



NEXT GENERATION ONCOLYTIC
IMMUNOTHERAPY

**Example responding skin cancer patients treated with RP1
combined with nivolumab in study RPL-001-16**

(Data cut-off 15th Oct 2020)

A microscopic background image showing a central, textured, purple, cone-shaped structure, possibly a cell or a virus, surrounded by numerous small, blue, spherical particles. The background is a gradient of blue and purple, with some yellow and orange structures visible on the left and right sides.

NEXT-GENERATION ONCOLYTIC
IMMUNOTHERAPY

Example CSCC patients

Patient 4403-1002 – 3rd January 2019

3



- Patient with extensive recurrent CSCC previously treated with surgery (including skin grafts), radiotherapy, cisplatin/5FU, then electrochemotherapy

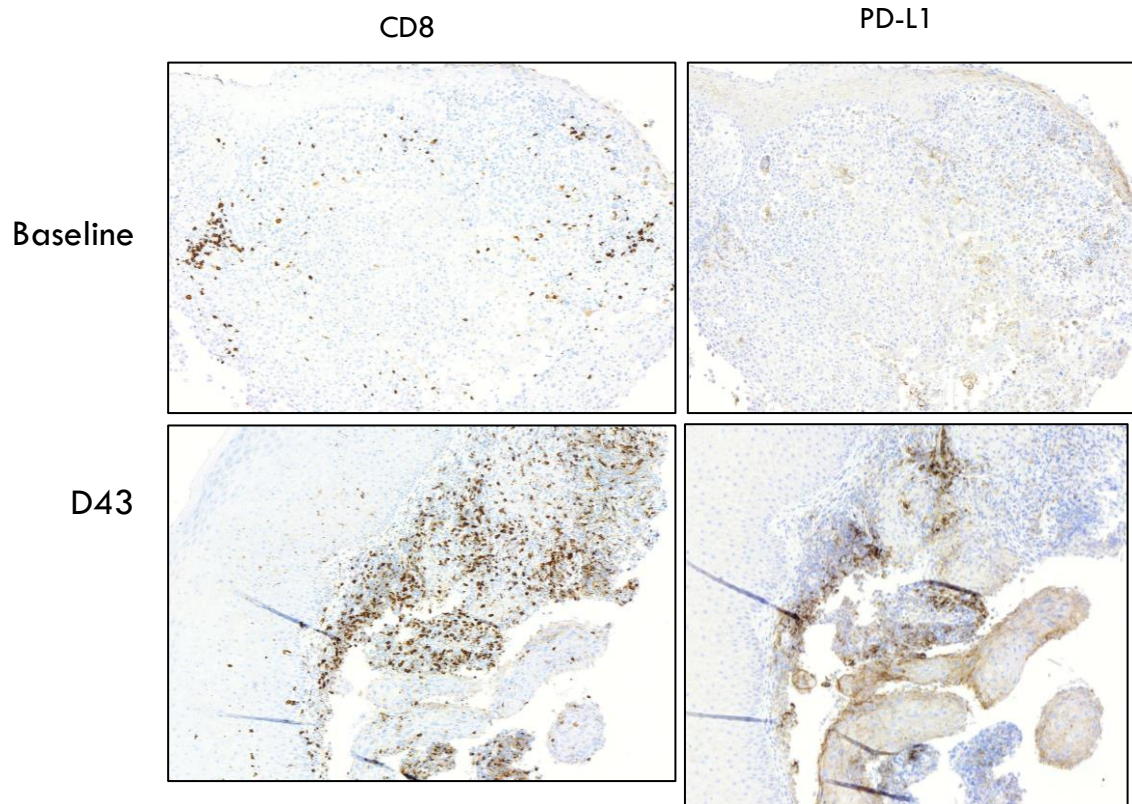
Patient 4403-1002 – 20th July 2020 (CR)

4



Patient 4403-1002 (CR)

5



Patient 4402-2001 (CR)

6

16th June 2019
(baseline)



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



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

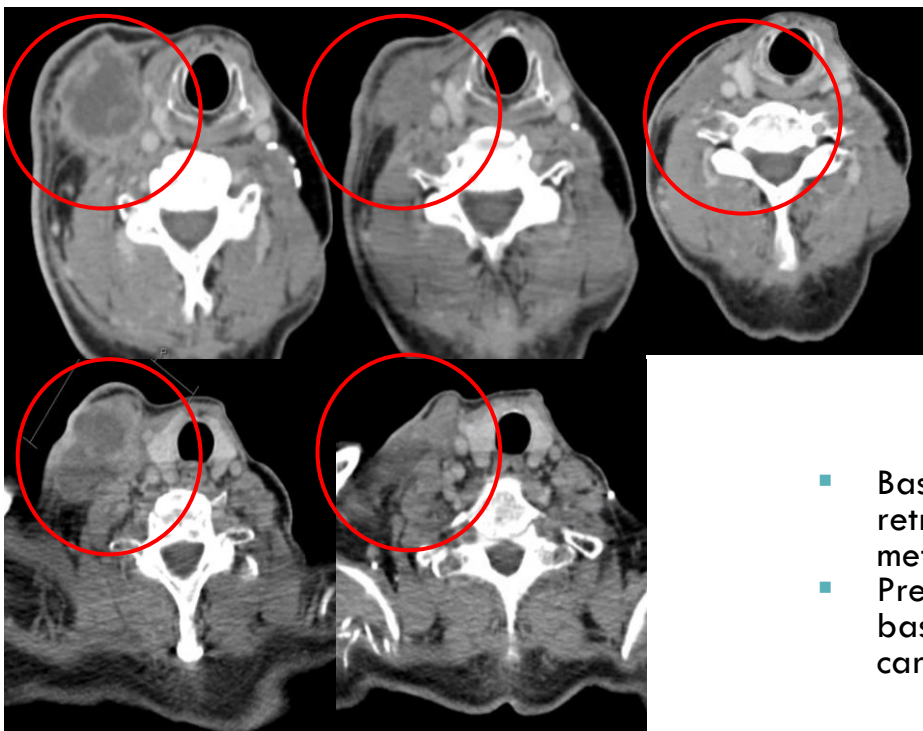


- Patient with recurrent CSCC of the neck (bilateral), previously treated with cisplatin-based chemoradiation & six cycles of carboplatin/5-FU, prior to entering the clinical trial
- Both the large injected tumor & the smaller contralateral tumor in the neck reduced considerably before the first nivolumab dose, i.e. after the first dose of RP1

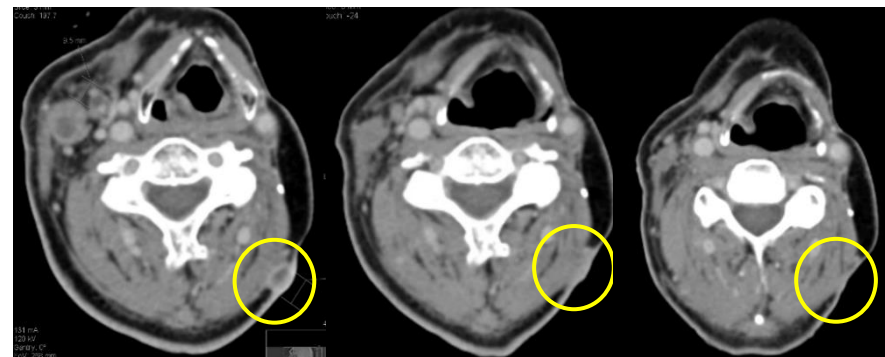
Patient 4402-2001 (CR)

7

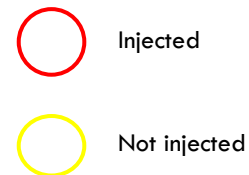
Baseline Right neck (injected)
8 weeks 24 weeks



Baseline Left neck (not injected)
8 weeks 16 weeks



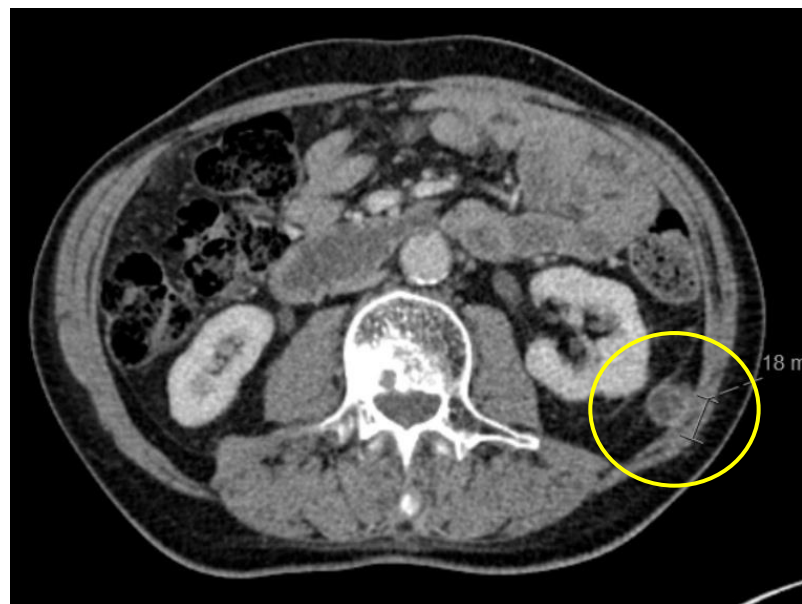
- Baseline disease: Bilateral neck, retroperitoneal lymph nodes, bone metastases
- Previously treated with cisplatin-based chemoradiation & carboplatin/5-FU



Patient 4402-2001 (CR)

8

Baseline



16 weeks



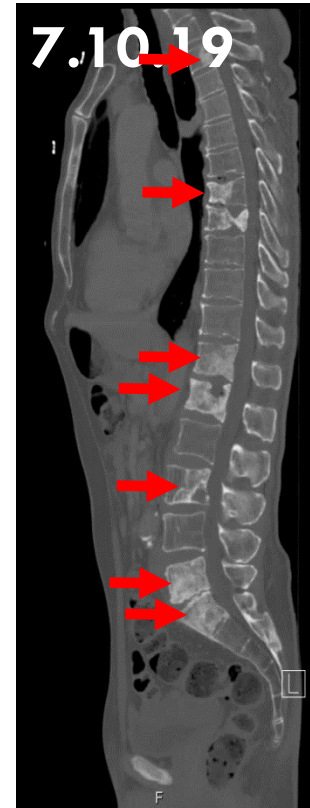
- The patient also had baseline retroperitoneal tumors which completely resolved



Not injected

Patient 4402-2001 (CR)

9

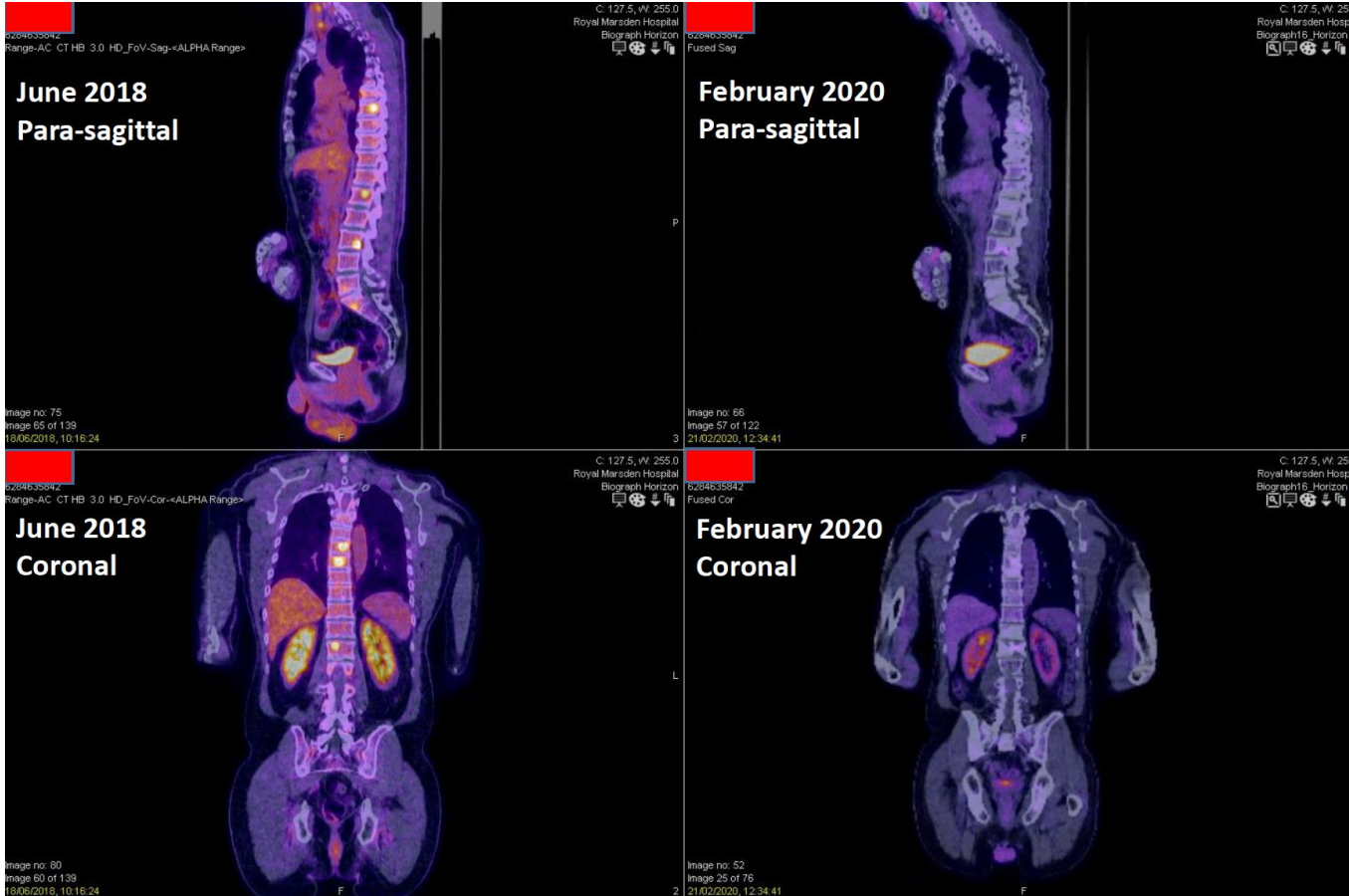


Complete sclerosis of all bone lesions with no areas of active disease. Declared radiological CR. Confirmed by PET scan (next slide)

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

Patient 4402-2001 (CR)

10

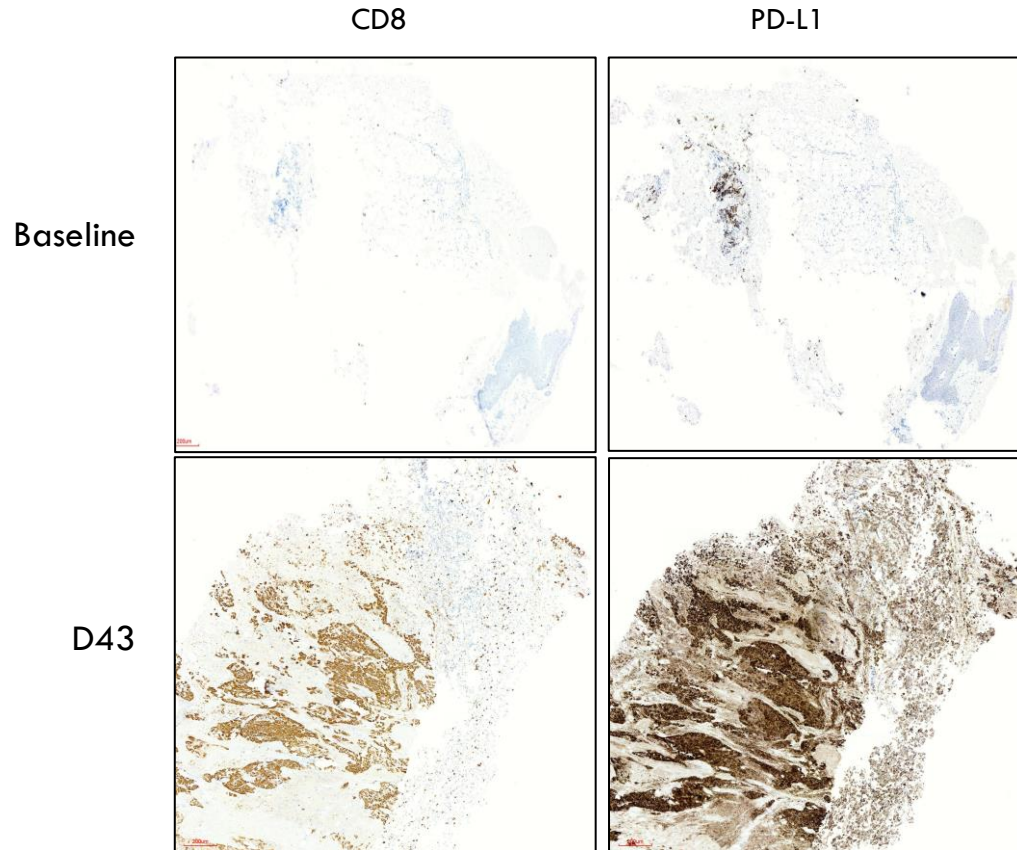


Bone metastases had substantially increased by CT between the prior PET scan (June 2018) and initiating the trial (June 2019), but no PET scan was performed at screening.

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

Patient 4402-2001 (CR)

11



Patient 4402-2004 (PR)

12

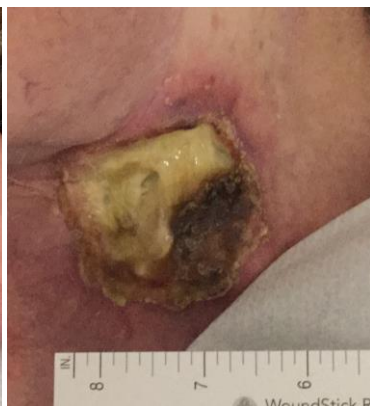
2nd Sept 2019
(pre-dosing)

16th Sept
(post single RP1 dose)

15th Oct

2nd Dec

13th Jan



Baseline scan



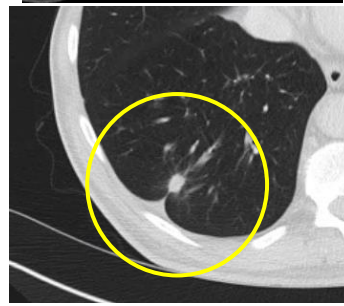
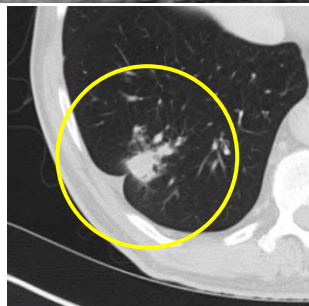
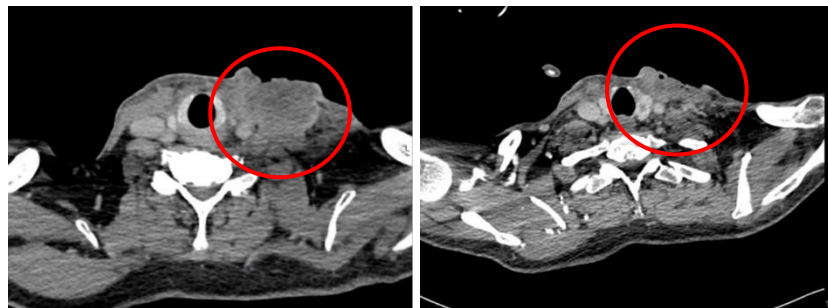
- Recurrent CSCC of the neck, previously treated with radiotherapy with immediate relapse after which the patient entered the clinical trial
- The large injected tumor in the neck flattened considerably after the first dose of RP1 (i.e. before the first nivolumab dose), & continued to reduce thereafter

Patient 4402-2004 (PR)

13

28th August 2019

25th October 2019

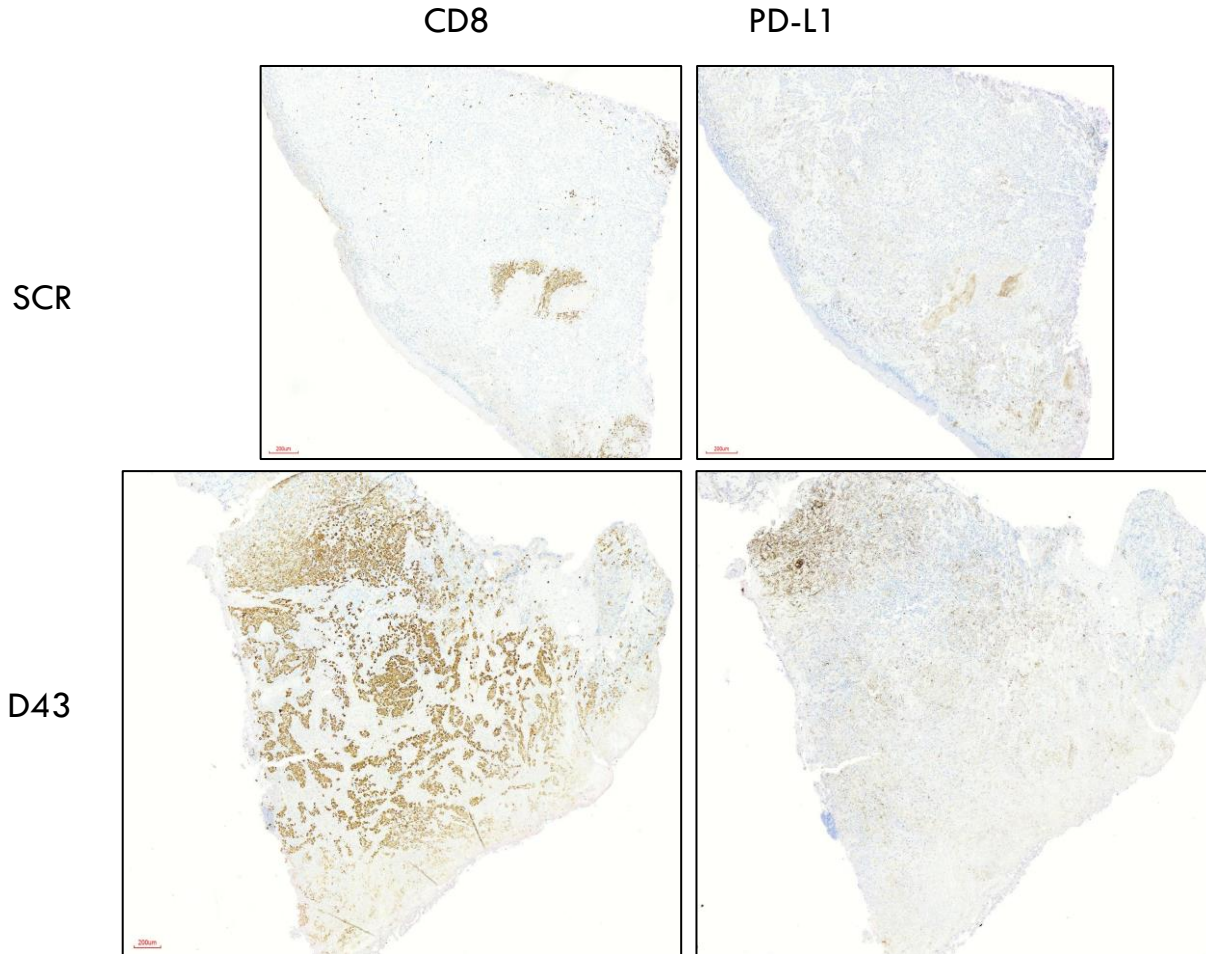


- The only other sites of disease were lesions in the lung, which also reduced



Patient 4402-2004 (PR)

14



Patient 4402-2005 (CR)

15

25th Sep 2019
(Baseline)

9th Oct 2019
(pre nivolumab)

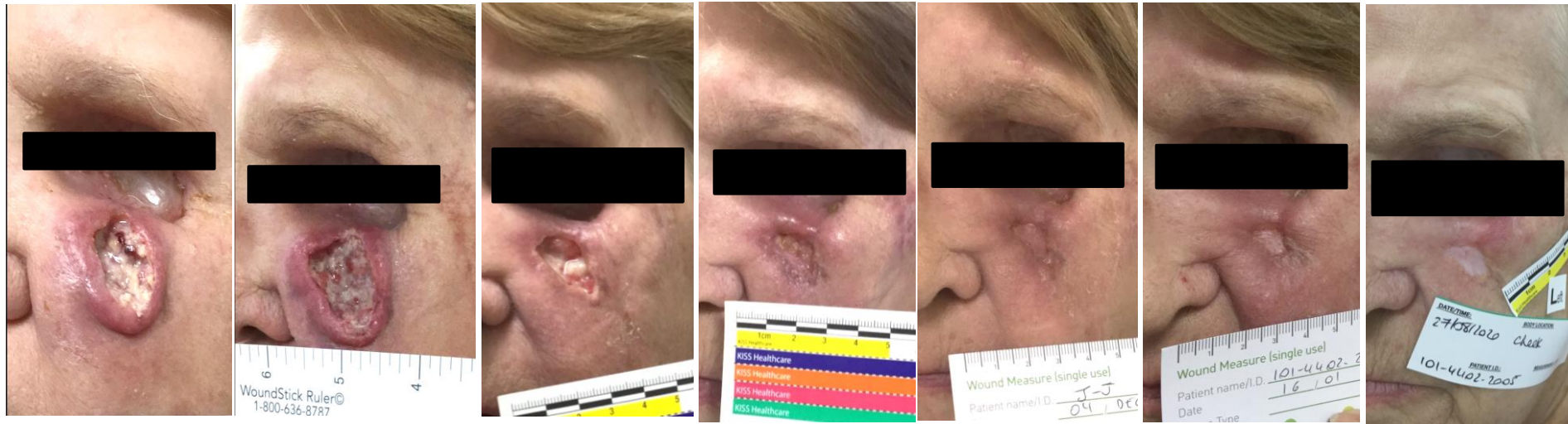
6th Nov 2019

20th Nov 2019

4th Dec 2019

16th Jan 2020

27th Aug 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 nivolumab
- CR confirmed by biopsy/CT in December

Patient 4402-2005 (CR)

16

19th Sep 2019



10th January 2020



- Biopsy confirmed CR in December
- At baseline, tumor was invading through the maxillary bones

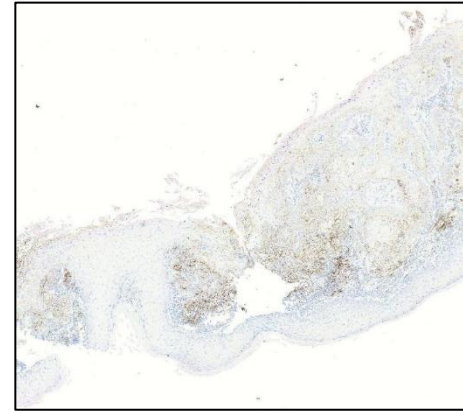
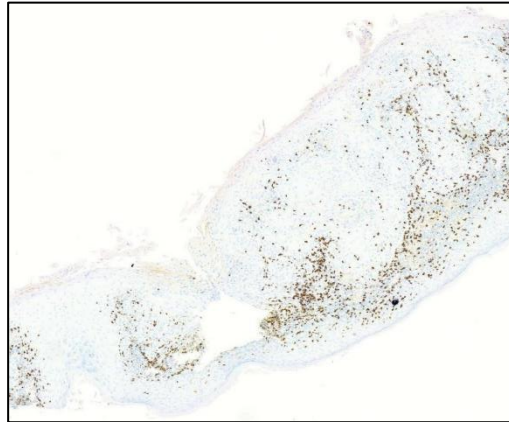
Patient 4402-2005 (CR)

17

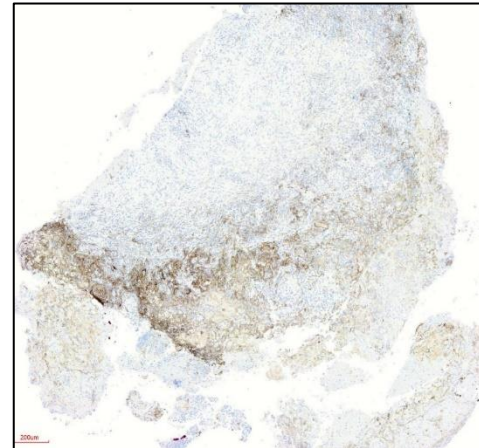
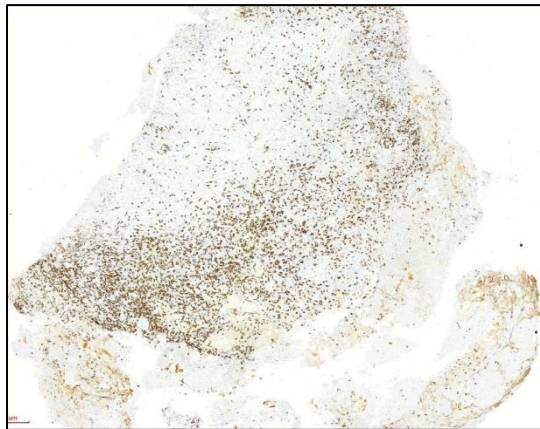
CD8

PD-L1

SCR



D43



Patient 4402-2006 (CR)

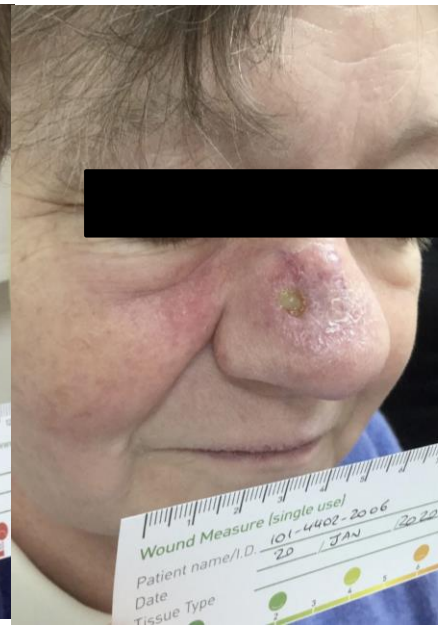
18

23rd December 2019
(Baseline)

6th January 2020
(pre nivolumab)

20th January 2020

2nd March 2020



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

Patient 4402-2006 (CR)

19

Baseline



Day 57



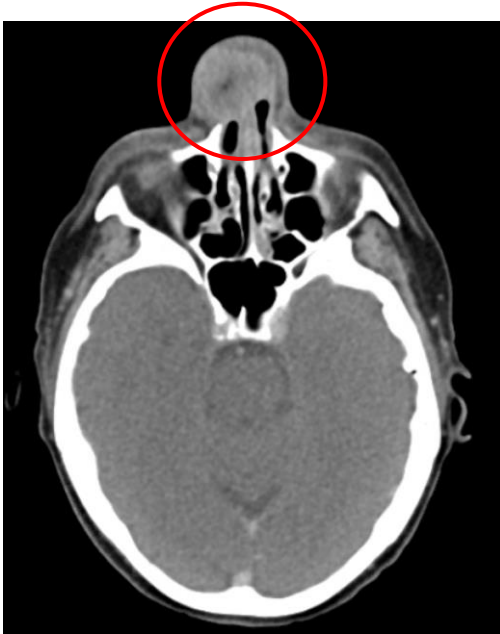
1st Sept 2020



Patient 4402-2006 (CR)

20

18th Dec 2019
(Screening)



2nd Feb 2020



14th April 2020*



- The alternative to study treatment was rhinectomy

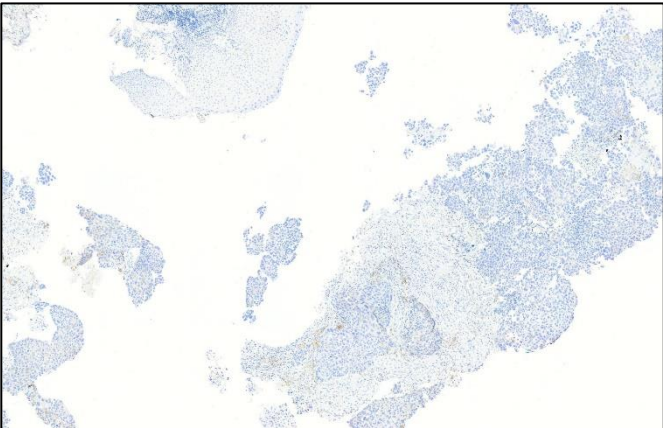
* CT done in a different plane to prior scans to maximally capture the affected area

Patient 4402-2006 (CR)

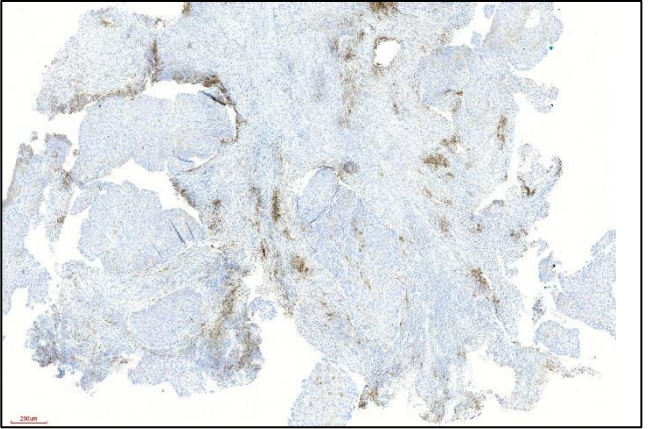
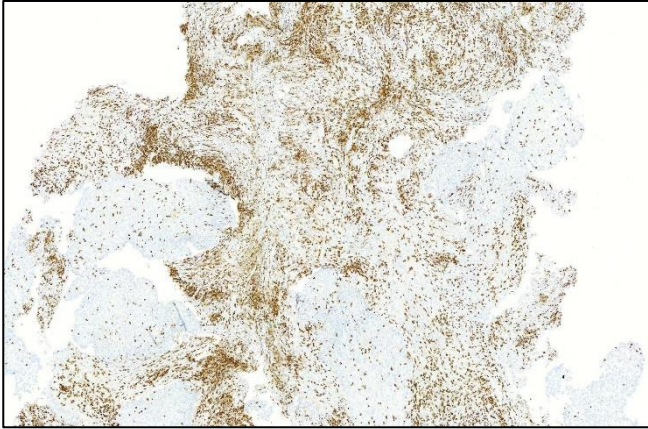
CD8

PD-L1

SCR



D43



Patient 1121-2003 (CR)

22

12th May 2020
(Baseline)

26th May 2020
(pre nivolumab)

9th June 2020

8th September 2020



- Prior cetuximab
- Injections into left neck lesion (1.7cm)
- Nivolumab subsequently discontinued due to dermatitis

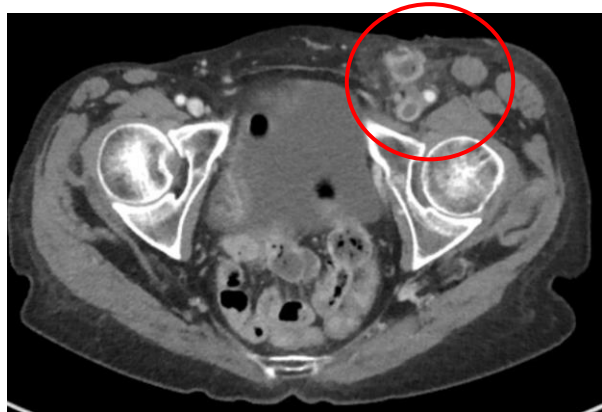
Patient 1122-2014 (PR; clinically assessed Oct; Oct CT pending)

23

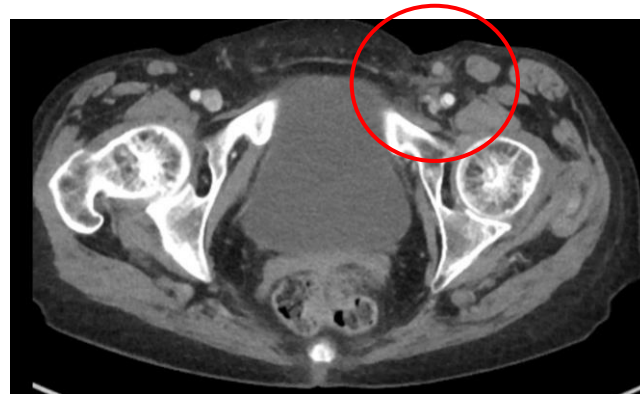
22nd May 2020



12th October 2020



Screening



17th Aug 2020

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

A microscopic background image showing a central, textured, purple, cone-shaped structure, possibly a virus or a cell, surrounded by numerous small, blue, spherical particles. The background is a gradient of blue and purple, with some yellow and orange structures visible on the left and right sides.

NEXT-GENERATION ONCOLYTIC
IMMUNOTHERAPY

Angiosarcoma patients

Patient 1122-2002 – Angiosarcoma (PR)

25



6th November 2019

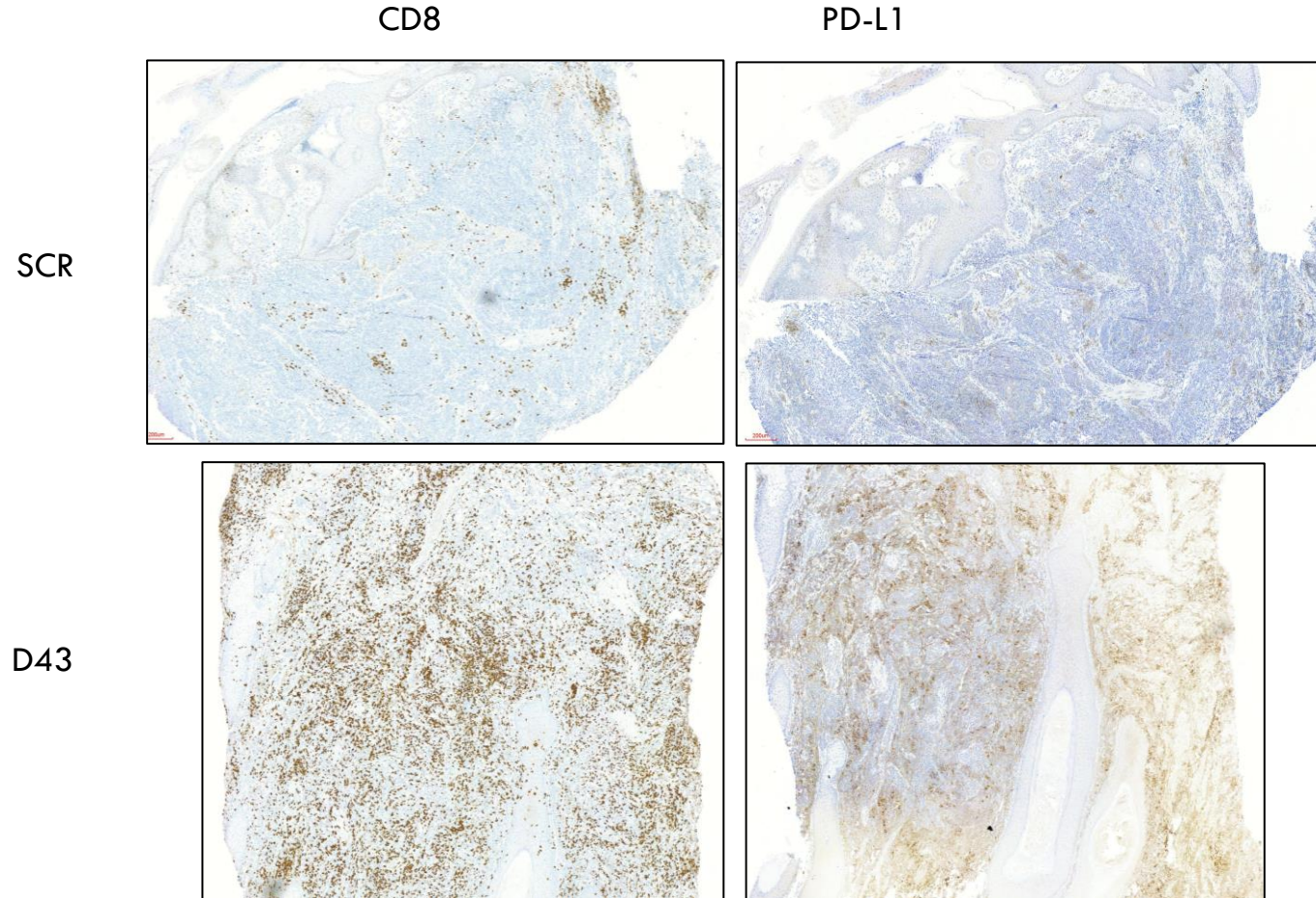


18th February 2020

- Patient subsequently withdrew from treatment due to nivolumab side effects

Patient 1122-2002 – Angiosarcoma (PR)

26



Patient 1122-2013 – Angiosarcoma (PR)

27



30th March (C1D1)



13th April 2020



27th May 2020



24th Sept 2020

- nivolumab stopped in April due to side effects
- Patient also has other disease on the scalp & uninjected nodal disease

Patient 1122-2019 – Angiosarcoma

28



12th Aug 2020 (CID1 2nd July 2020)



23rd Sept 2020

Formal response assessment awaited

A microscopic background image showing a central, textured, purple, cone-shaped structure, possibly a cell or a virus, surrounded by numerous small, blue, spherical particles. The background is a gradient of blue and purple, with yellow and orange structures on the left and right sides, suggesting a complex biological environment.

NEXT-GENERATION ONCOLYTIC
IMMUNOTHERAPY

Example melanoma patients

Anti-PD1 naïve cutaneous melanoma patients

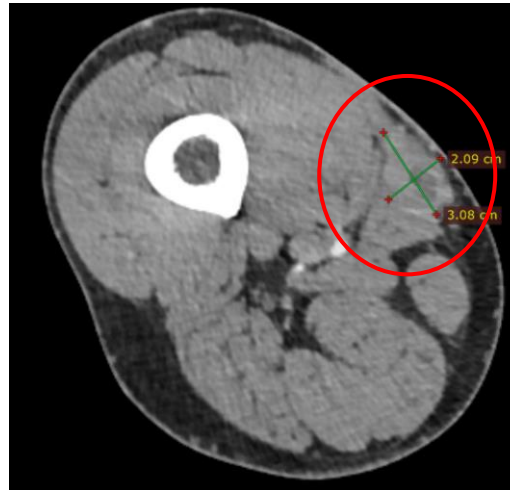
Patient #: 1103-2001 (CR)

31

12th Aug 2019
(screening)



20th Oct 2019



16th April 2020



- 6x3ml injections into medial right thigh (after which nothing left to inject into)
- Ongoing CR with marked reduction of multiple uninjected lesions including liver, lungs, resolved soft tissue lesion of right gluteus & injected lesion



Injected



Not injected

Patient #: 1103-2001 (CR)

32

12th Aug 2019
(screening)

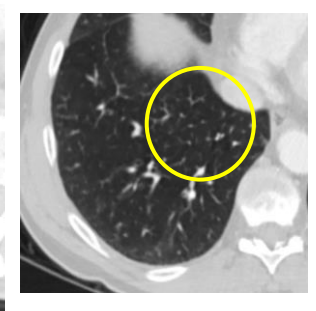
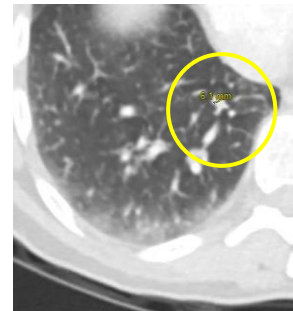
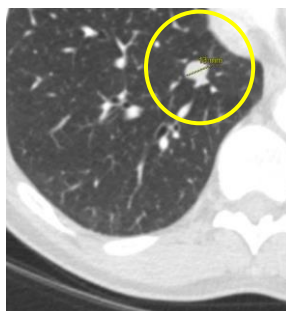
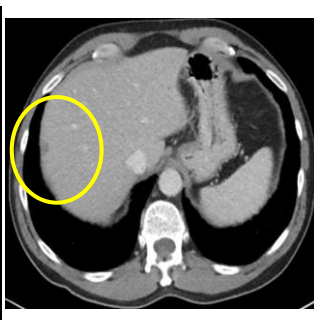
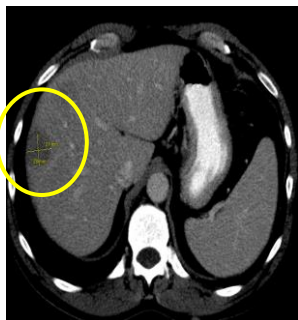
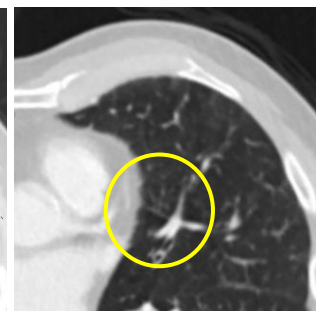
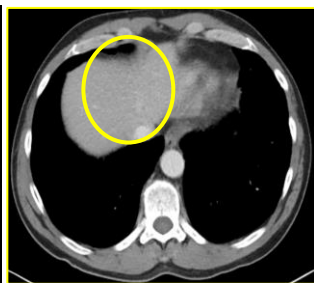
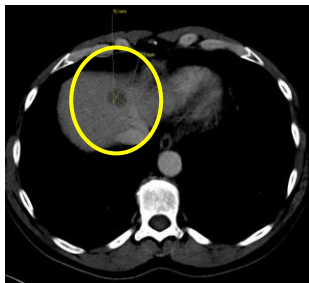
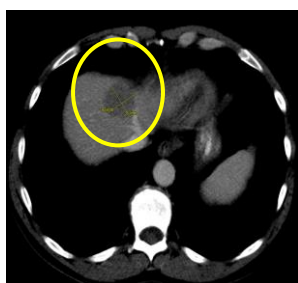
20th Oct 2019

10th Feb 2019

12th Aug 2019
(screening)

20th Oct 2019

10th Feb 2019



Injected



Not injected

Patient #: 1119-2001

33

Baseline

D57

D113

D169

D225



- Baseline disease in the foot, inguinal nodes and liver
- Heel injected once, subsequent injections into inguinal nodes only
- Initial increase seen in inguinal nodes and liver, followed by reduction (see next slides), then progression (liver) at 8 months

Patient #: 1119-2001

34

23rd May 2019

30th July 2019

10th September 2019

19th November 2019

14th January 2020



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



Injected



Not injected

Patient #: 1119-2001



Injected



Not injected

- Progression in the liver (uninjected) determined at C5 scan, reducing by 6 weeks later

35

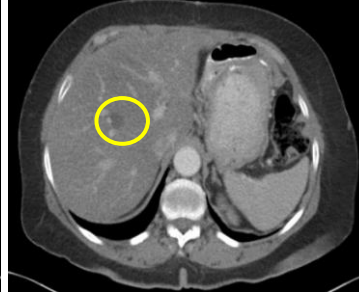
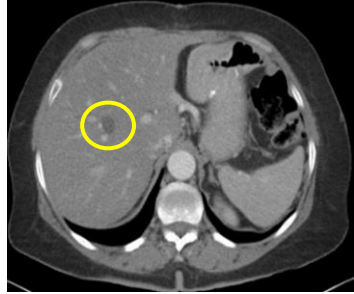
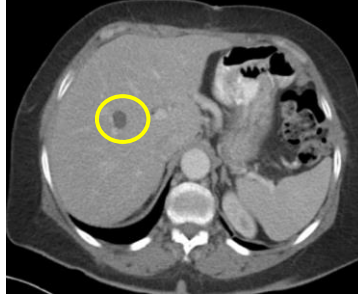
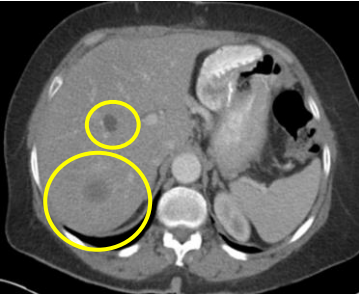
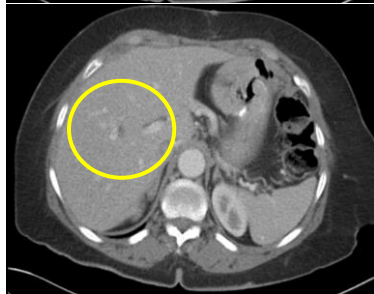
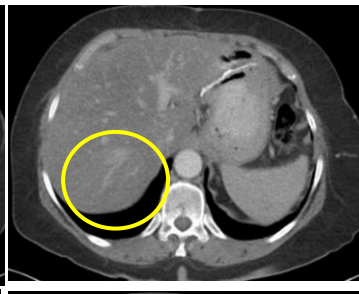
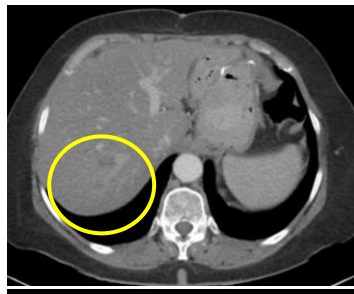
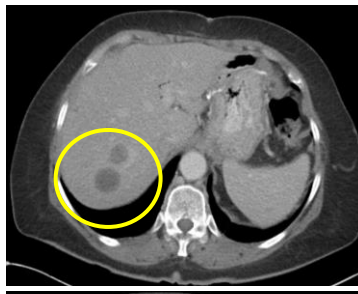
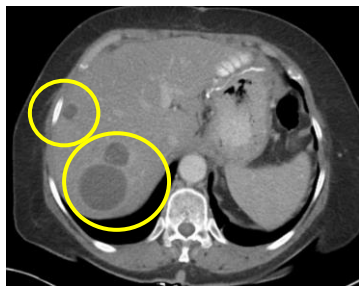
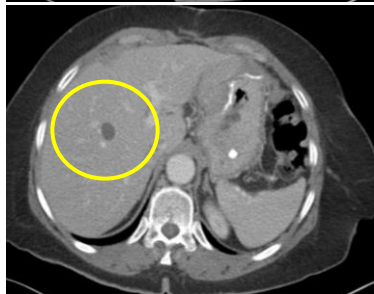
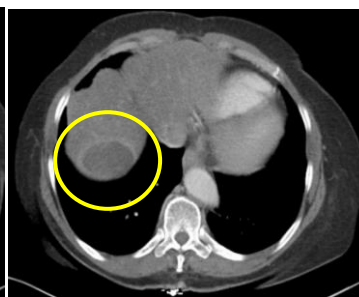
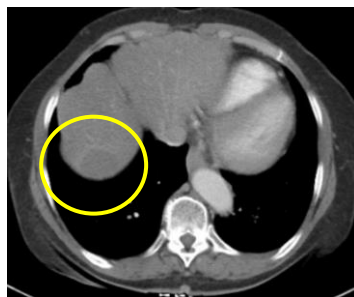
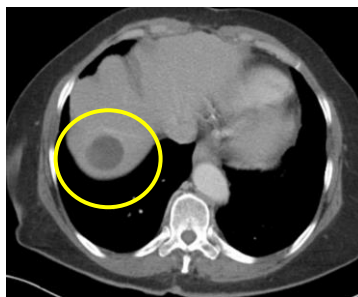
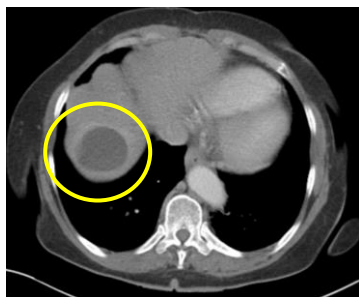
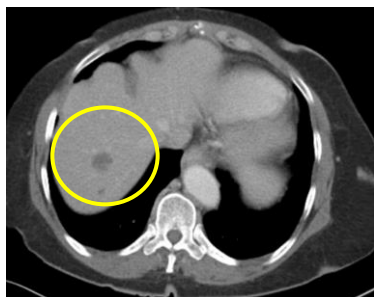
23rd May 2019

30th July 2019

10th September 2019

19th November 2019

14th January 2020



Patient #: 1119-2001 - Vitiligo

36



Left foot
(D113)



Right foot
(D169)



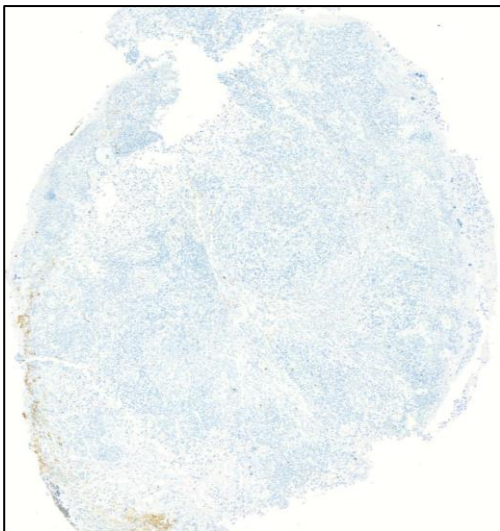
Left chest
(D169)

Patient #: 1119-2001

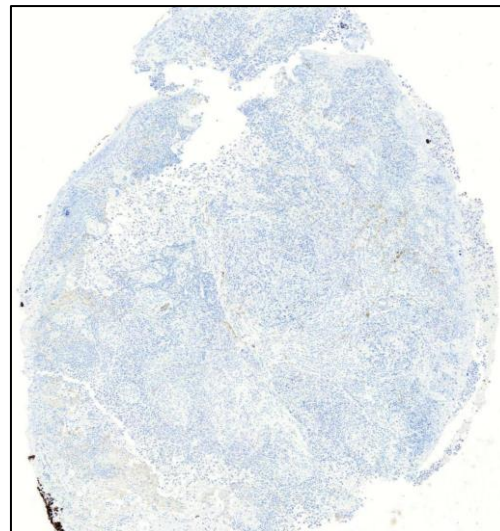
37

5X

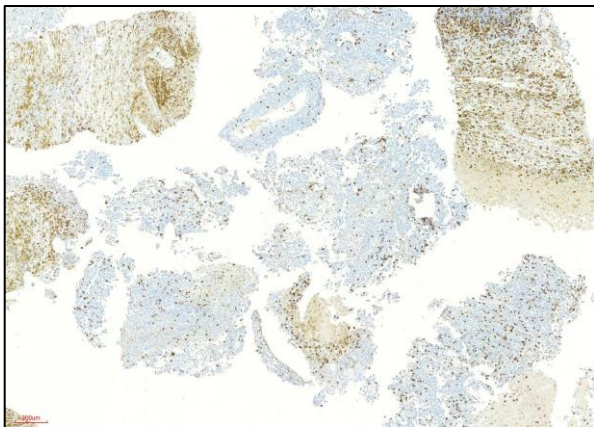
CD8
Baseline
biopsy



PD-L1
Baseline
biopsy



CD8
Day 43
biopsy
(injected tumor)



PD-L1
Day 43
biopsy
(injected tumor)



Patient #: 1119-2005 (PR)

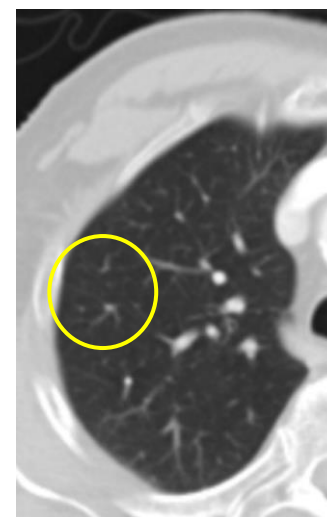
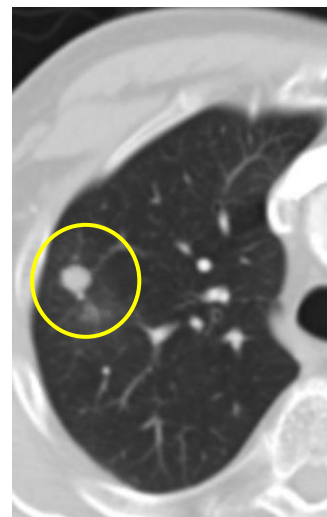
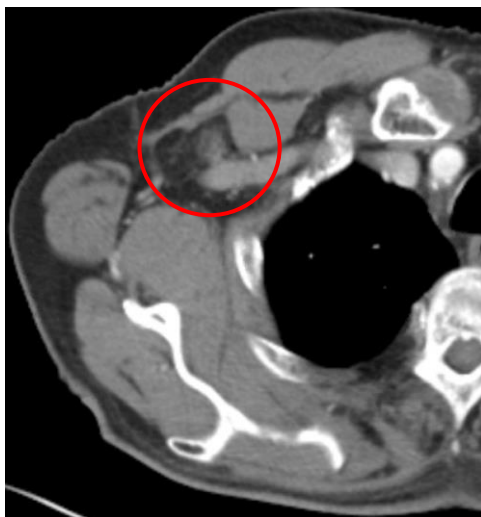
38

22nd Oct 2019
(screening)

11th Feb 2019

22nd Oct 2019
(screening)

11th Feb 2019



Baseline

- Injections into 3.1x2.4cm right axillary lymph nodes



Injected

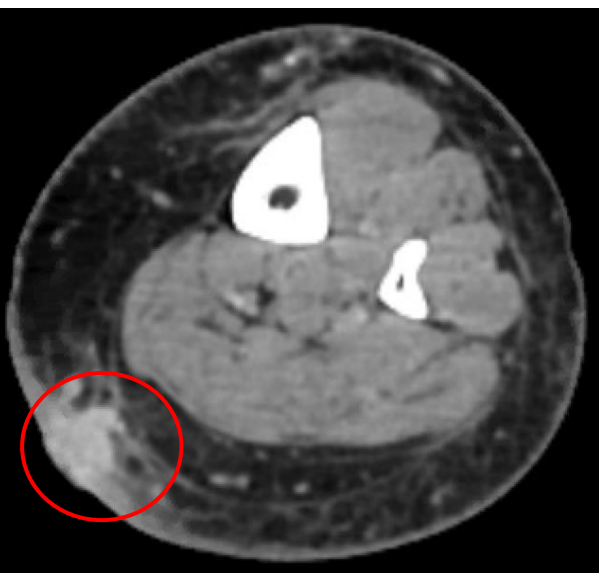


Not injected

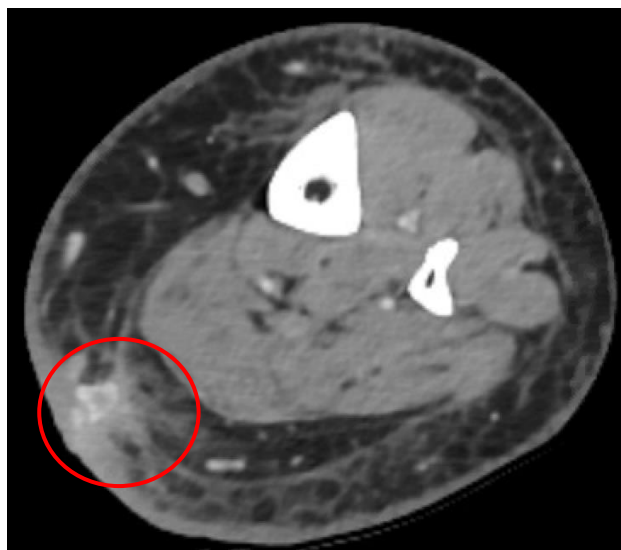
Patient #: 1121-2002 (CR)

39

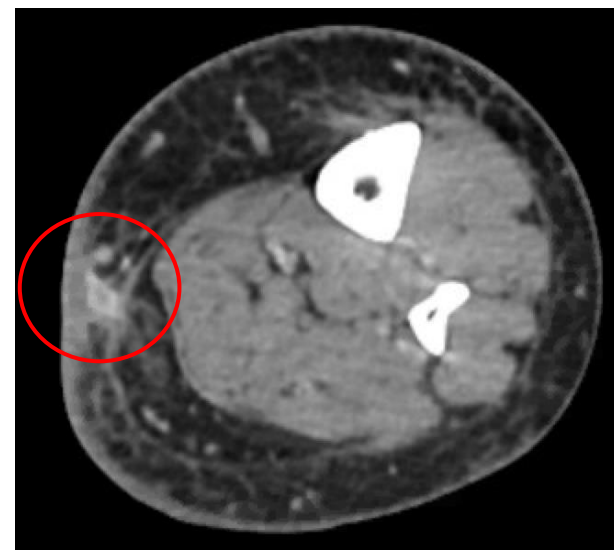
16th Dec 2019
(screening)



6th March 2020



5th May 2020



Patient #: 4403-2003 (PR)

5th August 2019
(DIC1)

19th August 2019

14th October 2019

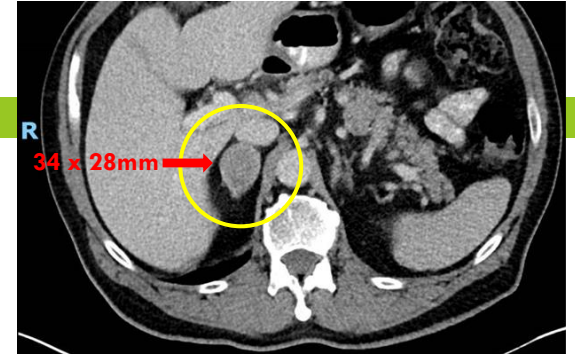


Injected

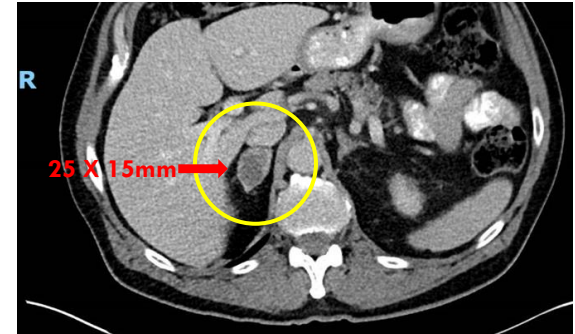


Not injected

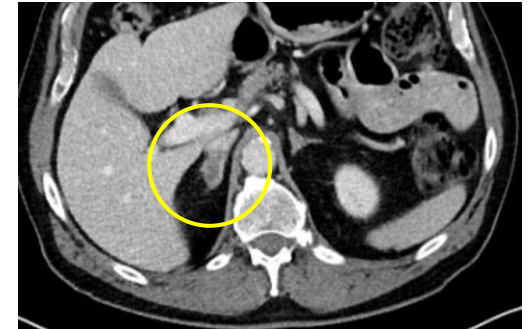
16th July 2019 (screening)



30th September 2019



25th November 2019



Patient #: 4403-2004 (SD)

41

25th Nov 2019
(screening)



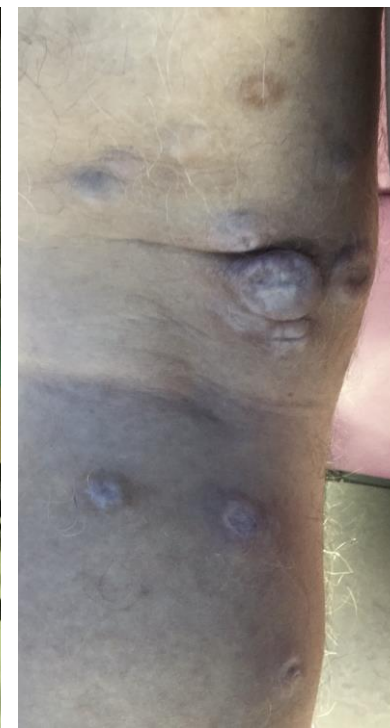
13th Dec 2019



13th Jan 2020



14th Sept 2020
(Awaiting biopsy results)



Baseline 23rd Oct 2019

- Left iliac node (24x18mm), intramuscular left thigh
- Numerous cutaneous/subcutaneous lesions left leg (representative area shown)

Patient #: 4401-2004

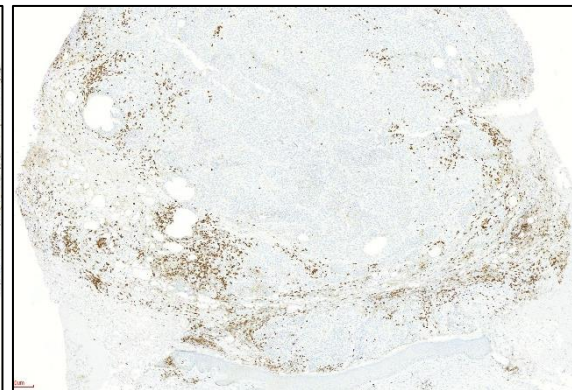
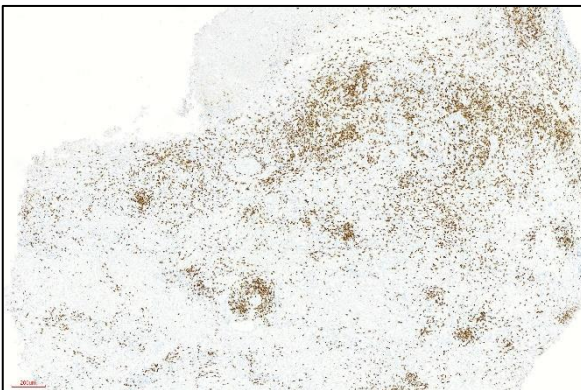
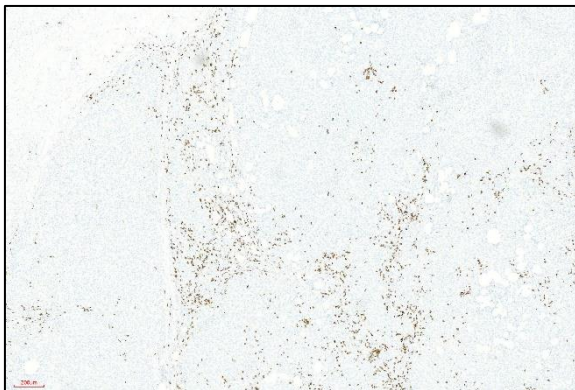
42

Archival/Screening

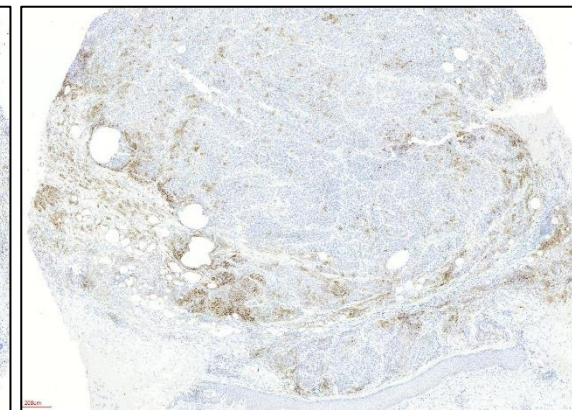
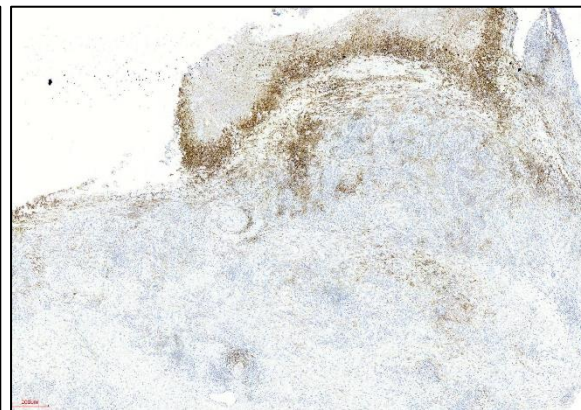
Day 43 - injected

Day 43 – Un-injected

CD8



PD-L1



Anti-PD1 experienced cutaneous melanoma patients

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

26th August 2019

1st July 2019
(screening)



5th November 2019



7th April 2020



25th Aug 2020



■ Initial progression followed by response

○ Injected

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

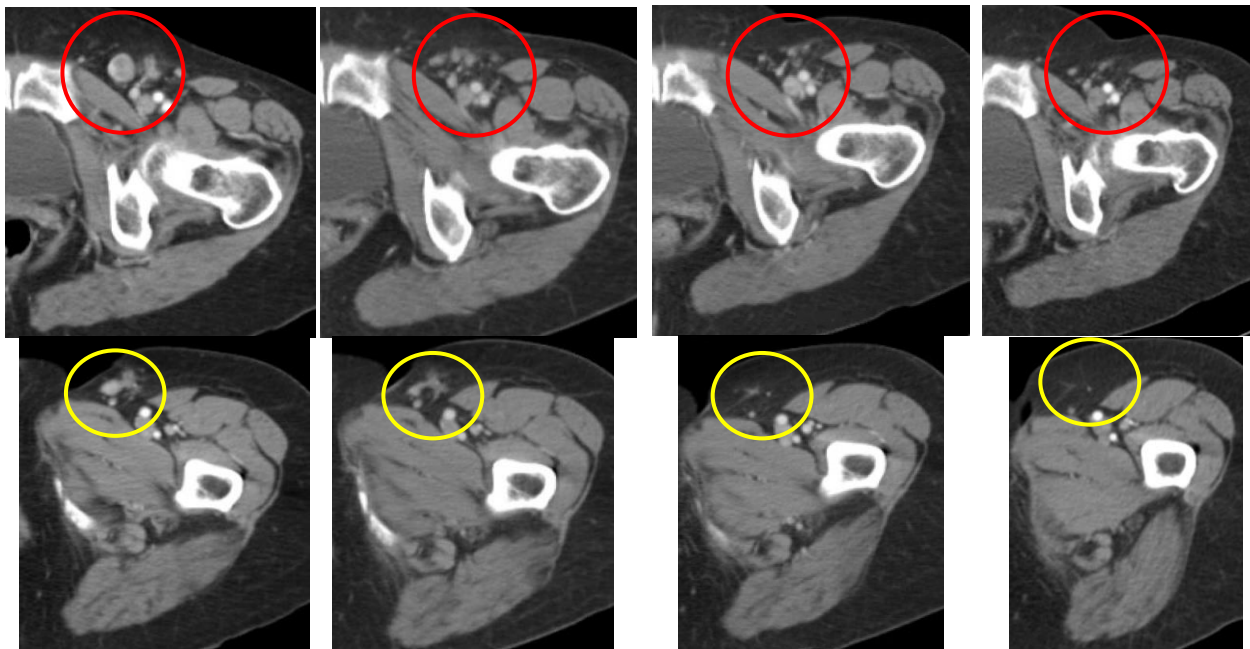
45

2nd July 2019
(screening)

17th Sept 2019

19th Nov 2019

7th April 2020



Injected once



Not injected



Injected

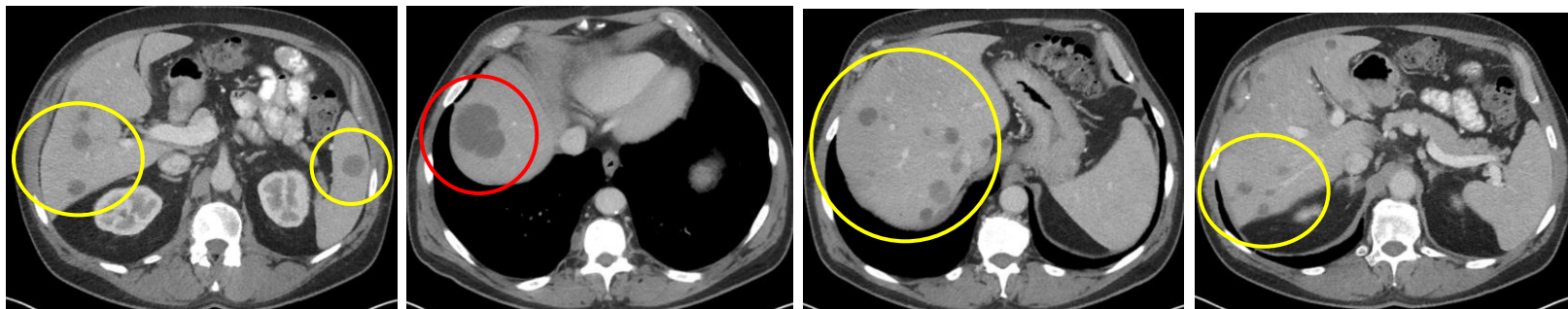


Not injected

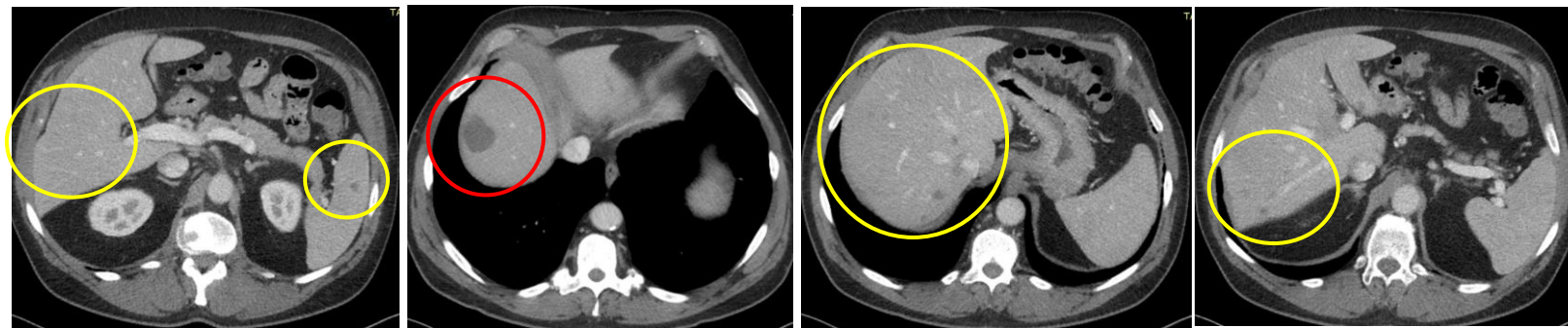
Patient 1122-2007 (ipilimumab/nivolumab refractory melanoma) – PR

46

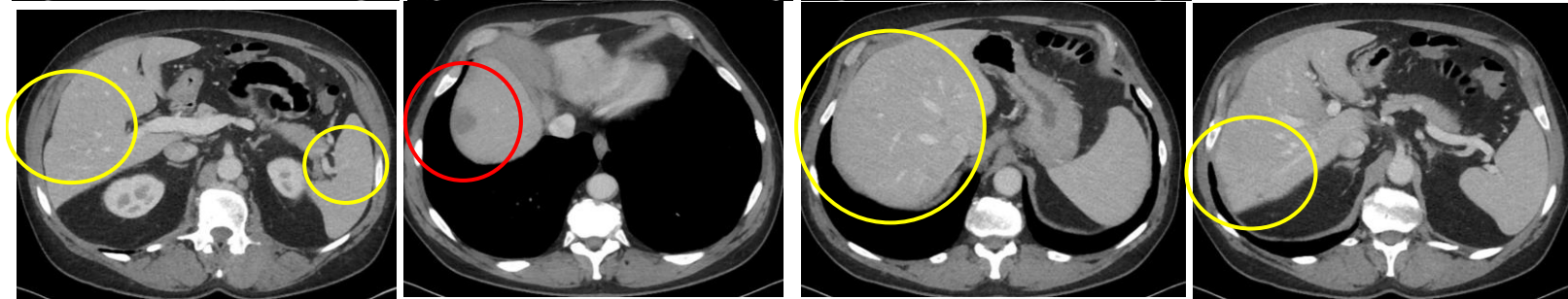
22nd Oct
2019
(Screening)



9th March
2020



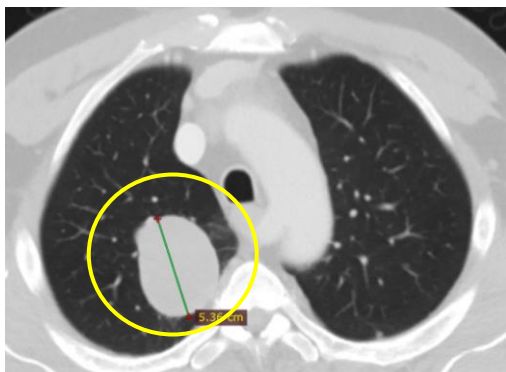
30th June
2020



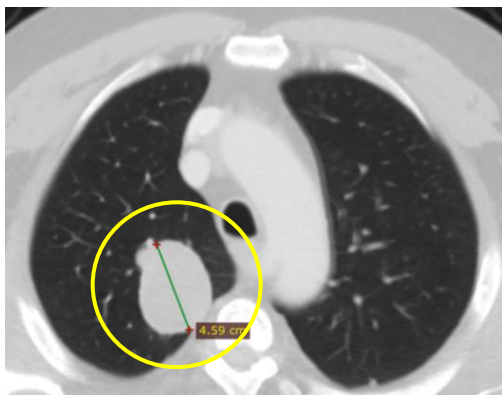
Patient: 1122-2007 (ipilimumab/nivolumab refractory melanoma) – PR

47

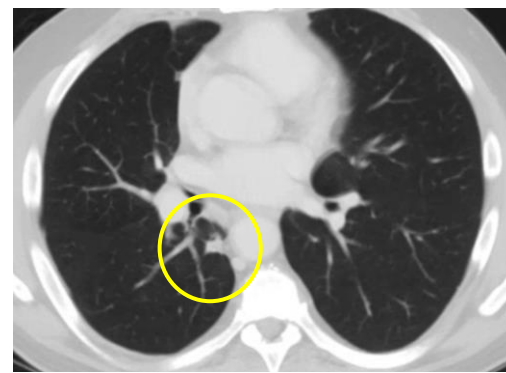
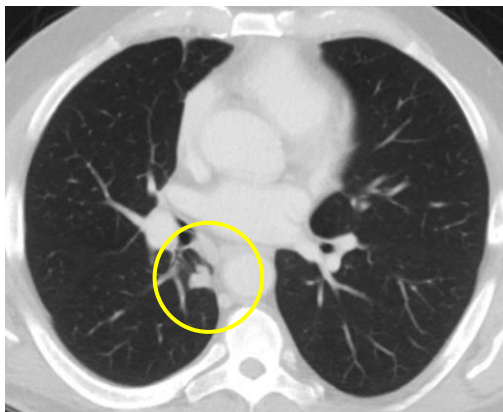
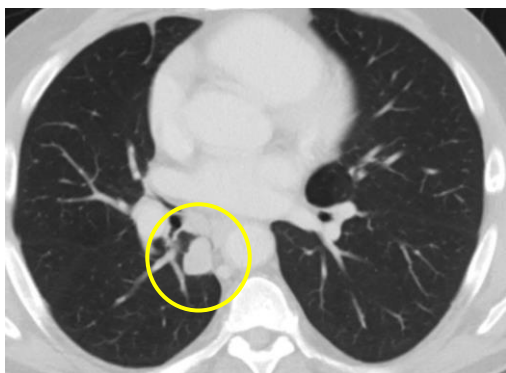
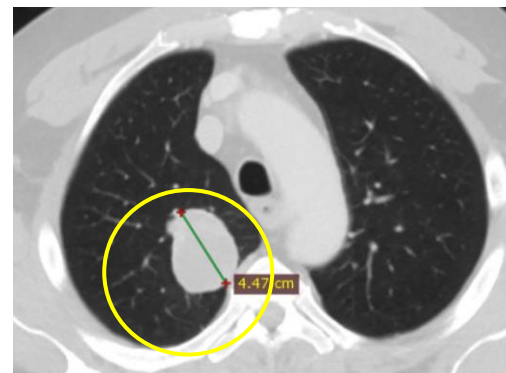
22nd Oct 2019
(Screening)



9th March 2020



30th June 2020

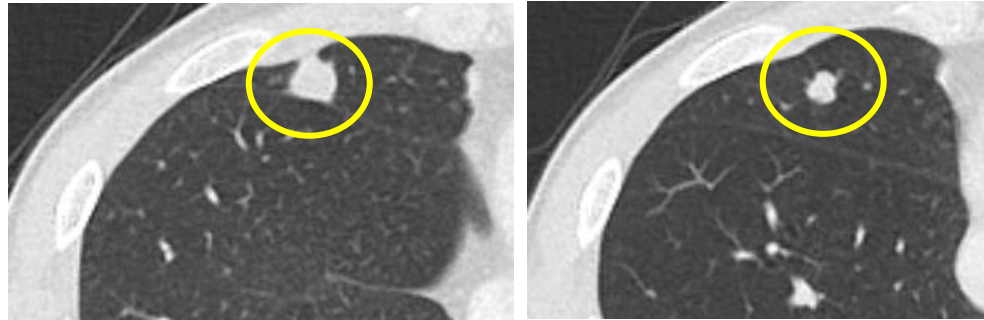


Patient #: 4401-1022 – PR

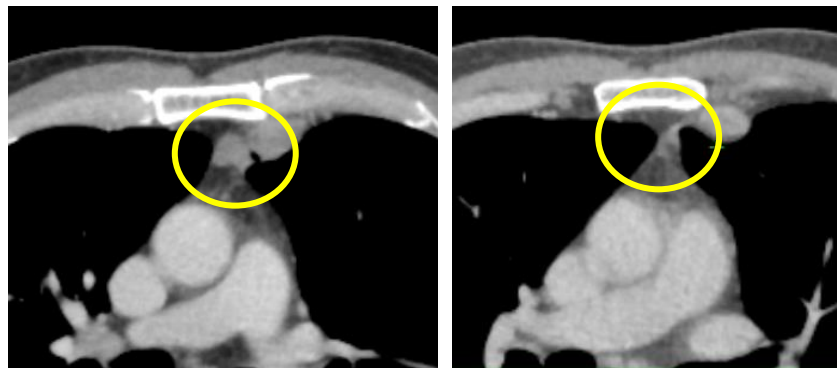
48

- 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

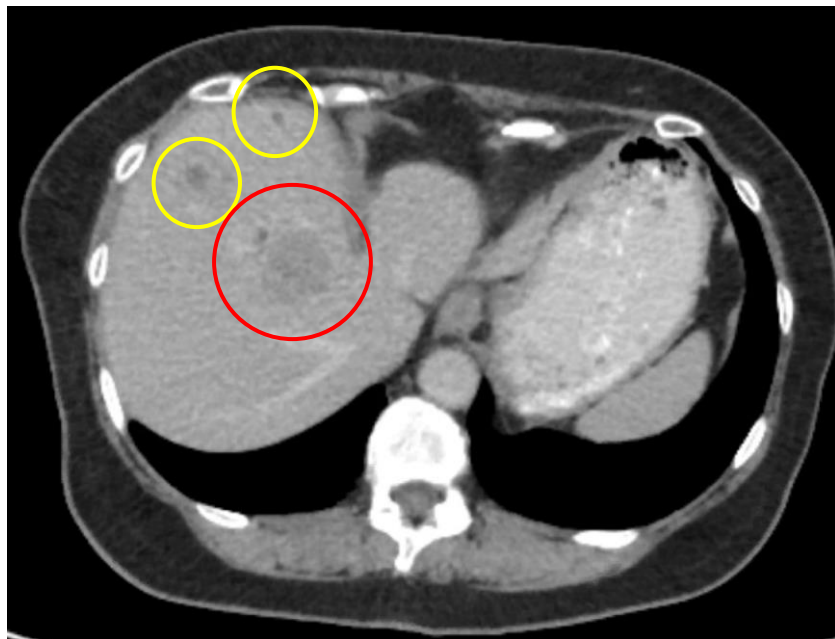


Not injected

Patient #: 4401-2007 (prior nivolumab) – PR

49

11th October 2019
(Screening)



4th May 2020



 Injected

 Not injected

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

50

10th June 2019

24th June 2019 (pre nivolumab)

2nd September 2019

6th July 2020

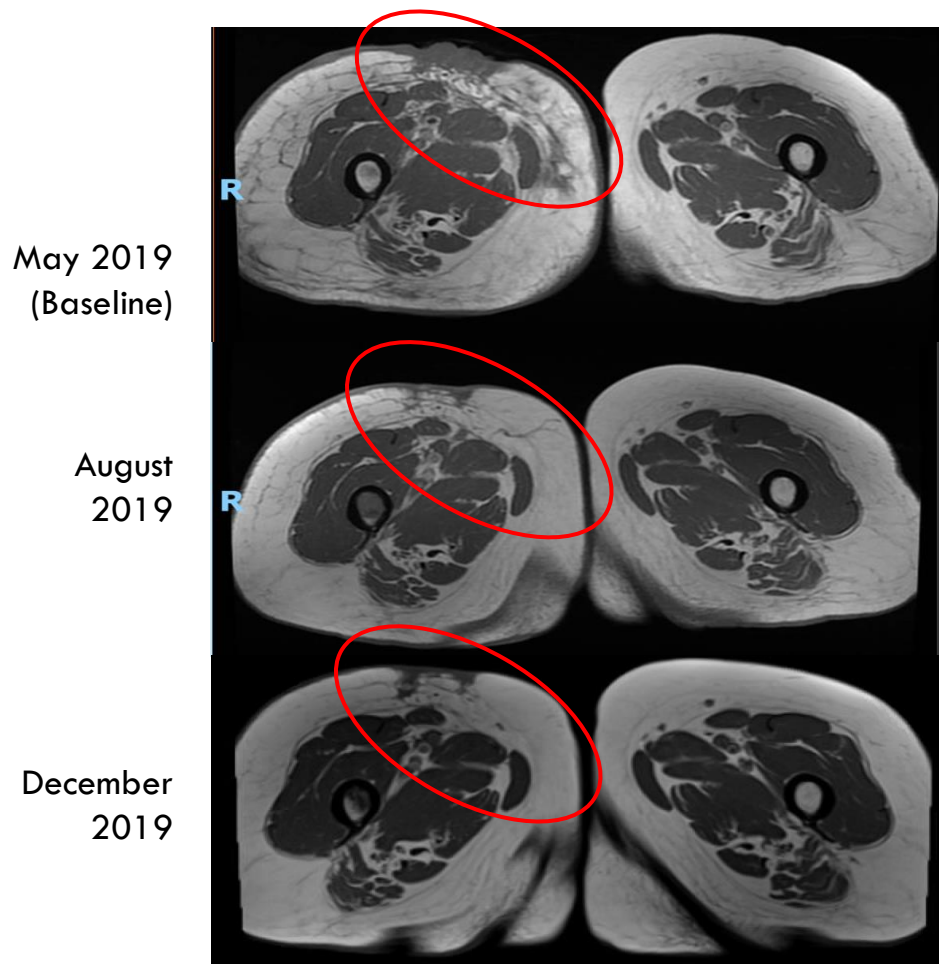


Patient history: Metastatic disease initially treated with ipi/nivo with best response of SD, then clear progression in the groin & thigh when radiotherapy followed by electrochemotherapy was added to continued nivolumab; following further clear progression, enrolled into the current trial

All tumors flattened after the first dose of RP1, i.e. prior to nivolumab & extensive oedema rapidly reduced

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

51



Injected



Not injected

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

52

22nd May 2019 16th March 2020



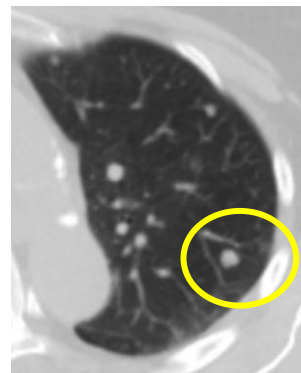
 Injected



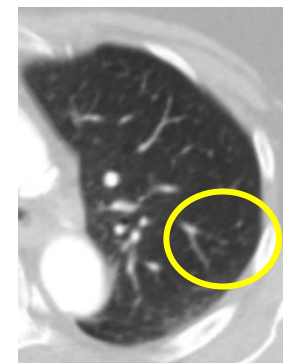
 Not injected



22nd May 2019



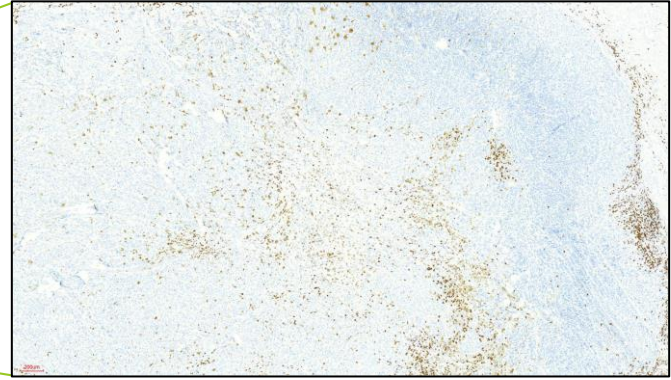
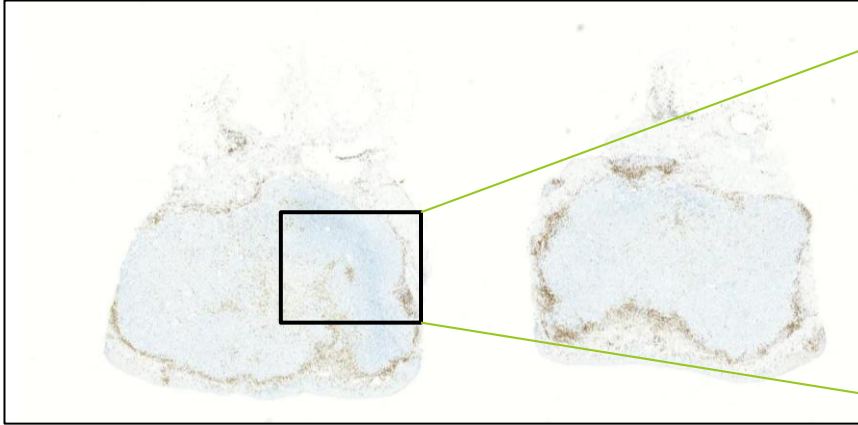
16th March 2020



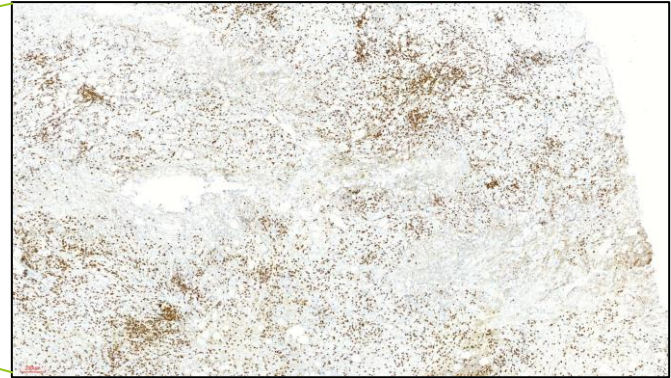
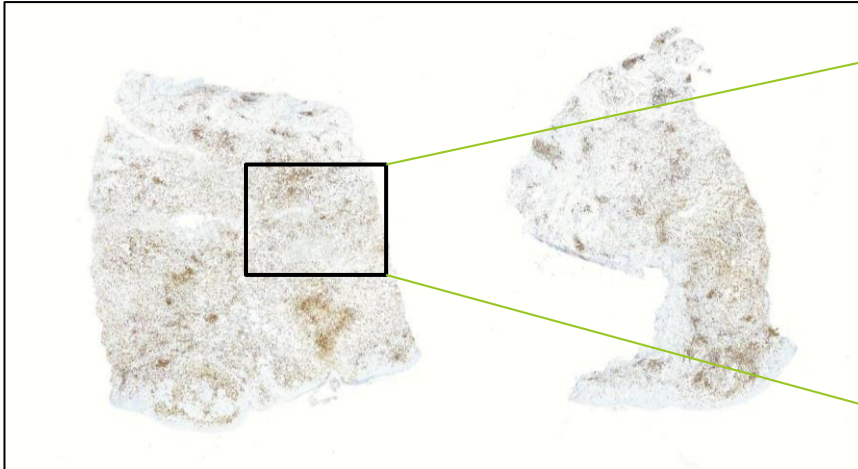
Reversal of T cell exclusion with RP1 combined with nivolumab

53

CD8
Baseline
biopsy



CD8
Day 43
biopsy

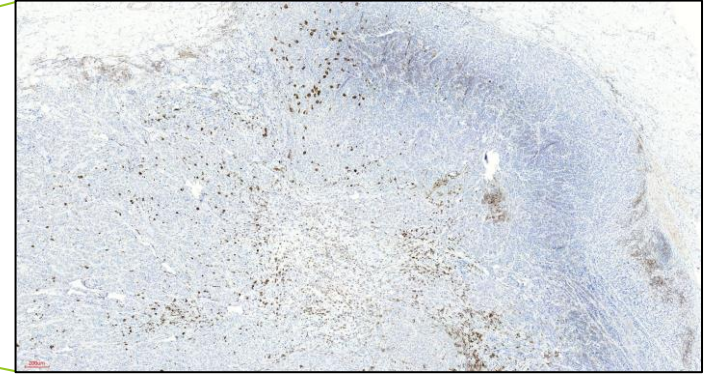
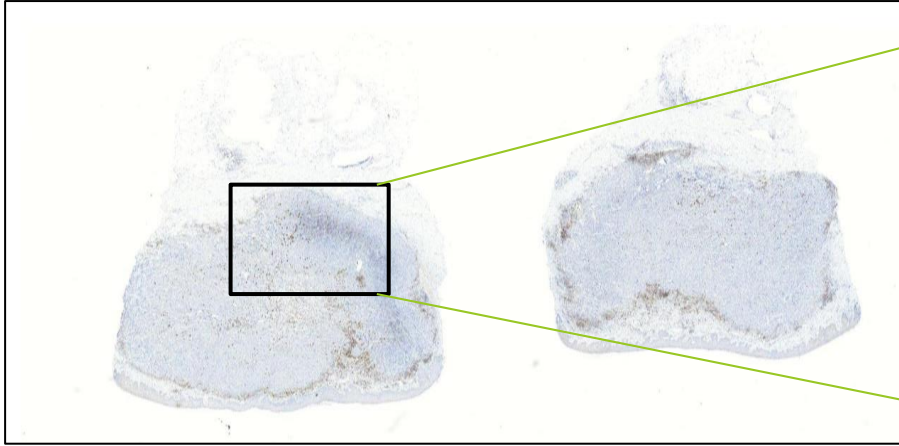


4403-1003 (PR)
Cutaneous melanoma
(ipilimumab/nivolumab refractory)

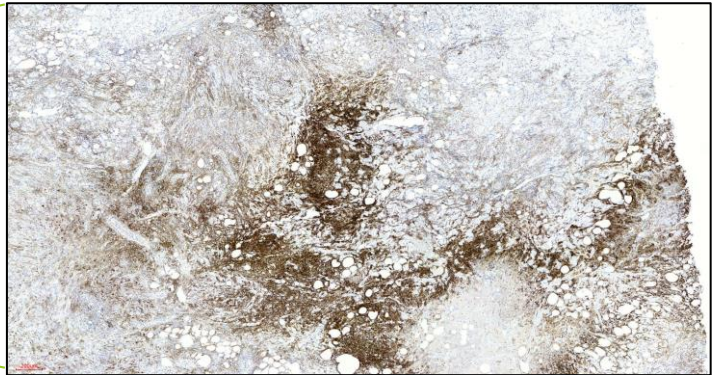
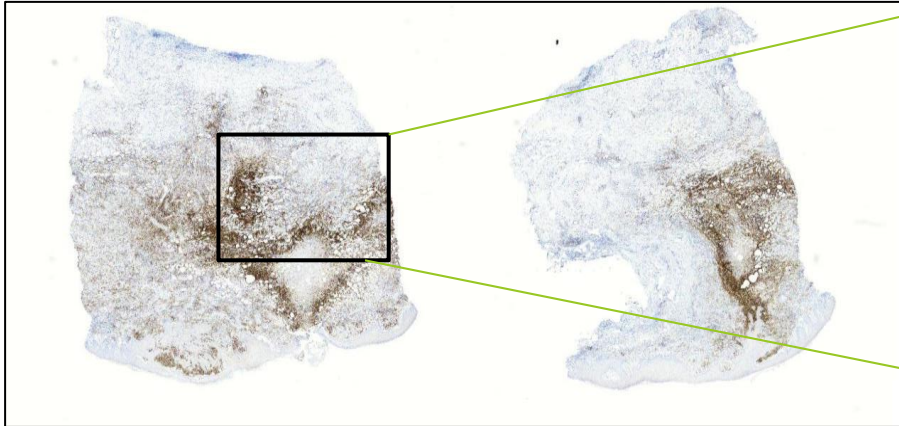
Reversal of T cell exclusion with RP1 combined with nivolumab

54

PD-L1
baseline
biopsy



PD-L1
Day 43
biopsy



4403-1003 (PR)
Cutaneous melanoma
(ipilimumab/nivolumab refractory)

Mucosal melanoma patients

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



Injected



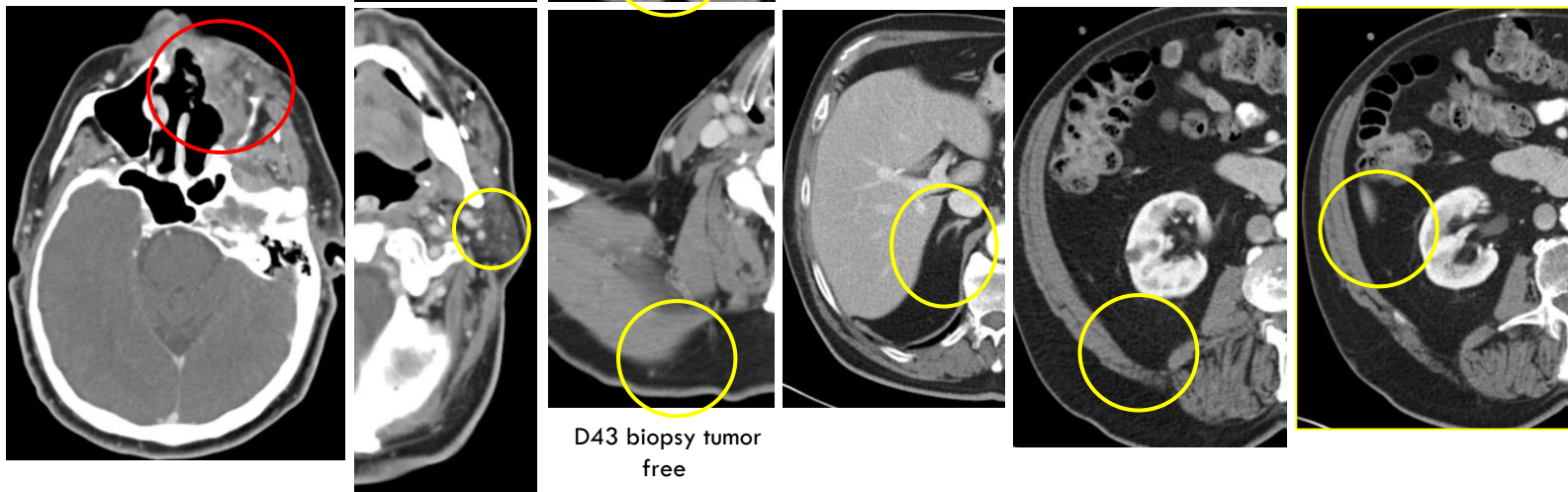
Not injected

56

12th Nov
2019
(Screening)



12th
March
2020



D43 biopsy tumor
free

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

57

20th Aug
2019
(Screening)



15th Jan
2020



Excision biopsy
tumor free 1st April
2020

Uveal melanoma patients

Patient #: 4403-1001 (ipilimumab/nivolumab refractory uveal melanoma)

59

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 (ipilimumab/nivolumab refractory uveal melanoma)

60

25th Sept
2019
(Screening)

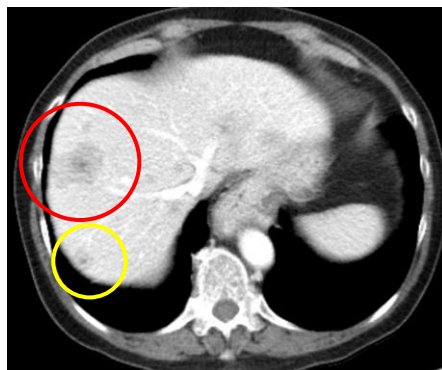
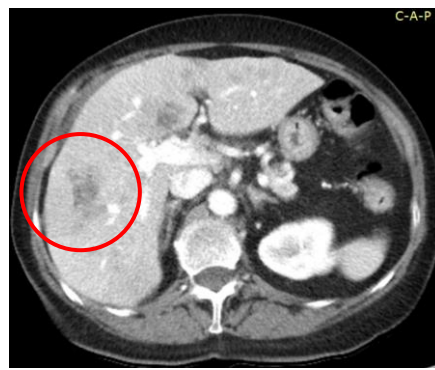
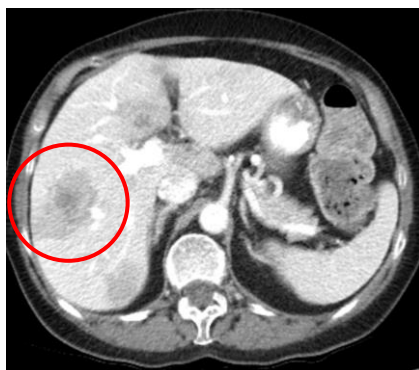
3rd April
2020



Injected



Not injected



Max 27.3% reduction by
RECIST (unidimensional),
61% reduction by WHO
(bi-dimensional)