



NEXT-GENERATION ONCOLYTIC IMMUNOTHERAPY

Summary of cutaneous melanoma patients treated so far in Replimune's Phase 1/2 clinical trial of RP1 alone & in combination with nivolumab in a range of solid tumor types

November 2019

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 our expectations about our use of cash, our advancement of our clinical trials, our goals to develop and commercialize our product candidates, our plans to establish our own in-house manufacturing capabilities, our proposed scientific presentations, 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 establishing, equipping, and operating our planned 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, and other risks set forth under the heading “Risk Factors” of our Annual Report on Form 10-K for the year ended March 31, 2019. 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.

Cutaneous melanoma patients treated on RPL-001-16 with RP1 +nivolumab

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Enrolled in Ph1

Enrolled in Ph2

Patient #	Prior therapy	D1C1	Comments/Current status
1105-1002	Ipi, IL2, nivo	25 th Mar 2019	Mixed response – some tumors reduced (including no tumor in injected 2.5cm liver lesion on biopsy), some progressed – off study for PD July 2019
4401-1022	Ipi, pembro	19 th Dec 2018	Ongoing PR; treatment ongoing SEE SLIDE 4
4403-1003	Ipi/nivo	10 th June 2019	Responding to ongoing treatment SEE SLIDES 5-8
1119-2001	None	4 th June 2019	Eightx9mL injected into heel lesion once & inguinal nodes thereafter. Initial increase in the liver (C5 scan) followed by reduction (next scan), heel & inguinal nodes also responding, vitiligo seen; treatment ongoing SEE SLIDES 9-11
1119-2003	Ipi/nivo	22 nd July 2019	1-3mLx7 injected into inguinal node & heel lesions. Ongoing PR after initial PD; nivolumab treatment ongoing (lesions too small to inject since C6 SEE SLIDE 12)
4403-2003	None	5 th Aug 2019	1-3mLx6 injected into popliteal lesion. D43 biopsy tumor free. C5 scan show reduction in adrenal mass (34x28 reduced to 25x15mm); treatment ongoing. Ongoing PR. SEE SLIDE 13
1101-2001	None	19 th Aug 2019	Injections into 2.5cm axillary node. “Tumor decreasing in size & responding well” per site PI; treatment ongoing
1103-2001	None	26 th Aug 2019	5x3mL injections into medial right thigh. Ongoing PR with marked reduction of multiple lesions including liver, lungs, resolved soft tissue lesion of right gluteus & injected lesion with necrotic center; treatment ongoing SEE SLIDE 14
TOO EARLY FOR FOLLOW UP SCANS BELOW THIS POINT			
4401-2003	Ipi/nivo	25 th Sept 2019	Injections into 4.6, 1.2 & 1.0cm nodules in the groin x3. No other info available
4405-2002	Ipi/nivo	2 nd Oct 2019	10mL injected x2 – baseline disease includes peritoneal 8.2cm, liver 6.5cm & 4.1cm, supraclavicular 2.6cm. No other info available
1115-2001	Ipi/nivo	10 th Oct 2019	1.5mL injected into two lung lesions (2.2cm & 1.7cm). No other info available
1112-2004	None	22 nd Oct 2019	One 6mL injection into 4.8cm femoral lymph node. No other info available
1105-2003	Pembro	9 th Oct 2019	Injections into multiple large scalp lesions. Reduced after first dose of RP1, prior to addition of nivo SEE SLIDE 15
1122-2003	UV-1+pembro	24 th Oct 2019	One injection into 3.1cm axillary node. No other info available (UV-1 is a peptide vaccine)

Anti-PD1 refractory patients with follow up scans highlighted

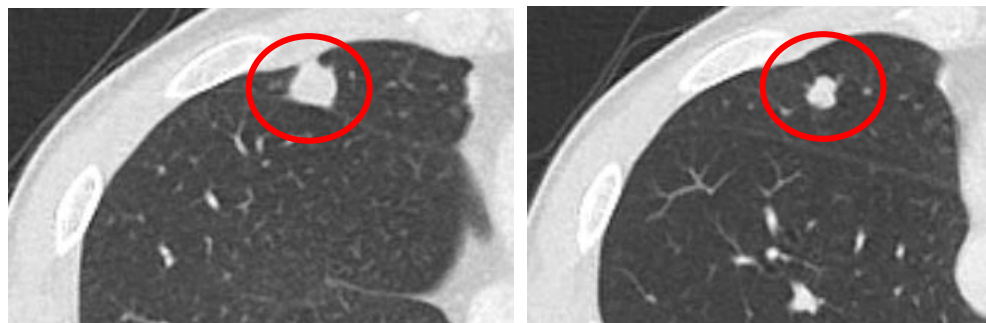
Patients receive a first dose of 1×10^6 pfu/mL of RP1 then subsequent doses of 1×10^7 pfu/ml every two weeks for up to 8 total RP1 doses. Combination with nivolumab is started from the second dose of RP1 & continues for up to two years

Patient #: 4401-1022 (ipilimumab & pembrolizumab refractory melanoma)

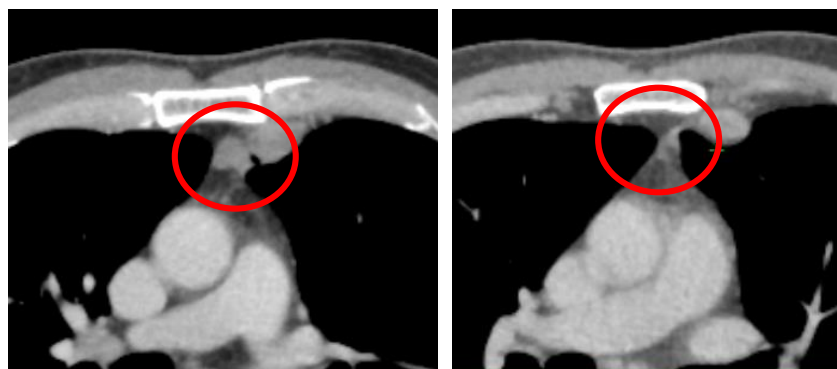
4

- Disease sites: Breast, lung, mediastinal and peritoneal anterior to the spleen
- RP1 injection site: Lesion behind the left ear

Lung



Anterior mediastinum



Baseline

10 months

- Confirmed progression on prior immune checkpoint blockade, where two sequential PET scans demonstrated new lesions while also concurrently being treated with local therapy for the lesion behind the ear, then entry into the RP1 clinical trial
- Ongoing PR
- Patient remains on treatment at 11 months

Patient #: 4403-1003 (ipilimumab/nivolumab refractory melanoma)

5

10th June 2019



24th June 2019 (pre nivolumab)



2nd September 2019



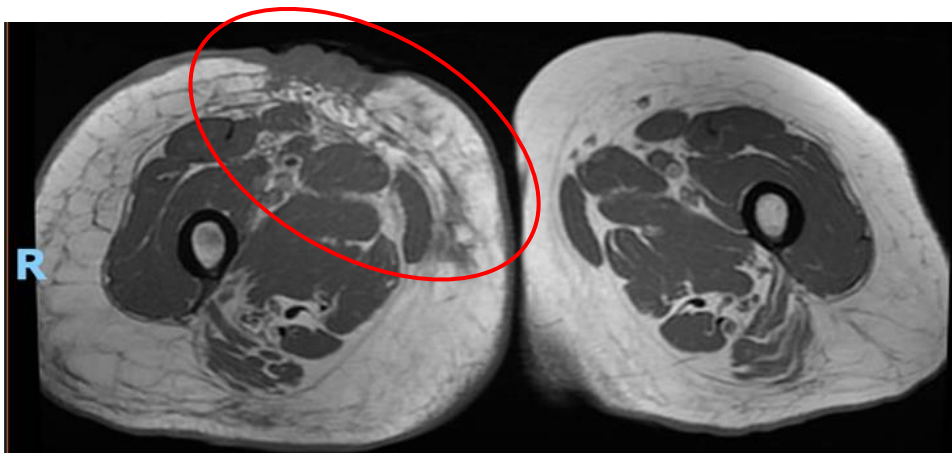
Patient history: Metastatic disease initially treated with ipili/nivo with best response of SD, then clear progression in the groin & thigh when radiotherapy followed by electrochemotherapy was added to continued nivolumab; following further clear progression, enrolled into the current trial

All tumors flattened after the first dose of RP1 (1×10^6 pfu/ml), i.e. prior to nivolumab & extensive oedema rapidly reduced

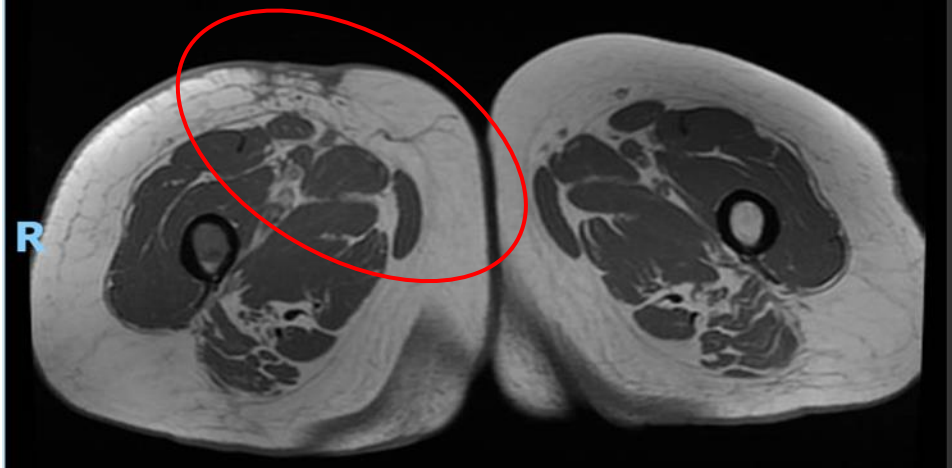
Patient #: 4403-1003 (ipilimumab/nivolumab refractory melanoma)

6

May 2019
(Baseline)



August
2019

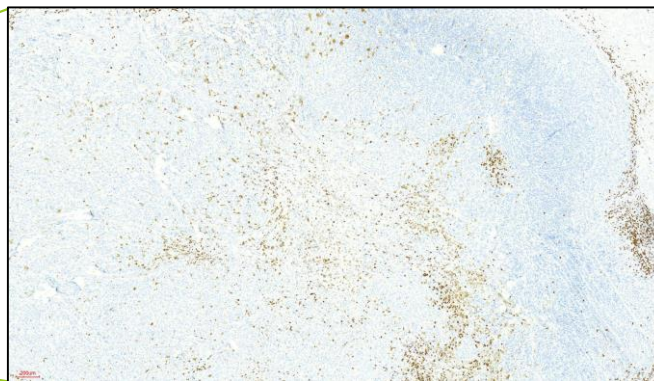
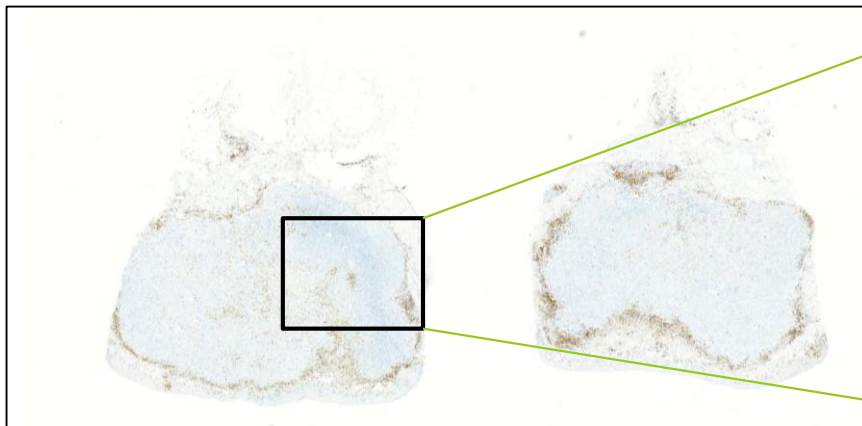


- Patient also had nodes in the groin which increased and are now reducing and lung metastases which following no change for prior 18 months are now reducing
- Patient quality of life has also greatly improved, from being essentially immobile at baseline to now able to go on long country walks
- Patient remains on treatment at >4 months

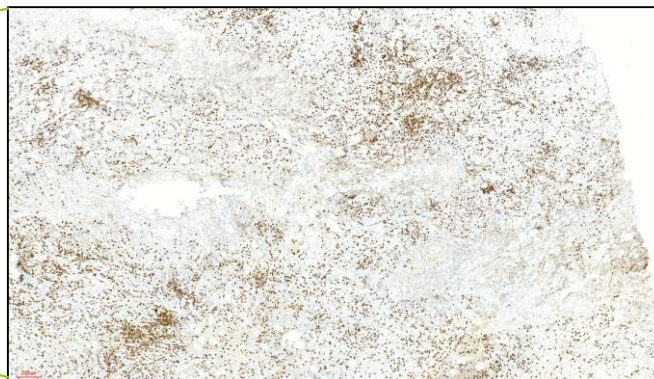
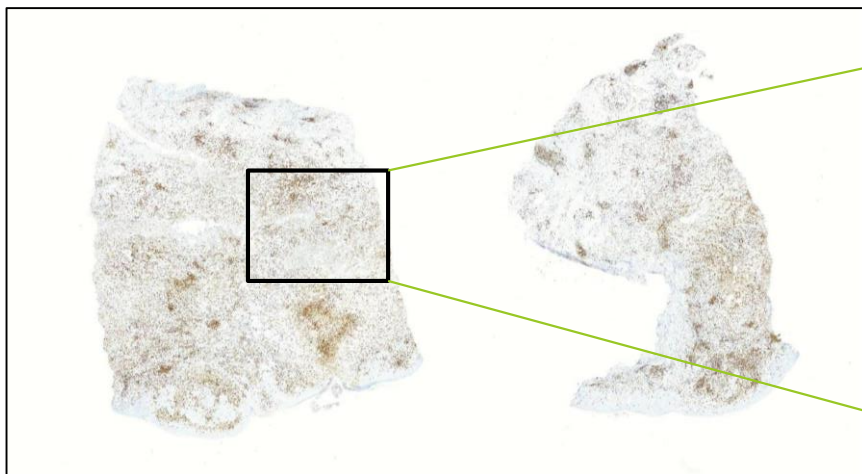
Reversal of T cell exclusion with RP1 combined with nivolumab

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CD8
Baseline
biopsy



CD8
Day 43
biopsy

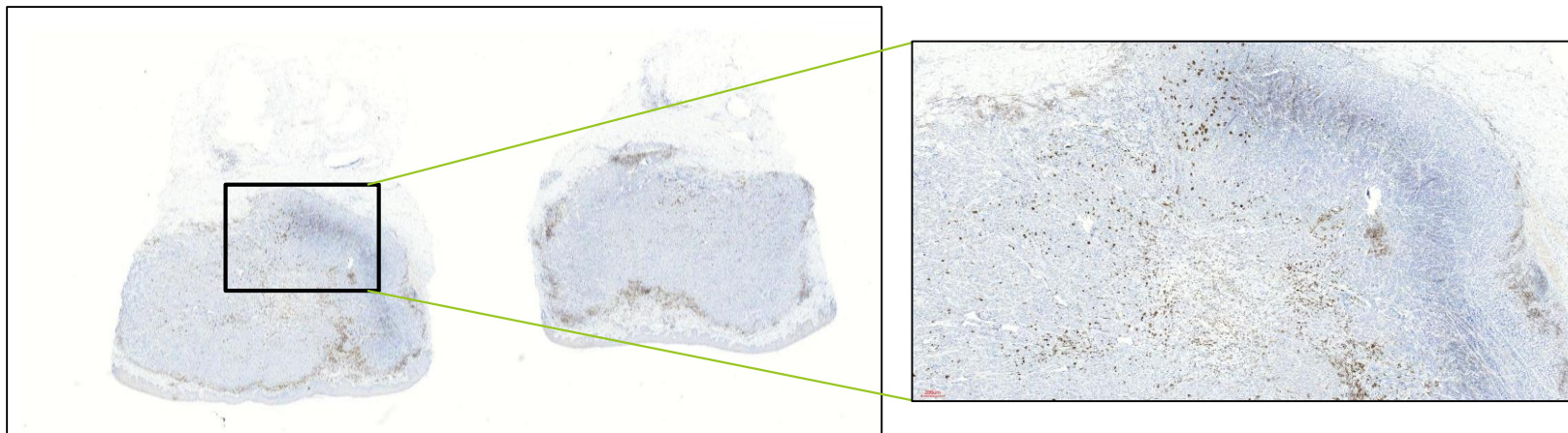


4403-1003
Cutaneous melanoma
(ipilimumab/nivolumab refractory)

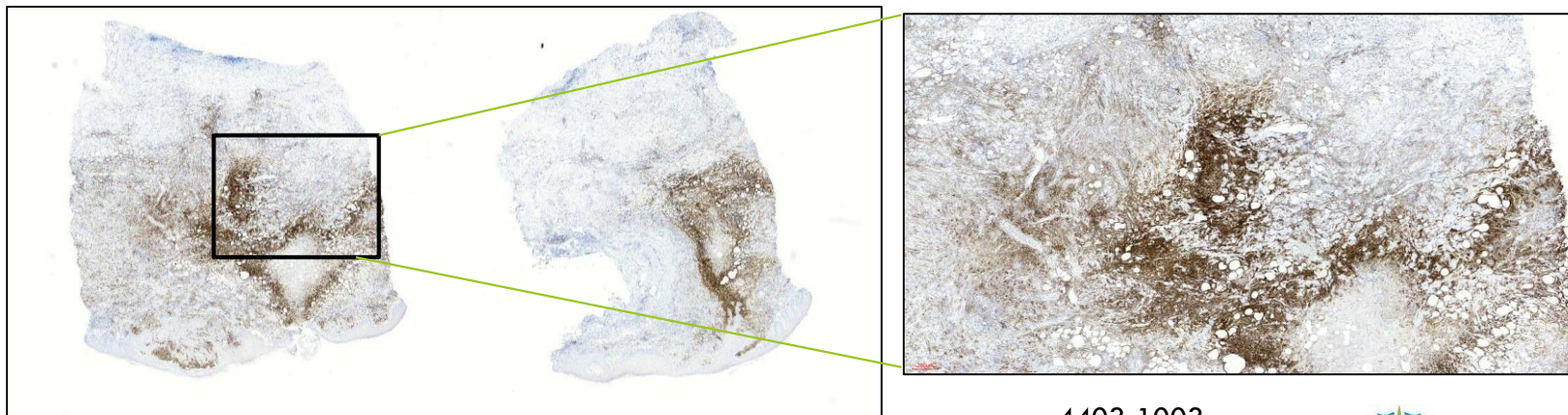
Reversal of T cell exclusion with RP1 combined with nivolumab

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PD-L1
baseline
biopsy



PD-L1
Day 43
biopsy



4403-1003
Cutaneous melanoma
(ipilimumab/nivolumab refractory)

Patient #: 1119-2001

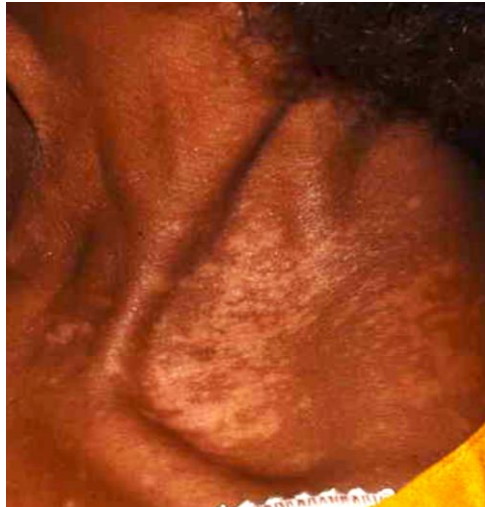
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Left foot



Vitiligo
D113

Left chest



Baseline



D57



D113



Right heel

(injected once with RP1; subsequent injections into inguinal nodes)

- Baseline disease in the foot, inguinal nodes and liver
- Initial increase seen in inguinal nodes and liver, followed by reduction (see next slides)
- Patient remains on treatment at 5 months

23rd May 2019

30th July 2019

10th September 2019

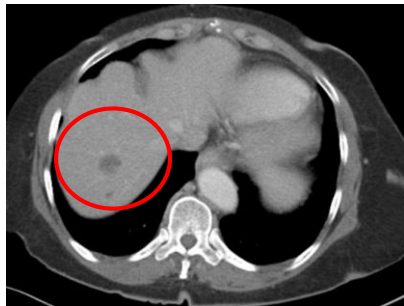


- Progression determined at C5 scan, reducing by 6 weeks later

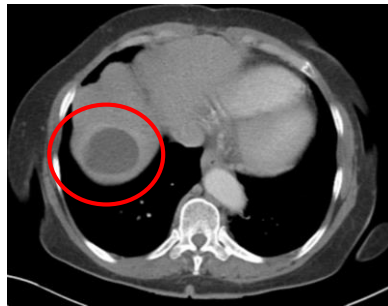
Patient #: 1119-2001

11

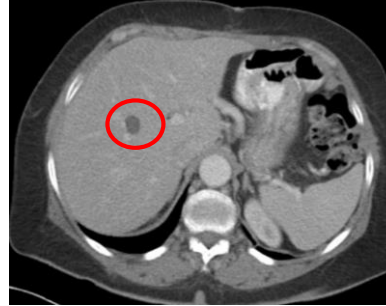
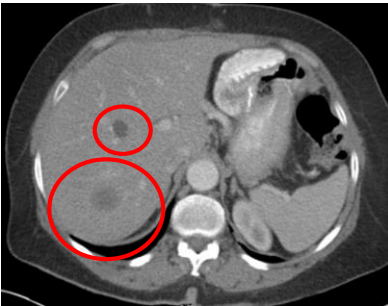
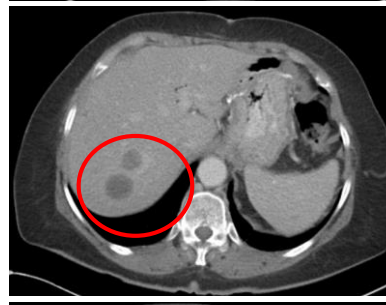
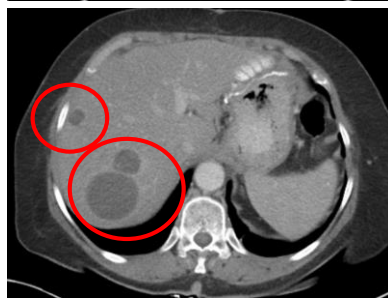
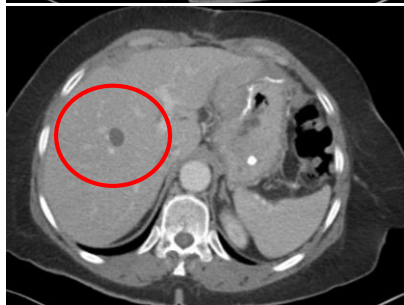
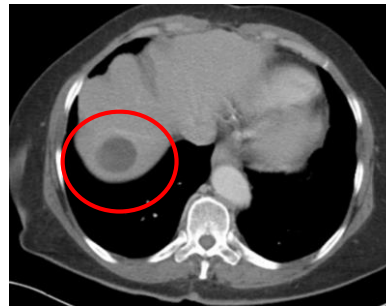
23rd May 2019



30th July 2019



10th September 2019



- Progression determined at C5 scan, reducing by 6 weeks later

Patient #: 1119-2003 (ipilimumab/nivolumab refractory melanoma)

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2nd July 2019
(screening)



17th Sept 2019



1st July 2019
(screening)



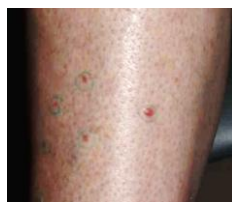
26th August 2019



24th October 2019



- The first ipilimumab/nivolumab refractory melanoma patient enrolled into the Phase 2 part of the study
- Patient remains on treatment at 3 months
- Current status: Ongoing partial response



Patient #: 4403-2003

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5th August 2019
(D1C1)



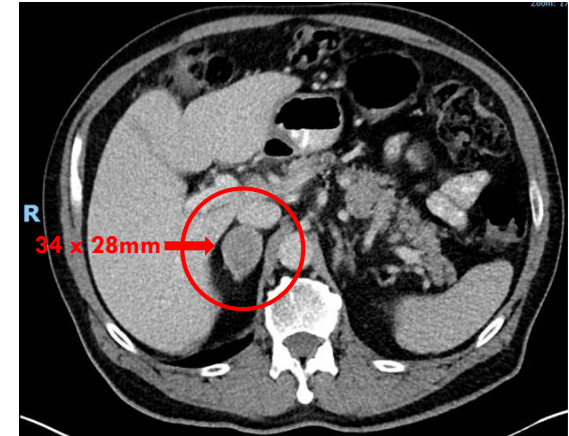
19th August 2019



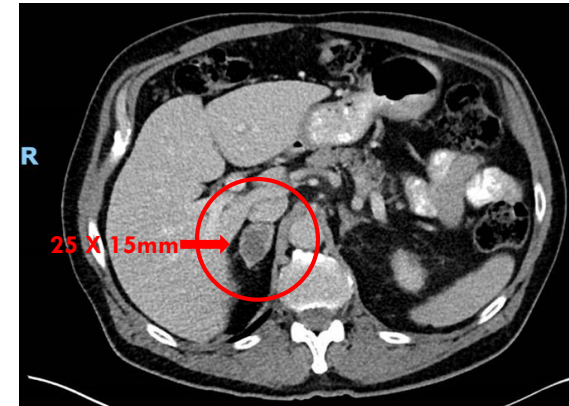
14th October 2019



16th July 2019 (screening)



30th September 2019



- D43 biopsy of the injected lesion tumor free
- Adrenal mass reduced from 34x28mm to 25x15mm at C5 scan
- Patient remains on treatment 3 months
- Current status: Ongoing partial response

Patient #: 1103-2001

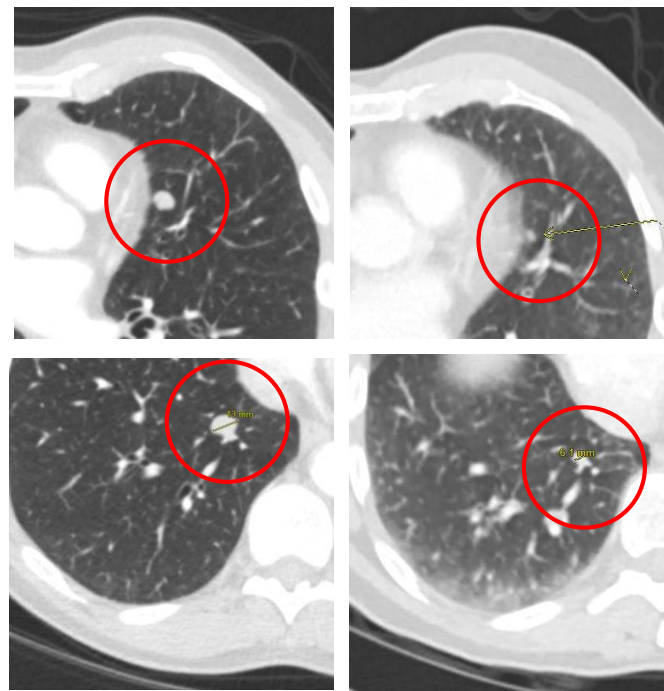
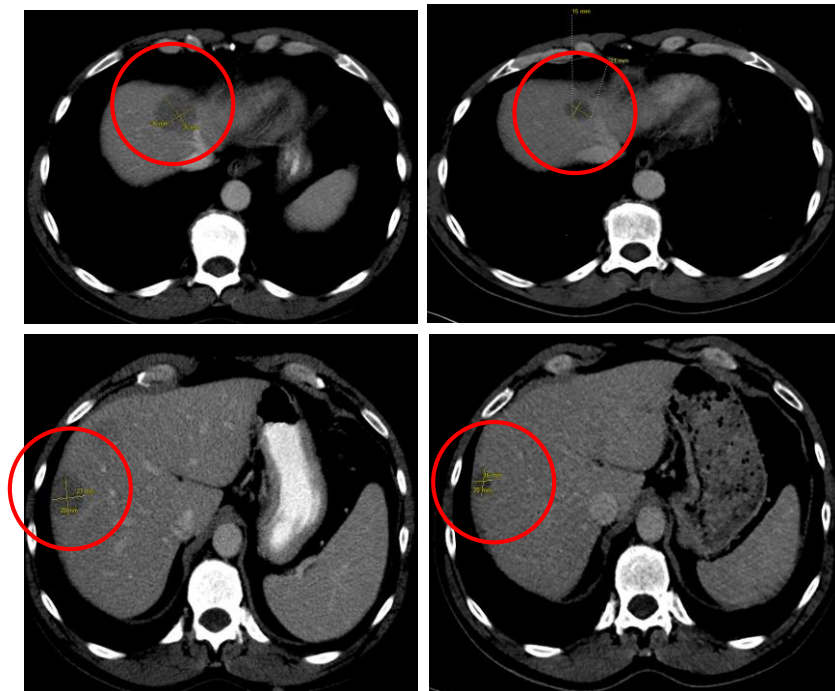
14

12th Aug 2019
(screening)

20th October 2019

12th Aug 2019
(screening)

20th October 2019



- Patient remains on treatment at 3 months
- Current status: Ongoing partial response

Patient #: 1105-2003 (pembrolizumab refractory melanoma)

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10th October 2019



16th October 2019



23rd October 2019
(pre-nivolumab)



- Increased drainage noted by day 6 prior to tumors reducing by day 13 (pre-nivolumab)
- Patient remains on treatment at 2-3 weeks