses of $1x10^7$ pfu/mL
- Opdivo: Given from the second dose of RP2 according to the current standard dosing regimen for up to 2 years in the combination cohort
- RP2 is directly injected into superficial or nodal tumors, or imaging guided injection used for injection into deeper tumors, including in visceral organs
- Since September 2020 a second course of up to 8 doses of RP2 has been allowed

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RP2 monotherapy & RP2 in combination with nivolumab Phase 1 clinical trial patient demographics

	RP2 Only (N = 9)	RP2 With Nivolumab (N = 27)
Medial age, years (range)	55 (36-76)	57 (36-82)
Female	1 (11.1%)	12 (44.4%)
Male	8 (88.9%)	15 (55.6%)
ECOG Performance		
0	6 (66.7%)	13 (48.1%)
1	3 (33.3%)	12 (44.4%)
Tumor Types		
Esophageal Adenocarcinoma	1	0
Colon Adenocarcinoma	1	0
Chordoma	0	2
Cutaneous Melanoma	2	9
Uveal Melanoma	3	6
Mucoepidermoid Carcinoma	1	0
Head and Neck, Squamous cell carcinoma	0	3
Sarcomatoidmyoepithelial carcinoma	0	1
Squamous Cell Carcinoma	1	0
Sarcoma	0	1
Rhabdomyosarcoma	0	1
Fibromyxoid Sarcoma	0	1
Nasopharyngeal carcinoma	0	1
Salivary gland malignancy unknown poorly differentiated	0	1
Metastatic acinic cell carcinoma of parotid gland	0	1

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Treatment related AEs for patients treated with RP2 combined with Opdivo

Preferred term	N=27 Grade 1-2 (>10%) # (%)	Grade 3 (all) # (%)
Pyrexia	14 (51.9)	2 (7.4)
Chills	12 (44.4)	0
Influenza like illness	9 (33.3)	0
Fatigue	5 (18.5)	1 (3.7)
Pruritus	5 (18.5)	0
Hypotension	4 (14.8)	1 (3.7)
Nausea	4 (14.8)	0
Vomiting	4 (14.8)	0
Diarrhoea	3 (11.1)	0
Arthralgia		2 (7.4)
Dysphagia		2 (7.4)
Abdominal pain upper		1 (3.7)
Abscess limb		1 (3.7)
Haemorrhage		1 (3.7)
Hyponatraemia		1 (3.7)
Immune-mediated hepatitis		1 (3.7)
Infusion related reaction		1 (3.7)
Myalgia		1 (3.7)
Transaminases increased		1 (3.7)

No Grade 4 or 5

- RP2 combined with Opdivo has been generally well tolerated, with no new safety signals identified
- As for RP1, injection into visceral organs has also been well tolerated, with in general only procedure related AEs seen, which are of similar severity & frequency as seen for imaging-guided biopsy

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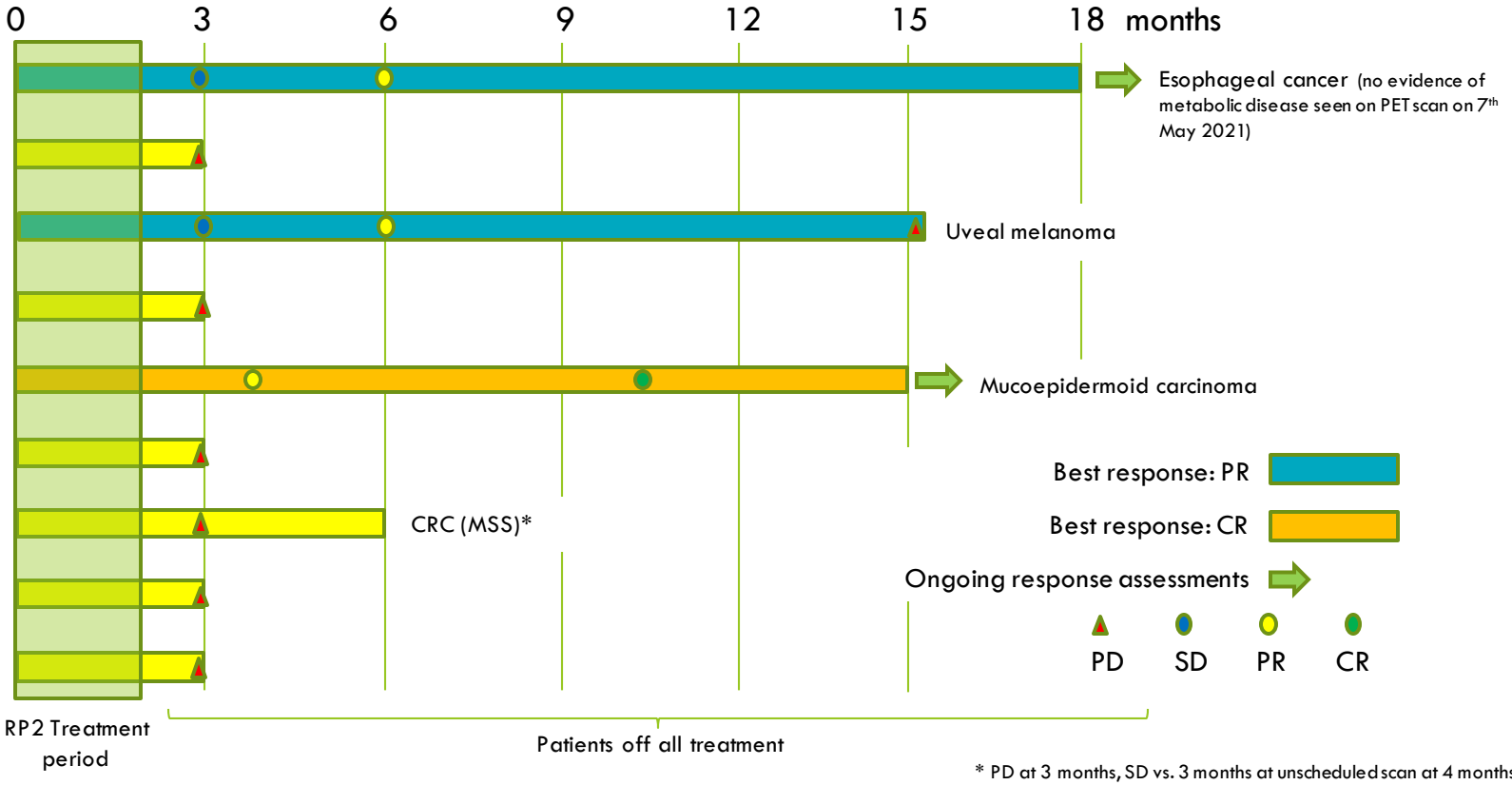
RP2 monotherapy swimmers plot (updated from October)



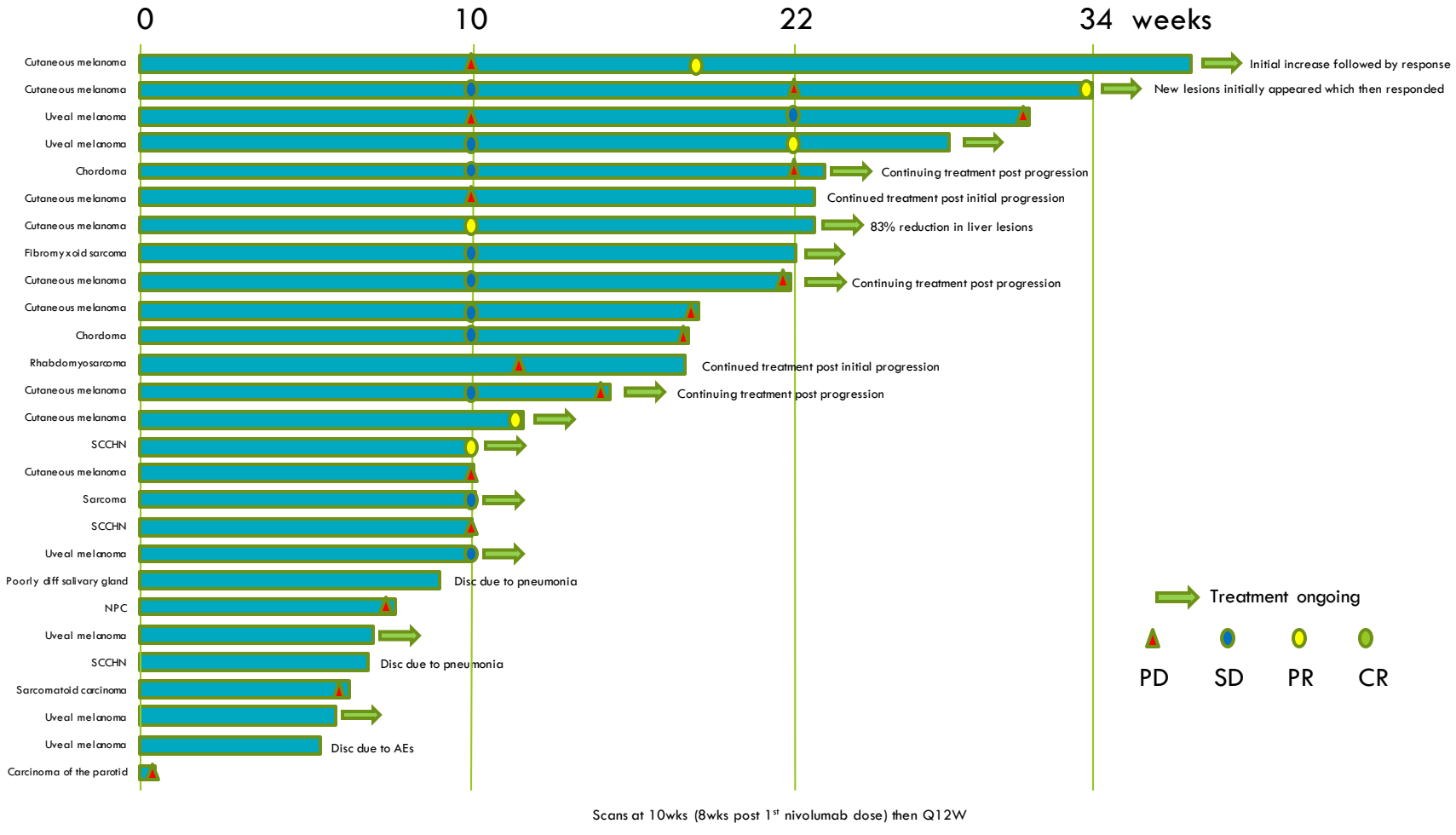
* PD at 3 months, SD vs. 3 months at unscheduled scan at 4 months, PD at 6 months (lung lesions stable, liver lesions/peritoneal carcinomatosis progressing, 1 lymph node [uninjected] reduced in size)

RP2 combined with Opdivo patient disposition

Tumor type (Prior therapies)	All	Cutaneous melanoma (Anti-PD1 or anti-PD1/anti-CTLA-4 x9)	Uveal melanoma (IMCgp100 x1; anti-PD1 or anti-PD1/anti-CTLA-4 x2)	Uveal melanoma (Anti-PD1 naïve x2; prior therapy unknown x1)	SCCHN (Chemo/anti-PD1 failed x2; RT failed x1)	NPC (multiple chemo failed)	Salivary gland cancer (naïve; tipfarnib/RT failed)	Sarcoma/ sarcomatoid carcinoma (multi-chemo; multi-surgery/RT x2; brachytherapy)	Chordoma (OSI-906/imatinib/ afatinib; afatinib/RT)
# of patients	**27**	**9**	**3**	**3**	**3**	**1**	**2**	**4**	**2**
Ongoing PR	**6**	**4[a]**	**1**	-	**1[b]**	-	-	-	-
Best response SD[c]	9	3	-	2	-	-	-	2	2
Ongoing SD	3		-	1	-	-	-	2	-
Best response PD	7	2	-	-	1	1	1	2	
Continuing treatment post initial progression	3	2	-	-	-	-	-	-	1
On treatment with no follow up	2	-	2	-	-	-	-	-	-
On study with the opportunity for response	**8**	**2**	**2**	**1**	**0**	**0**	**0**	**2**	**1**
Current ORR	**22%**	**44%**	**33%**	**0%**	**33%**	**0%**	**0%**	**0%**	**0%**

[a]Two not yet confirmed [b]Not yet confirmed; prior nivolumab, 5-FU/cisplatin, radiotherapy [c]Ongoing SD or SD followed by PD

RP2+Opdivo: Best response and duration on study treatment



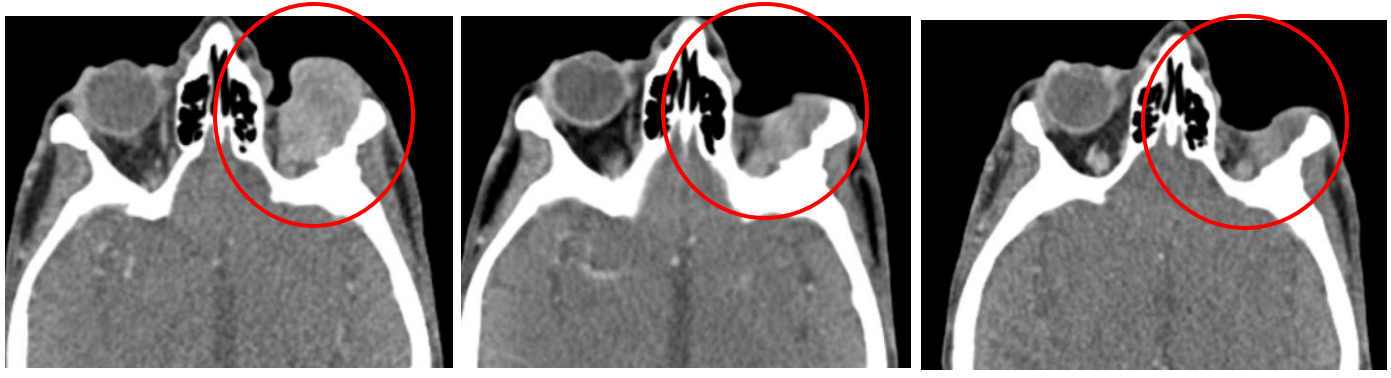
Scans at 10wks (8wks post 1st nivolumab dose) then Q12W

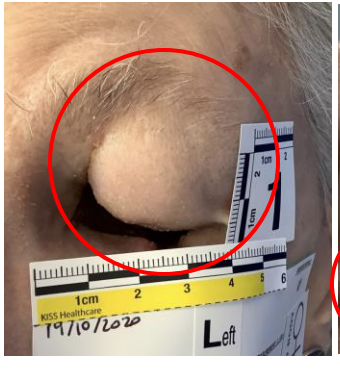
Patient 4402-0007: Uveal melanoma (Opdivo failed) - PR

30th Sept 2020 (Screening)

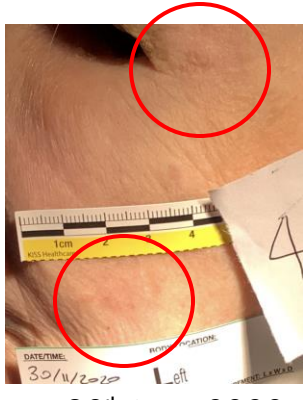
29th Dec 2020 (SD)

22nd March 2021 (PR)

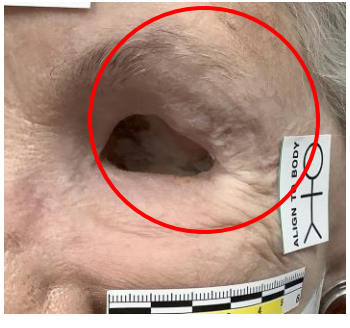




19th Oct 2020 (Baseline)



30th Nov 2020



27th Jan 2021

Also has iliac bone metastases which are responding

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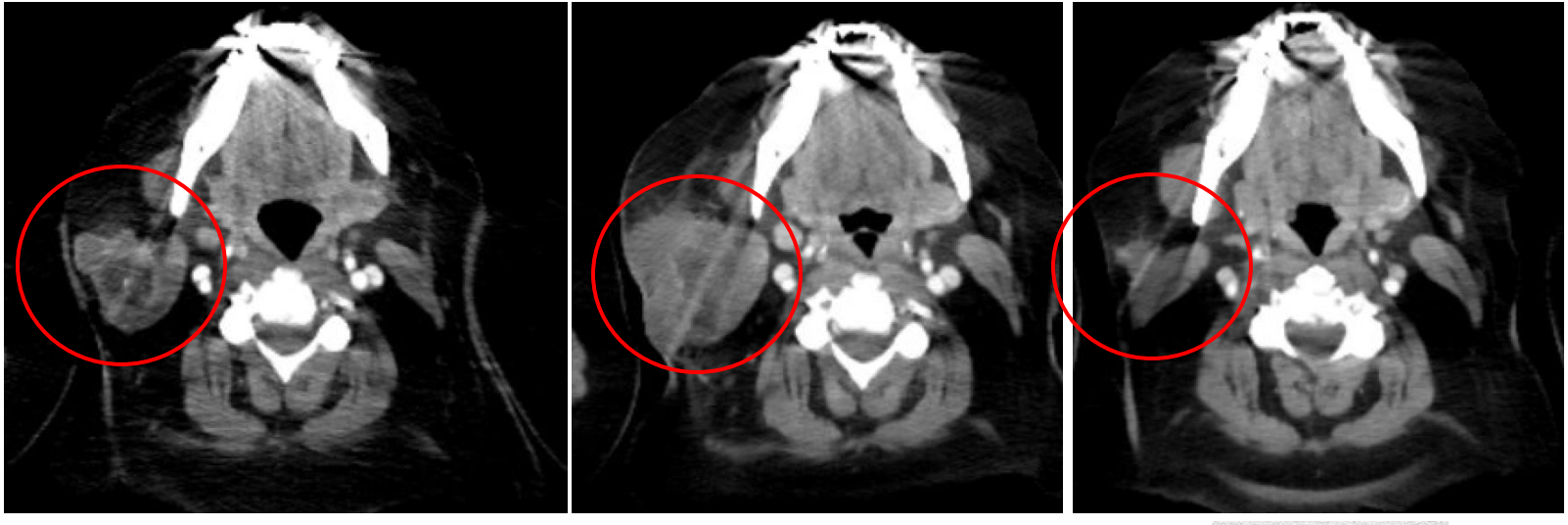
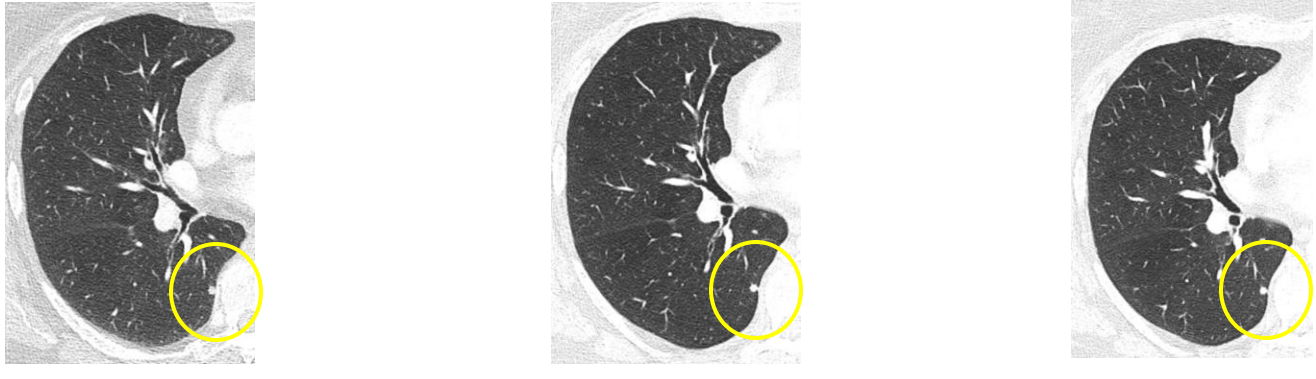
Patient 4403-0004: Cutaneous melanoma (Opdivo failed): PR

23rd Jul 2020 (baseline) | 26th Oct 2020 (PD) | 1st Feb 2021 (PR)



Had been off work for three years & in significant pain: Now off all pain meds & back at work

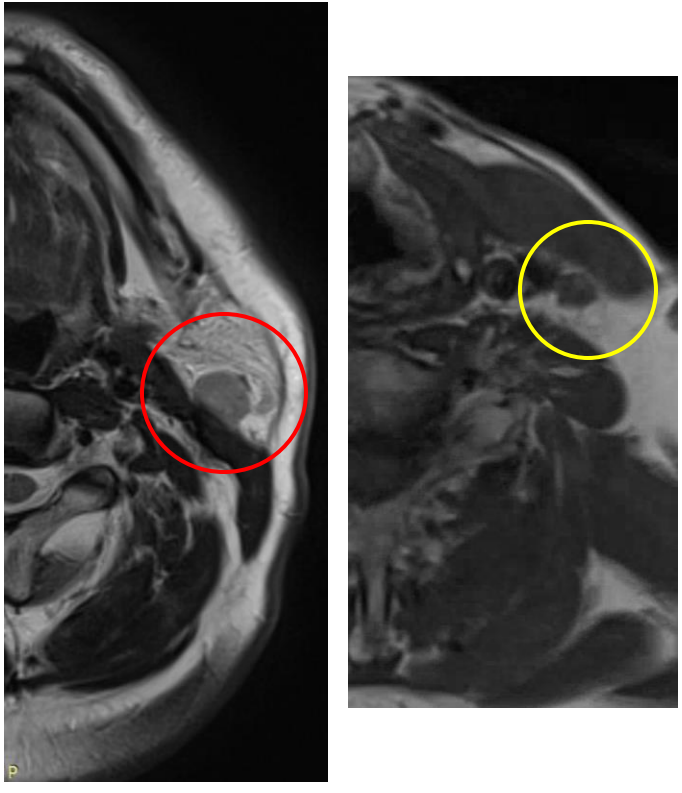


Other small lung & brain lesions also stable since baseline

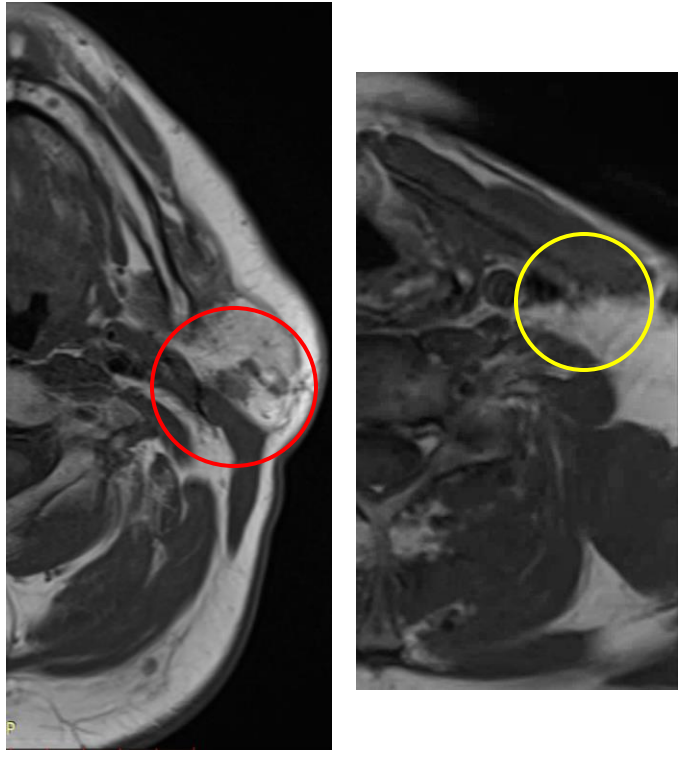
Patient 4403-0011: SCCHN (Opdivo, 5-FU/cisplatin, RT failed): PR

15.9x12.5mm lesion posterior to the left parotid gland & 9x8mm in the sternocleidomastoid muscle

19th Feb 2021(Screening)



20th April 2021



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Conclusions

- RP1 combined with Opdivo continues to provide deep & durable responses in skin cancer
- RP1 combined with Opdivo continues to be well tolerated
  - Includes following injection into visceral organs which is both feasible and effective
- RP1 dose re-initiation is well tolerated & has shown evidence of clinical activity in all patients treated so far
- Biomarker data (presented at AACR) continues to support the mechanism of action of igniting an anti-tumor immune response and turning immunologically 'cold' tumors 'hot'
- RP2 monotherapy and RP2 combined with Opdivo have been generally well tolerated
- RP2 monotherapy & combined with Opdivo has demonstrated compelling initial activity in hard to treat & anti-PD1 failed patients with cancer

Beyond skin cancers – what next?

In addition to developing in specific less immune responsive tumor types, Replimune believes there to be particular opportunity for the treatment with patients with liver metastases

Liver metastases – Background/rationale

- Liver is one of the most common sites of metastases across tumors (including lung, breast, and colon cancer)
- Prognosis for patients with liver metastases is poor with limited effective treatment options
  - Liver metastases across tumor types are associated with systemic resistance to immune checkpoint blockade
- Liver metastases are associated with the antigen-specific elimination of T cells from the circulation by macrophages resident in the liver metastases
  - Leads to systemic loss of T cells and diminished immunotherapy efficacy
- The oncolytic immunotherapy MOA is intended to
  - Directly kill tumors
  - Induce systemic T cell mediated (& other) immune responses to the antigens released
- Intratumoral RP1 & RP2 alone & combined with anti-PD1 is well tolerated & has demonstrated compelling evidence of efficacy, including in liver mets

Sources: Riihimaki et al Cancer Med 2018; Yu et al Nat Med Jan 2021

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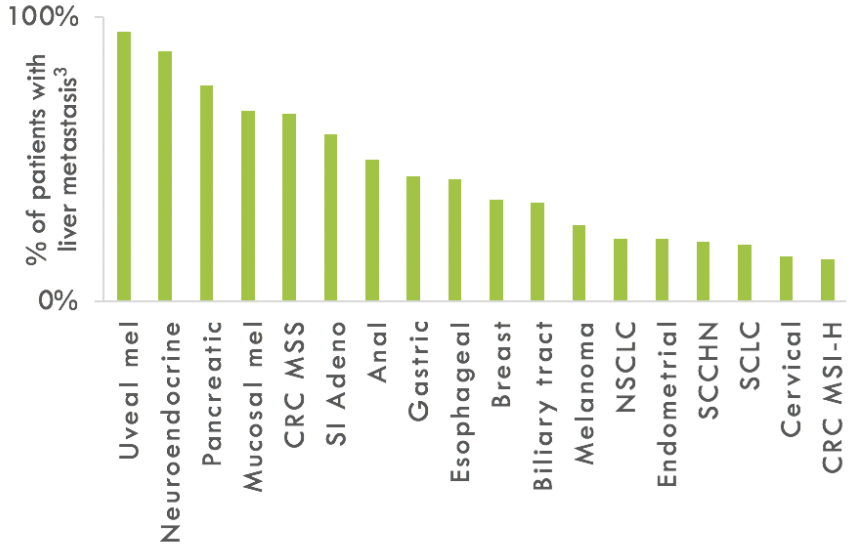
Significant numbers of patients with liver metastases have the potential to benefit from an effective treatment option

In three example major indications, large numbers of patients with liver metastases could benefit from an effective treatment option

	Breast	Colon	Lung
Estimated annual US deaths[1]	43,600	52,980	131,880
Autopsy liver metastasis frequency[2]	36%	69%	23%
Rough estimate of eligible patient #	~16k	~37k	~30k

Numerous additional cancer types have liver metastases, suggesting impact across tumor types



1) SEER 2021 Estimated Deaths. From SEER Cancer Stat Facts by indication
2) Riihimaki Cancer Med (2018)
3) Data displays % of liver metastases at initial diagnosis or death Source: Independent analysis conducted on behalf of Replimune

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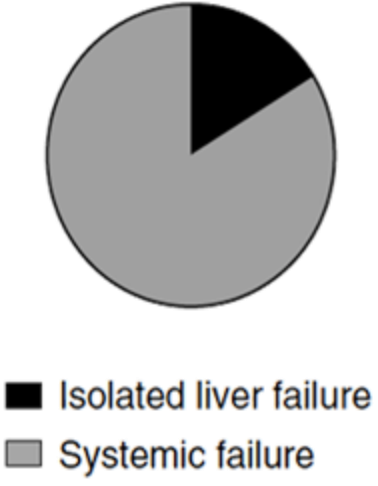
Liver metastases negatively impact immunotherapy efficacy

The presence of liver metastasis correlates with **poor outcomes** to immunotherapy

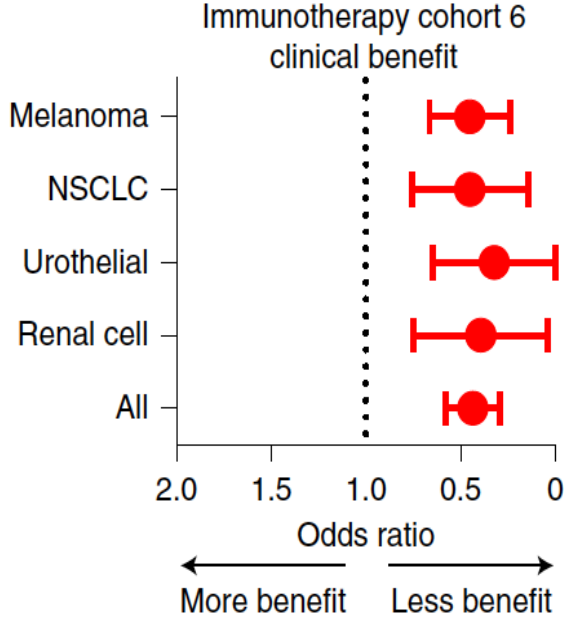
- *Systemic treatment failure*
- *Significantly reduced clinical benefit*

Treatment failure in patients with liver metastases are most frequently systemic, not only in liver



Study of melanoma patients showed 84% of failures are systemic

Patients with liver metastases have an immunotherapy efficacy gap across tumor types



Clinical benefit is reduced in patients with liver metastases

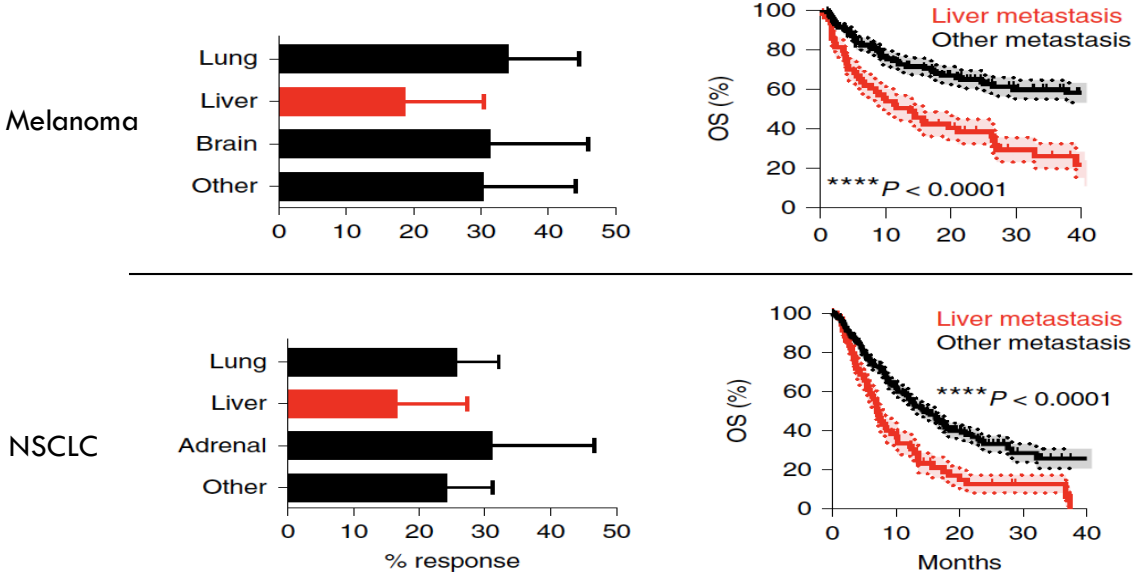
Yu et al Nat Med Jan 2021

There is a significant unmet need for patients with liver metastases

The presence of liver metastasis correlates with **poor outcomes** to immunotherapy

- *Lower objective response rates*
- *Survival significantly reduced*

Two illustrative tumor types show substantial outcome gap between patients with and without liver mets



Response rates by metastatic site

Survival by metastatic site

Yu et al Nat Med Jan 2021

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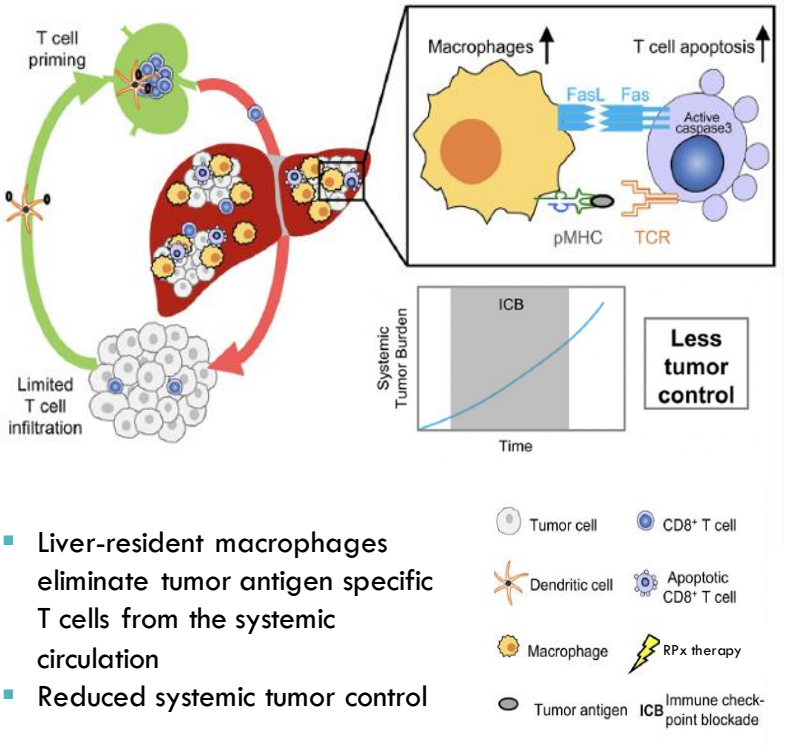
Liver metastases adversely impact response to immunotherapy

Immunotherapy with liver metastases

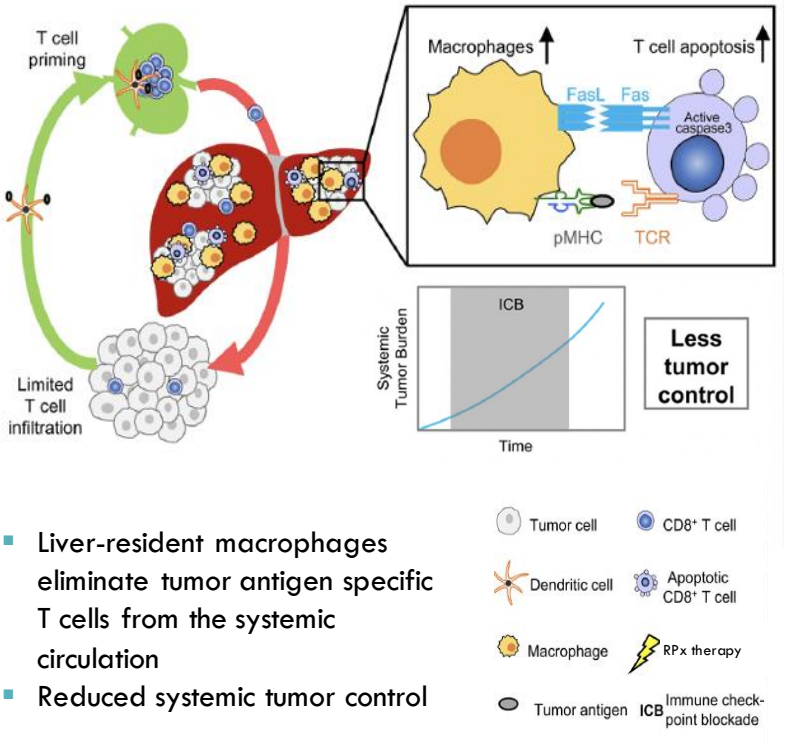


- Liver-resident macrophages eliminate tumor antigen specific T cells from the systemic circulation
- Reduced systemic tumor control

Modified from Yu et al Nat Med Jan 2021

RPx injection into liver metastases aims to re-ignite the immune response, clearing lesions locally and increasing T cells in circulation for systemic efficacy

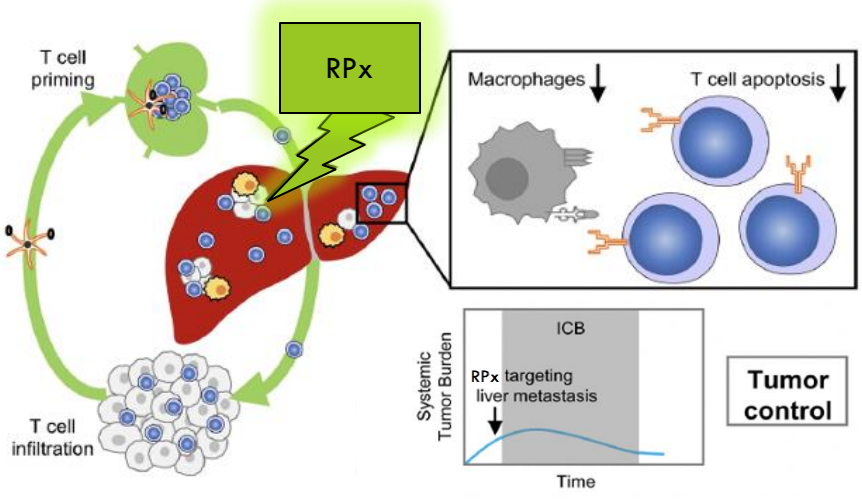
Immunotherapy with liver metastases



- Liver-resident macrophages eliminate tumor antigen specific T cells from the systemic circulation
- Reduced systemic tumor control

Modified from Yu et al Nat Med Jan 2021

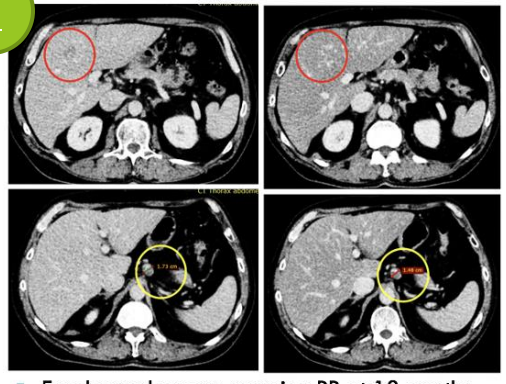
Immunotherapy with liver metastasis depletion



- Liver metastases together with resident macrophages reduced by RPx
- Activation of innate & adaptive anti-tumor immunity – increased T cells
- CD40L/4-1BBL in RP3 also intended to reduce T cell apoptosis
- Restored/increased systemic tumor control

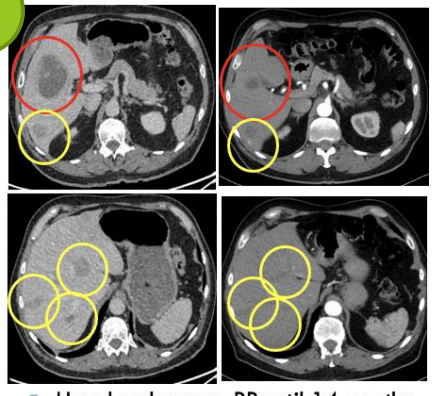
Six example patients with liver metastases across tumor types responding to RP1 or RP2

1



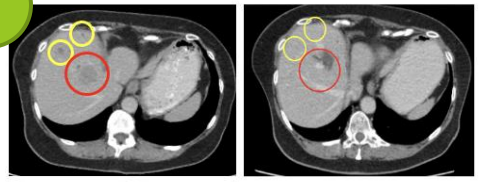
- Esophageal cancer, ongoing PR at 18 months

2



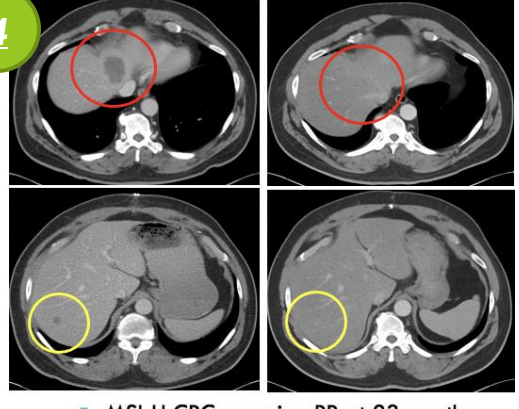
- Uveal melanoma, PR until 14 months

3



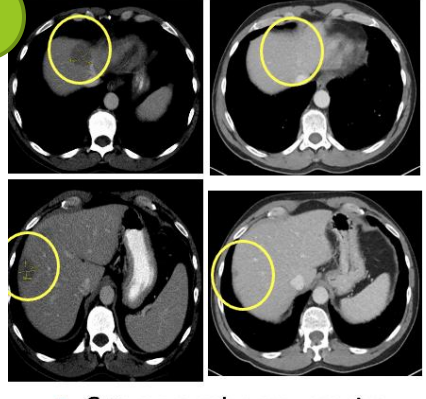
- Cutaneous melanoma, ongoing metabolic CR at 19 months

4



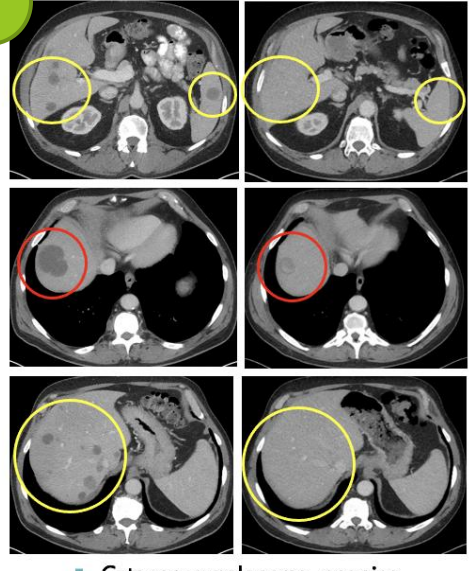
- MSI-H CRC, ongoing PR at 23 months

5



- Cutaneous melanoma, ongoing CR at 15 months

6



- Cutaneous melanoma, ongoing PR at 15 months

Liver metastases – Development strategy

- Expand RP2 enrollment to include patients with liver metastases of defined tumor types
  - GI cancers, breast, lung & further signal confirmation in uveal melanoma
    - Further confirm the ability of RPx to treat patients with liver metastases
    - With signal confirmation in uveal melanoma, proceed to registration-directed development
- Determine safety of RP3, including when injected into liver metastases
  - Ongoing phase 1 clinical trial of RP3 alone & combined with anti-PD1 therapy
- Assess RP2 or RP3 (data dependent) in a multi-cohort phase 2 clinical trial in patients with liver metastases
  - N=20-40 per cohort
  - e.g. CRC (MSS), breast cancer, NSCLC, SCLC, SCCHN, etc + basket of the rest
  - Depending on activity & risk benefit, un-gate
    - Tumor type agnostic registration-directed clinical trial, &/or
    - Indication specific registration-directed clinical trial(s)

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Conclusions

- Replimune intends a broad development program with RP2/3, intended to largely target tumor types beyond skin cancers
- While indication-specific development is intended as part of a broader roll out of the development strategy for RP2/3 post Phase 1, Replimune believes there to be a particular opportunity in patients with liver metastases across tumor types
  - High un-met need with reduced efficacy of checkpoint blockade
  - Rationale for the use of RP2/3 in patients with liver metastases
  - Safety & feasibility of administration of RPx to patients with liver metastases
  - Initial clinical efficacy data with RP1/2 in patients with liver metastases
- A specific liver metastasis strategy is therefore being developed, with initiation of multi-cohort Phase 2 development intended for late 2021/22
  - The approach to be taken is intended to allow for rapid un-gating to registration directed development in one or more tumor types, and/or in a tumor type agnostic approach

Upcoming data sets expected in 2021/22

- End 2021
  - RP2 + Opdivo updated data from combination cohort in all comers study
  - RP3 phase 1 initial single agent data in all comers
  - RP1 + Opdivo anti-PD1 failed NSCLC initial data
  - RP1 ARTACUS single agent initial data in CSCC organ transplant patients
  - Further granularity on RP2/3 development strategy
- 2022
  - RP1 + Opdivo anti-PD1 failed CSCC initial data
  - CERPASS (CSCC registration directed study) primary read out
  - IGNYTE (anti-PD1 failed melanoma registration directed study) primary read out
  - RP1 + Opdivo anti-PD1 failed NSCLC updated data
  - RP2 liver metastases cohort expansion data
  - RP1 ARTACUS single agent data in CSCC organ transplant patients
  - RP3 initial data from anti-PD1 combination cohort in all comers study

Well capitalized to deliver on all potential catalysts with cash into H2 2024