# Igniting a Systemic Immune Response to Cancer

Replimune's mission is to revolutionize cancer treatment with therapies designed to activate a powerful and durable full-body anti-tumor response. We imagine a world where cancer is a curable disease.

Dec 5, 2023

## RP1 Program Update Investor Event

# 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, timing and sufficiency 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, statements regarding our expectations about our cash runway, 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, the ongoing military conflict between Russia and Ukraine and the impact on the global economy and related governmental imposed sanctions, 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.

# Today's speakers/Q&A panel

**PHILIP ASTLEY-SPARKE**
**Chief Executive Officer**
*Replimune*

**ROBERT COFFIN**
**Founder, President & Chief Research & Development Officer,** *Replimune*

**MICHAEL MIGDEN**
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*Dept of Dermatology*
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**MICHAEL WONG**
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*Melanoma Medical Oncology, University of Texas MD Anderson Cancer Center*

**NIKHIL KUSHALANI, MD**
**Vice Chair**
*Cutaneous Oncology at Moffitt Cancer Center*

**CAROLINE ROBERT**
**Professor**
*Head of Dermatology Unit, Institute Gustave Roussy and Co-Director Melanoma Research Unit INSERM, Paris-Sud University.*

# AGENDA

SECTION I

## RP1: Exec Summary and Overview

SECTION II

## RP1: 1L CSCC (CERPASS)

SECTION III

## RP1 IGNYTE and ARTACUS Skin Cancer Data and Anti-PD1 Failed Melanoma Update

SECTION IV

## RP1 Regulatory Update/Overall Summary

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## Panel Q&A

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# AGENDA

# Establishing a skin cancer franchise

| | | |
|---|---|---|
| 1 | **IGNYTE anti-PD1 failed melanoma registrational cohort** *N=140* | Updated data presented today for 156 patients (140 patients from the anti-PD1 failed melanoma cohort + 16 anti-PD1 failed patients from the initial melanoma cohort) |
| 2 | **CERPASS – first-line CSCC randomized controlled clinical trial** *N=211* | **Top-line primary analysis data being presented today** |
| 3 | **IGNYTE initial NMSC cohort (anti-PD1 naïve)** *N=30 (fully accrued)* | **Demonstrated activity in other NMSCs**; Commercialization in MCC, BCC etc, likely to be based on compendia listing |
| 4 | **IGNYTE anti-PD1-failed NMSC cohort** *N=80* | Updated snapshot data (30 patients) being presented today |
| 5 | **ARTACUS skin cancers in solid organ transplant recipients** *N=65* | Data presented at SITC 2023 showed 34.8% ORR (27 patients, 23 evaluable for efficacy) - also to be reviewed today |
| 6 | **Neoadjuvant CSCC** *(study in development)* | **Study in collaboration with INCYTE**: expected to capture significant high-risk patient population |

- RP1 establishes confidence in easy-to-administer settings
- Deep and durable responses across multiple settings in skin cancer, including high CRs in 1L CSCC
- Durable responses in anti-PD1 failed patients with melanoma & a range of NMSCs
- Trial in planning to provide proof-of-concept in neoadjuvant setting

# RP1 Executive Summary

## CERPASS/ NMSC

*Active in both combination and as monotherapy*

- **While RP1 did not meet statistical significance* in 1L CSCC for its dual primary endpoints in the CERPASS study, clinical benefit was demonstrated in terms of CRs and DOR**
- **In solid organ transplant recipients RP1 monotherapy (ARTACUS study) shows approx. 35% ORR[1] in a setting where anti-PD1 therapies are contra-indicated**
- Updated data from **RP1 in anti-PD1 failed NMSC cohort shows approx. 30% ORR** in hard-to-treat patients

## IGNYTE

*Continued, compelling benefit in anti-PD1 failed melanoma demonstrated in the full data set and longer follow up*

- **Snapshot data from the full (140 patient) cohort** in anti-PD1 failed melanoma **shows durable benefit consistent with the data from the first 75 patients** presented at ASCO[2]

## Regulatory

*Regulatory approval strategy*

- **Intend to share CERPASS data in 1L CSCC with FDA**
- **FDA** confirmed the IGNYTE population is one of unmet need and has **agreed to a confirmatory trial design concept to support a potential filing under the accelerated approval pathway**
- **Assuming supported by positive IGNYTE primary analysis data a BLA filing planned for 2H 2024**

***"Breadth and consistency of clinical data for RP1 across a range of skin cancers [including in high un-met need, difficult to treat settings] demonstrated. REPL is well positioned to commercialize with a regulatory pathway to first approval"***

*Per the protocol $p<0.025$ is required for formal statistical success in CERPASS for CRR or ORR alone.
[1]SITC 2023, [2]ASCO 2023

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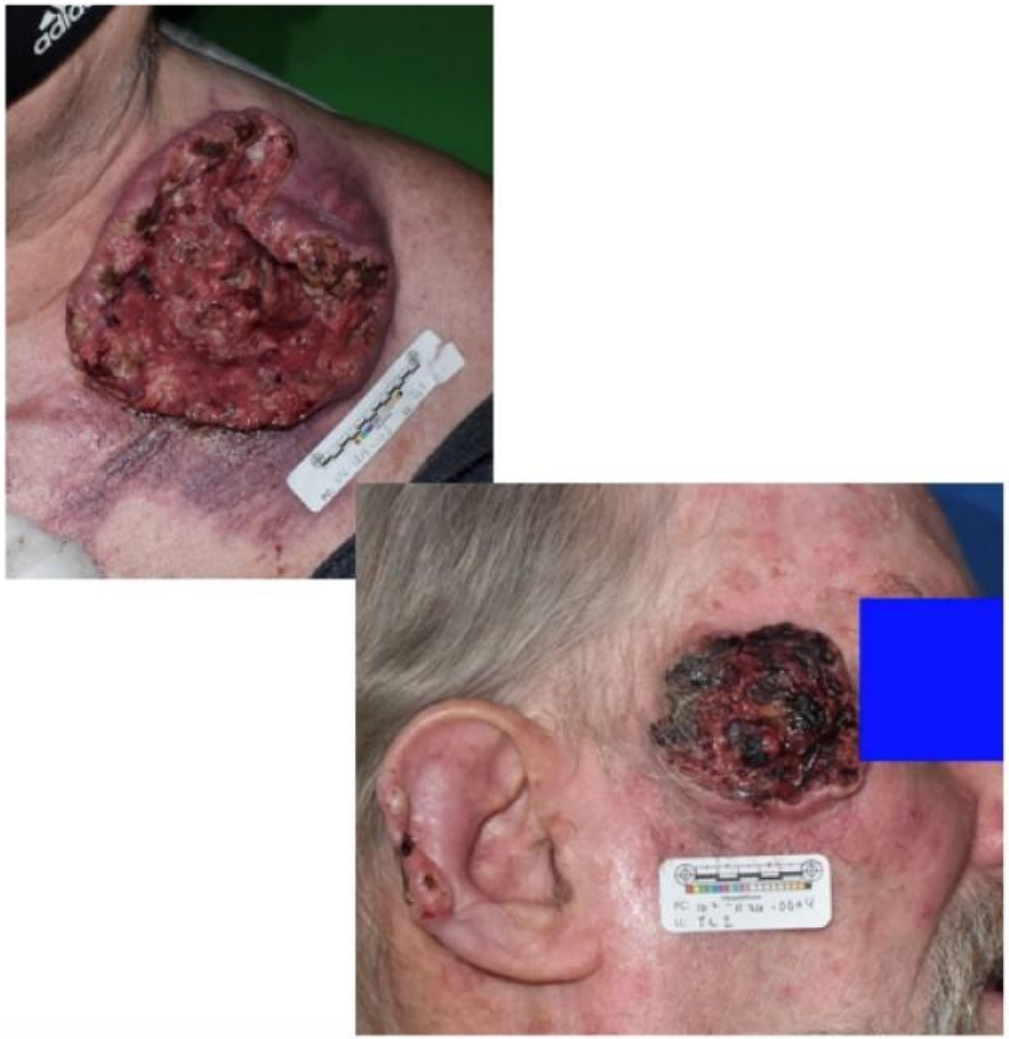
# CSCC disease characteristics and typical patient presentation

- **Second most common skin cancer** with ≈700,000 patients annually in the U.S.[1]
- **Approximately 7,000-15,000 US deaths** annually[1-3]
  - 80% of patients die from locoregional progression, not metastatic disease[4,5]
- **Patients tend to be older**, >60 yrs old
- Usually develops from precursor lesions (actinic keratosis) but may be *de novo;* ***m*ajority (80–90%) occur on the head and neck**
- **CSCC** is a predominately outward growing disease with large, painful, superficial tumors which **can impact quality of life and contribute to social isolation**
  - Disfiguring, painful
  - Foul smelling drainage
  - Delay in seeking medical care
- **~15-30% of patients have underlying immune deficiencies** from solid organ transplant, RA, MS, CLL, HIV



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

# Remaining unmet needs in CSCC

***Durability of CRs vs. PRs Achieved by Cemiplimab in CSCC**

| Study | Patients | Complete response | Partial response |
|---|---|---|---|
| Rischin 2021 | 35 laCSCC pts<br>54 mCSCC pts | 0 of 10 pts progressed<br>1 of 21 pts progressed | 6 of 25 pts progressed<br>11 of 33 pts progressed |
| Strippoli 2021 | 25 laCSCC pts<br>5 mCSCC pts | 0 of 9 pts progressed; no deaths | 9 of 14 pts progressed; 6 deaths |

- **While anti-PD1s are effective for 1L CSCC approximately 50% of patients don't achieve a clear benefit**
  - Typically, ORRs range from 40-50% and CRs from approx. 5-20%[1-4] – **CRs most effectively result in long-term clinical benefit***
  - Large outwardly growing tumors have significant impact on QoL
- **No FDA approved options for anti-PD1-failed CSCC/NMSC**
  - Roughly 70% of treated patients still ultimately progress
  - Low ORR and/or limited durability with significant toxicity for both chemotherapy and/or Erbitux[5] based regimens
- **Treatment of populations at high-risk such as immunocompromised patients** (e.g., those with auto-immune diseases, transplant recipients) who often develop NMSC, including CSCC, remains challenging[6,7]
  - Anti-PD1 therapy used cautiously in organ transplant patients due to risk of organ rejection

[1]Libtayo Package Insert
[2]Keytruda Package Insert
[3]Migden et al ESMO 2022, Annals of Oncology
[4]Hughes et al Annals of Oncology 2021
[5]Marin-Acevedo et al Cancers 2023, 15(12), 3180
[6]Lam JKS, et al. Head Neck. 2018;40:985-992.
[7]Friman T, et al. Int J Cancer. 2022;150(11):1779-91.

# Primary analysis data for CERPASS
## *November 2023*

# CERPASS registration-directed Ph2 study in CSCC

**Key Eligibility Criteria:**

- Locally-advanced/metastatic CSCC
- ECOG PS 0 or 1
- No active autoimmune disease
- No prior treatment with a PD-1/PD-L1 inhibitor
- No untreated brain metastases


## Key Endpoints

- **Dual independent primary endpoints: Complete Response Rate & Overall Response Rate***
  - Approx. 15% absolute difference in CRR and/or ORR required
  - Secondary endpoints: DOR, PFS, OS, disease-specific survival, safety/tolerability

**Note p≤0.05 is required if both dual primary endpoints hit for statistical success, if only one of the dual endpoint hits need a p≤0.025 is needed*

†First dose of RP1 to be given as monotherapy with cemiplimab to be given with second dose of RP1
‡57 weeks treatment for the combination arm; treatment duration for cemiplimab-only arm is 54 weeks

# CERPASS summary

- While neither primary endpoint (ORR or CRR) was met[1], RP1+cemiplimab demonstrated clinically meaningful activity vs. cemiplimab alone, supporting RP1+anti-PD1 therapy as an active combination in a randomized controlled setting
  - RP1+cemiplimab increased the complete response rate vs. cemiplimab alone (38.1% vs 25%; p=0.040[1]), even though the overall number of responses was not materially increased (52.5% vs 51.4%; p=0.692[1])
    - Among the 83 patients with locally advanced disease, a CR rate of 48.1% vs. 22.6% was observed
  - 72.6% of responses in the RP1+cemiplimab arm were CRs vs. 48.6% of responses in the cemiplimab arm (p=0.013[2])
  - RP1+cemiplimab also increased the duration of response as compared to cemiplimab alone (HR 0.45) – *Immature data: further follow up is required for this to mature*
  - RP1+cemiplimab is a well tolerated, with predominantly transient Grade 1-2 flu-like symptoms vs. cemiplimab alone
- RP1+cemiplimab provided particularly meaningful benefit for patients with "difficult to treat tumors" (anatomically challenging locations and/or large/disfiguring) which have the greatest impact on quality of life
- Overall, RP1+cemiplimab increased the quality (depth, durability & clinical meaningfulness) of the responses achieved in 1L CSCC
- PFS & OS are currently immature

*All time-based endpoints require further follow up to allow these to mature – a further analysis will then be conducted to support the overall BLA filing strategy for RP1*

[1]Per the protocol p≤0.025 is required for formal statistical success in CERPASS for either CRR or ORR alone [2]Not a pre-specified analysis. N.B. While this is the primary analysis the data analysis is still immature, with additional responses still able to develop and improve over time

# Demographics & baseline characteristics

| | Cemiplimab n=72 | RP1+cemiplimab n=139 |
|---|---|---|
| **Sex** (n/%) | | |
| Male | 57 (79.2) | 100 (71.9) |
| Female | 15 (20.8) | 39 (28.1) |
| **Age** | | |
| Mean | 74.3 | 74.0 |
| Median | 75.0 | 74.0 |
| Min, Max | 38, 94 | 40, 96 |
| **Race** (n/%) | | |
| White | 52 (72.2) | 103 (74.1) |
| Other | 20 (27.8) | 36 (25.9) |
| **Disease characteristics** (n/%) | | |
| Metastatic CSCC | 41 (56.9) | 87 (62.6) |
| Locally advanced CSCC | 31 (43.1) | 52 (37.4) |
| Baseline tumor burden* ≤10cm | 63 (87.5) | 107 (77.0) |
| Baseline tumor burden* >10cm | 9 (12.5) | 32 (23.0) |
| **Prior therapy for CSCC** (n/%) | | |
| Radiation | 31 (43.1) | 55 (39.6) |
| Chemotherapy | 7 (9.7) | 12 (8.6) |
| Other | 3 (4.2) | 5 (3.6) |

## Key Takeaways

- In general, baseline demographics were well balanced
- However, there was a substantial imbalance in patients with >10cm of baseline tumor burden between the arms

*Baseline tumor burden was a prespecified analysis in the SAP

# Safety (treatment-Related AEs)

| | TRAEs which occurred in >5% of RP1+cemiplimab patients (all other Grade 3-5 are listed) | | | |
|---|---|---|---|---|
| | Cemiplimab (N=72) | | RP1+cemiplimab (N=139) | |
| Preferred Term | Grade 1-2 | Grade 3 | Grade 1-2 | Grade 3 |
| Patients with TRAEs | 46 ( 63.9) | 8 ( 11.1) | 97 ( 69.8) | 23 ( 16.5) |
| | | | | |
| Fatigue | 10 ( 13.9) | 0 ( 0.0) | 24 ( 17.3) | 2 ( 1.4) |
| Pruritus | 12 ( 16.7) | 0 ( 0.0) | 23 ( 16.5) | 0 ( 0.0) |
| Pyrexia | 0 ( 0.0) | 0 ( 0.0) | 20 ( 14.4) | 1 ( 0.7) |
| Nausea | 4 ( 5.6) | 0 ( 0.0) | 16 ( 11.5) | 0 ( 0.0) |
| Hypothyroidism | 3 ( 4.2) | 0 ( 0.0) | 15 ( 10.8) | 0 ( 0.0) |
| Chills | 1 ( 1.4) | 0 ( 0.0) | 13 ( 9.4) | 0 ( 0.0) |
| Diarrhoea | 8 ( 11.1) | 1 ( 1.4) | 13 ( 9.4) | 1 ( 0.7) |
| Asthenia | 7 ( 9.7) | 0 ( 0.0) | 12 ( 8.6) | 0 ( 0.0) |
| Infusion related reaction | 1 1.4) | 0 ( 0.0) | 10 ( 7.2) | 1 ( 0.7) |
| Rash | 10 ( 13.9) | 0 ( 0.0) | 10 ( 7.2) | 0 ( 0.0) |
| Rash maculo-popular | 2 ( 2.8) | 0 ( 0.0) | 8 ( 5.8) | 2 ( 1.4) |
| Vomiting | 0 ( 0.0) | 0 ( 0.0) | 7 ( 5.0) | 0 ( 0.0) |

## Key Takeaway

RP1+cemiplimab is well tolerated, with predominantly additional transient Grade 1-2 flu-like symptoms being seen as compared to cemiplimab alone.

**List of additional Grade 3-5 events**
**(one event each unless indicated in parentheses)**

**RP1+cemiplimab:**
**Grade 3:** Injection site pain, confusional state, pneumonitis, anaemia, tumour haemorrhage, groin abscess, headache, hypotension, acute kidney injury, autoimmune anaemia, dermatitis bullous, dermo-hypodermitis, diabetic ketoacidosis, immune-mediated enterocolitis, immune-mediated hepatitis(2), neuralgia, pemphigoid, pulmonary oedema, syncope, troponin increased
**Grade 4:** Immune-mediated myocarditis, myocarditis
**Grade 5:** None

**Cemiplimab:**
**Grade 3:** Pneumonitis, lipase increased, immune-mediated hepatitis, autoimmune nephritis, colitis, guttate psoriasis, immune-mediated pancreatitis
**Grade 4-5:** None

# Confirmed ORR & CRR (ITT population)

| BOR (confirmed response) | All N=211 | |
|---|---|---|
| n/% | Cemiplimab n=72 | RP1+ cemiplimab n=139 |
| PR | 19 (26.4) | 20 (14.4) |
| SD | 14 (19.4) | 18* (12.9) |
| PD | 12 (16.7) | 27 (19.4) |
| **OR** | **37 (51.4%)** | **73 (52.5%)** |
| | **P=0.692[1]** | |
| **CR** | **18 (25.0%)** | **53 (38.1%)** |
| | **P=0.040[1]** | |
| **% responders which are CR**** | **48.6%** | **72.6%** |

## Key Takeaways

- While ORR was not improved with RP1+cemiplimab, the number of patients who achieved a CRR was substantially increased in the RP1+cemiplimab arm
- A higher proportion of CRs were achieved with RP1+cemiplimab as compared to cemiplimab alone
- CRs are the key driver of long-term clinical benefit in CSCC

*One patient shown as SD was a CR due to the confirmatory assessment happening 21 days rather than later 28 days as required per protocol (CRR if included = 38.8%; p=0.031); **&Nominal p value 0.013

[1]Per the protocol p≤0.025 is required for formal statistical success in CERPASS for CRR or ORR alone and p≤0.05 if both endpoints were met

BOR=best overall response

# Confirmed ORR & CRR by type of disease

| BOR (confirmed response) | Locally advanced CSCC n=83 | | Metastatic CSCC n=128 | |
|---|---|---|---|---|
| n/% | Cemiplimab n=31 | RP1+ cemiplimab n=52 | Cemiplimab n=41 | RP1+ cemiplimab n=87 |
| **OR** | 18 (**58.1%**) | 33 (**63.3%**) | 19 (**46.3%**) | 40 (**46.0%**) |
| **CR** | 7 (**22.6%**) | 25 (**48.1%**) | 11 (**26.6%**) | 28 (**32.2%**) |

**Key Takeaways**

- The rate of complete response is improved in both locally advanced & metastatic CSCC
- In LA CSCC, there was a more than doubling of the CRs for the combination of RP1+cemiplimab vs cemiplimab (48.1% vs 22.6%)

BOR=best overall response

# Confirmed ORR & CRR by baseline tumor burden

| BOR (confirmed response) | Baseline target tumor burden* | | | |
|---|---|---|---|---|
| | ≤10cm (n=170) | | >10cm** (n=41) | |
| n/% | Cemiplimab n=63 | RP1+ cemiplimab n=107 | Cemiplimab n=9 | RP1+ cemiplimab n=32 |
| **ORR** | 34 (**53.4%**) | 64 (**59.8%**) | 3 (**33.3%**) | 9 (**28.1%**) |
| **CR** | 17 (**27.0%**) | 46 (**43.0%**) | 1 (**11.1%**) | 7 (**21.9%**) |

**Key Takeaways**

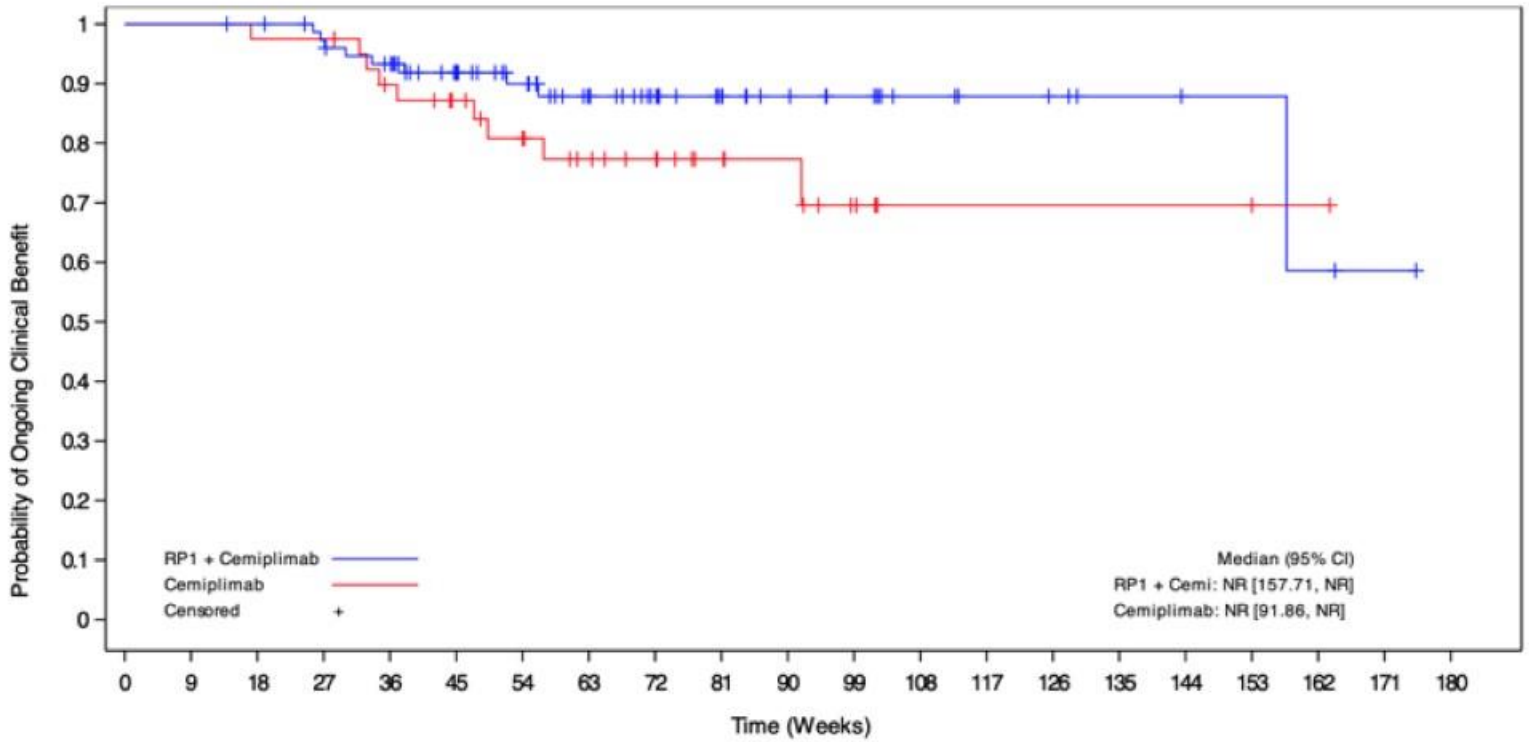
- There was an imbalance in extent of disease burden across the arms with significantly less large tumors (>10 cm) treated on the cemiplimab alone arm
- Despite tumor burden imbalance impacting ORR, CRR is improved in patients with both high & lower baseline tumor burden for patients treated with RP1+cemiplimab vs. cemiplimab alone

*Baseline tumor burden was a prespecified analysis in the SAP
**While 23.0% of RP1+cemiplimab patients had baseline tumor burden >10cm, only 12.5% of cemiplimab patients had baseline tumor burden >10cm

BOR=best overall response

# Duration of response (immature data)
## Time from baseline to end of response for responders

All responding patients




Number of subjects at risk:

| | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| RP1 + Cemi | 78 | 78 | 77 | 73 | 68 | 58 | 48 | 37 | 29 | 22 | 17 | 14 | 9 | 7 | 6 | 4 | 3 | 3 | 2 | 1 | 0 |
| Cemiplimab | 40 | 40 | 39 | 39 | 34 | 29 | 25 | 20 | 17 | 12 | 10 | 6 | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 0 | |

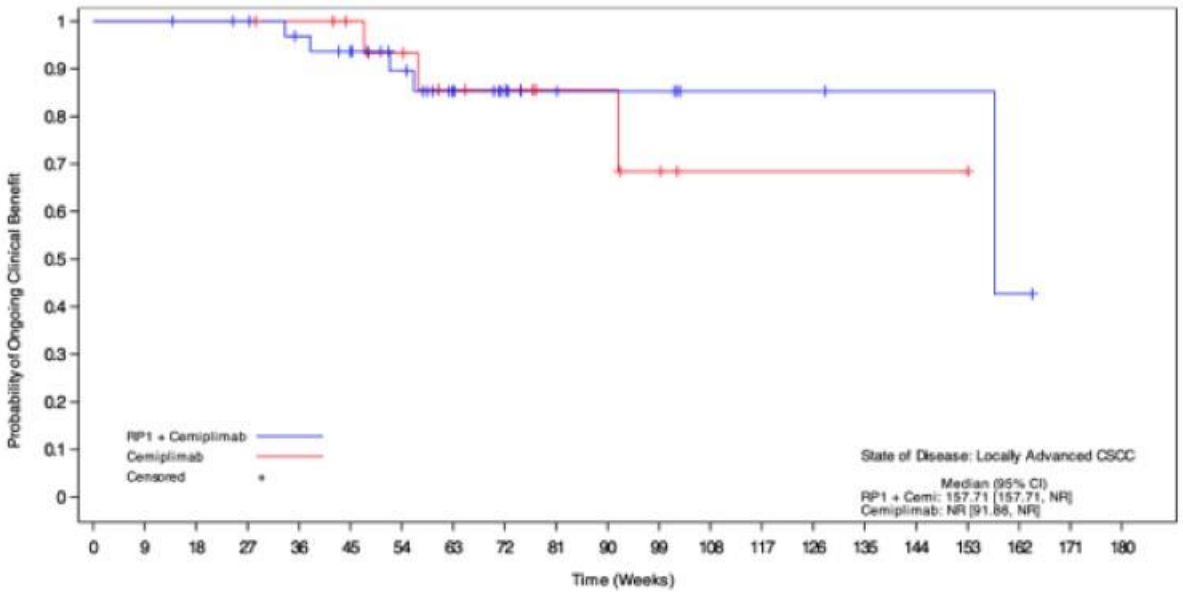
### Key Takeaway

Duration of response is improved with RP1+cemiplimab as compared to cemiplimab alone (immature data).

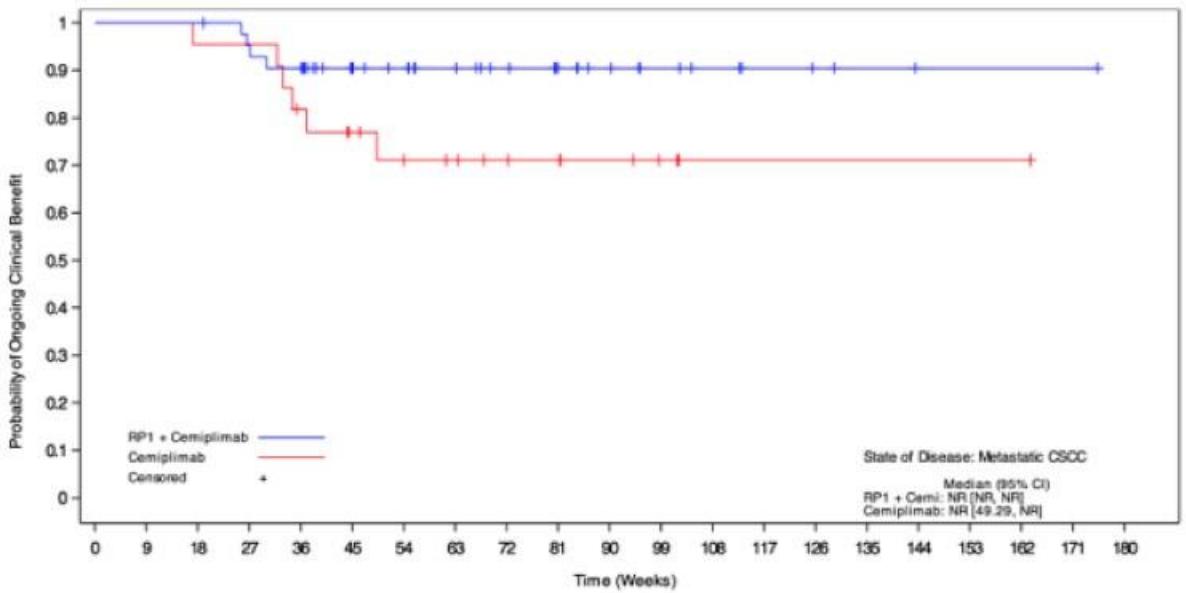
# Duration of response by disease type
## (Immature data)

Replimune

### Locally advanced patients




### Metastatic patients

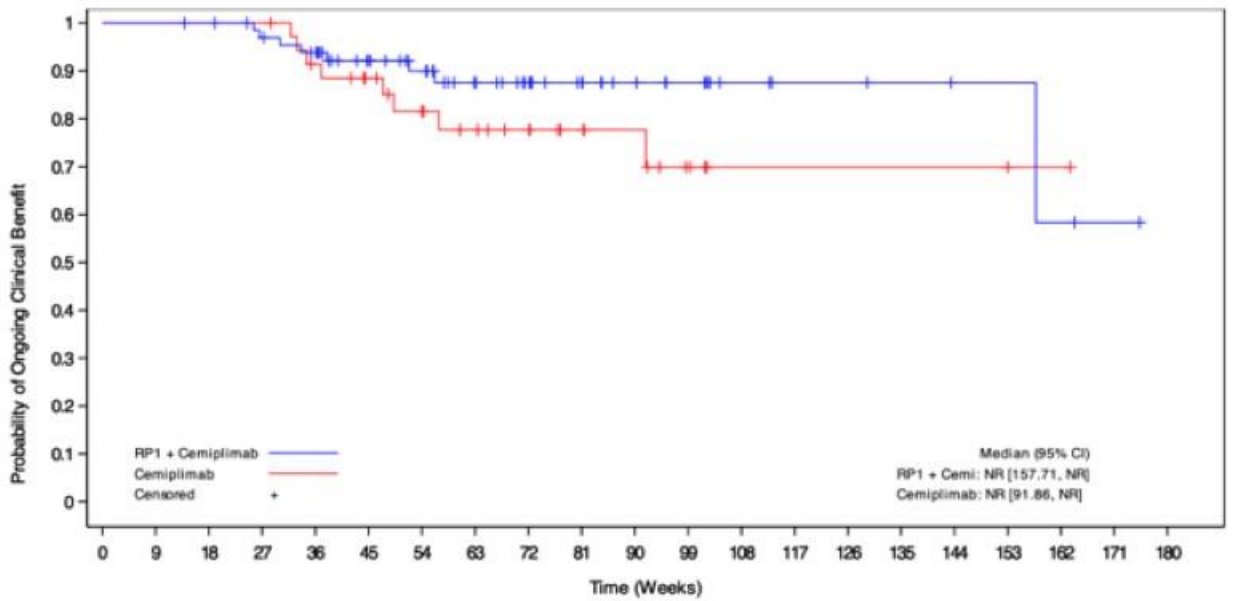



**Key Takeaway**

Duration of response is improved in patients with metastatic disease, locally advanced patient data is too immature to draw conclusions.

# Duration of response by baseline disease burden
## (Immature data)

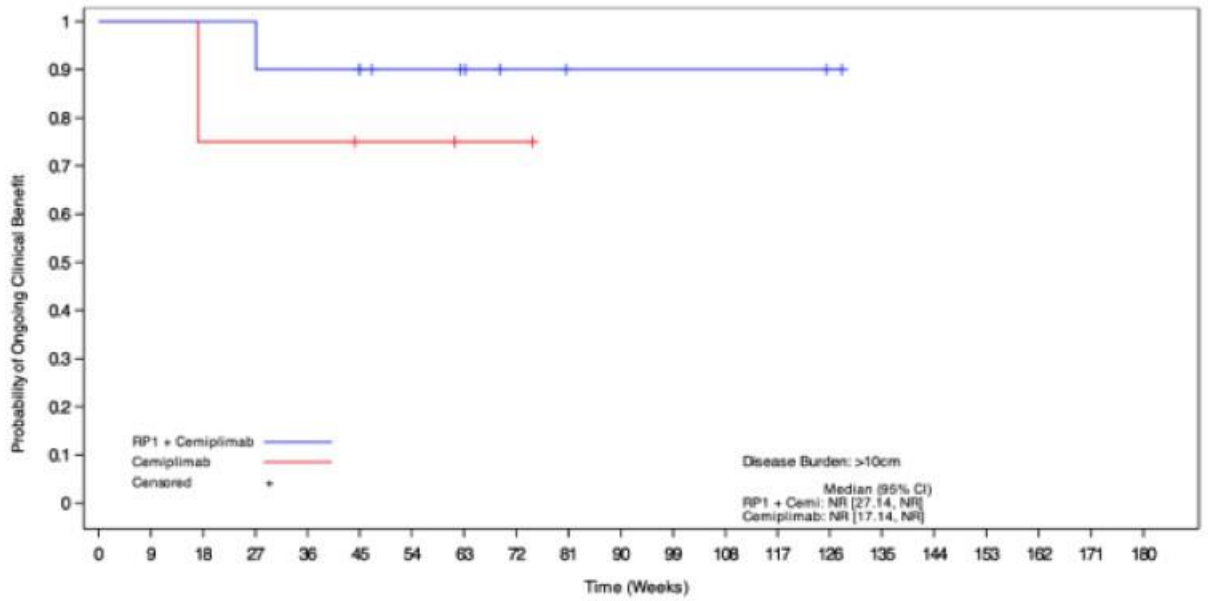
≤10cm of baseline disease (target lesions)




Number of subjects at risk:

| | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| RP1 + Cemi | 68 | 68 | 67 | 63 | 59 | 49 | 42 | 32 | 26 | 20 | 15 | 12 | 7 | 5 | 5 | 4 | 3 | 3 | 2 | 1 | 0 |
| Cemiplimab | 36 | 36 | 36 | 36 | 31 | 27 | 23 | 19 | 16 | 12 | 10 | 6 | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 0 | |

>10cm of baseline disease (target lesions)




Number of subjects at risk:

| | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| RP1 + Cemi | 10 | 10 | 10 | 10 | 9 | 9 | 6 | 5 | 3 | 2 | 2 | 2 | 2 | 2 | 1 | 0 | | | | | |
| Cemiplimab | 4 | 4 | 3 | 3 | 3 | 2 | 2 | 1 | 1 | 0 | | | | | | | | | | | |

**Key Takeaway**

Duration of response is improved in patients with both ≤10 cm as well as >10cm of baseline disease for RP1+cemiplimab

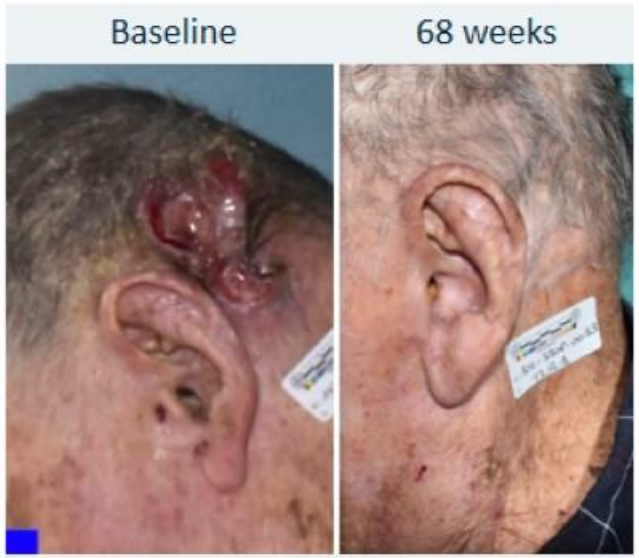
# RP1+cemiplimab addresses the key unmet need in patients with CSCC

# RP1+cemiplimab impact on "difficult to treat" tumors
# A key unmet need in CSCC

- In CSCC, due to the nature of the disease many tumors are difficult to treat (anatomically challenging locations and/or large/disfiguring) and therefore increasing the proportion of patients for whom external disease is eradicated has the greatest impact on patient quality of life
  - CSCC is relentlessly outgrowing, and erodes anatomic structures, with locoregional progression frequently resulting in death
- Study images demonstrate that RP1+cemiplimab eradicates bulky externally visible and/or anatomically challenging disease more frequently than does cemiplimab alone
  - These RP1+cemiplimab-mediated responses in more difficult to treat tumors would be expected to be of high clinical impact for patients

# The five most visually impactful CRs with cemiplimab

Replimune

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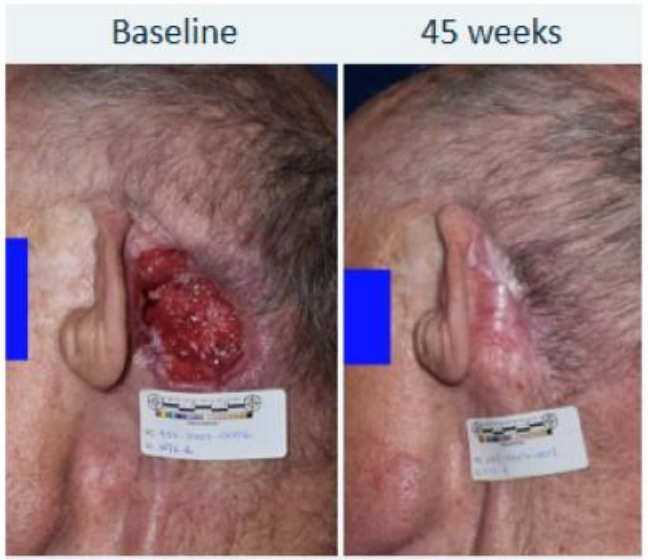


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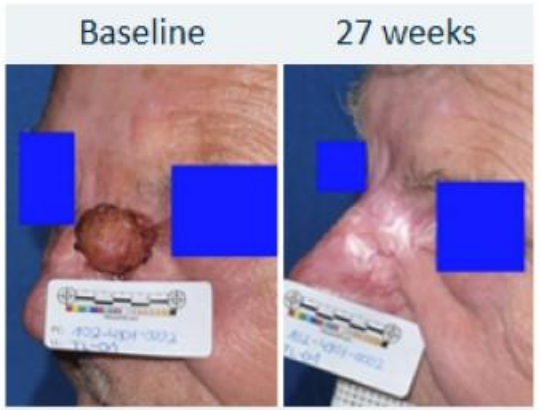


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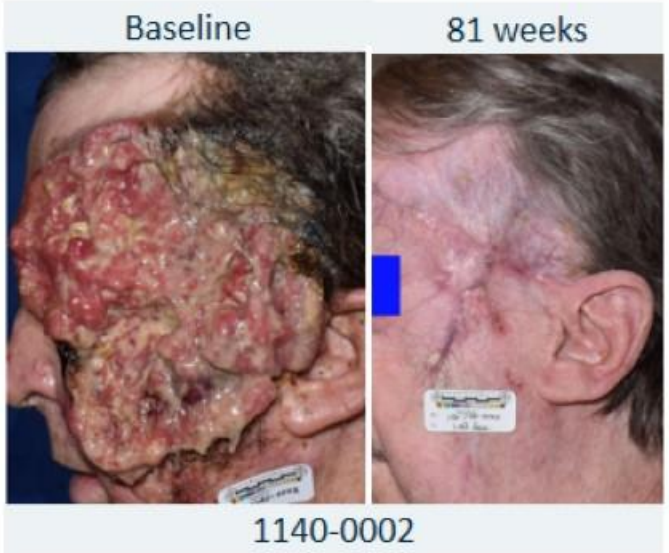
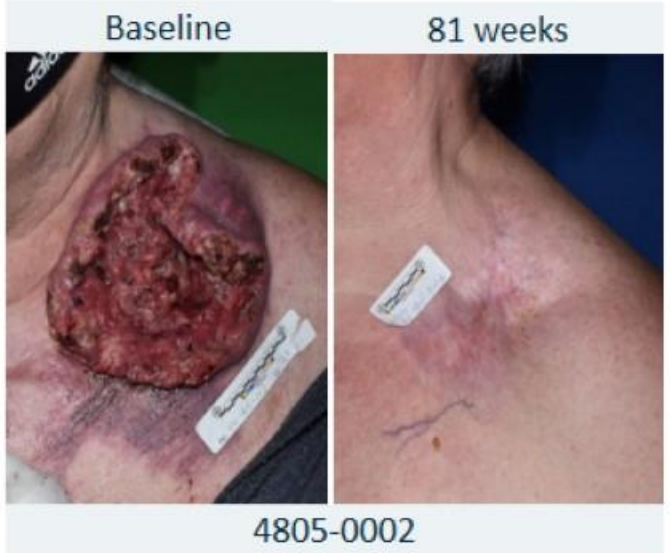
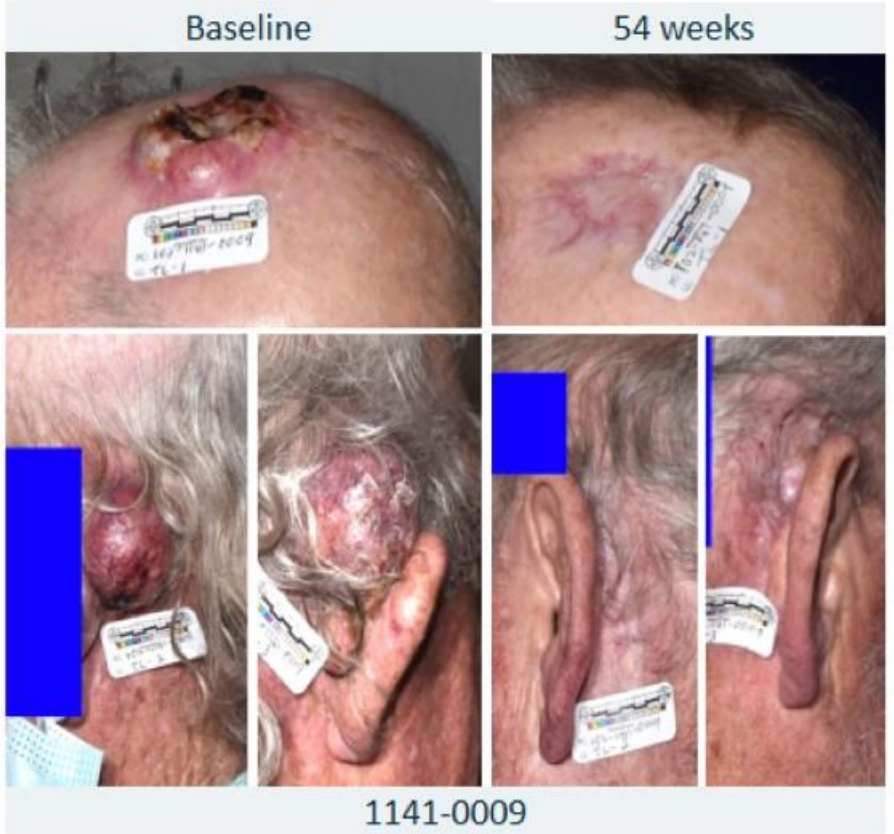
# Five of the most visually impactful CRs with RP1+cemiplimab



1140-0002



4805-0002



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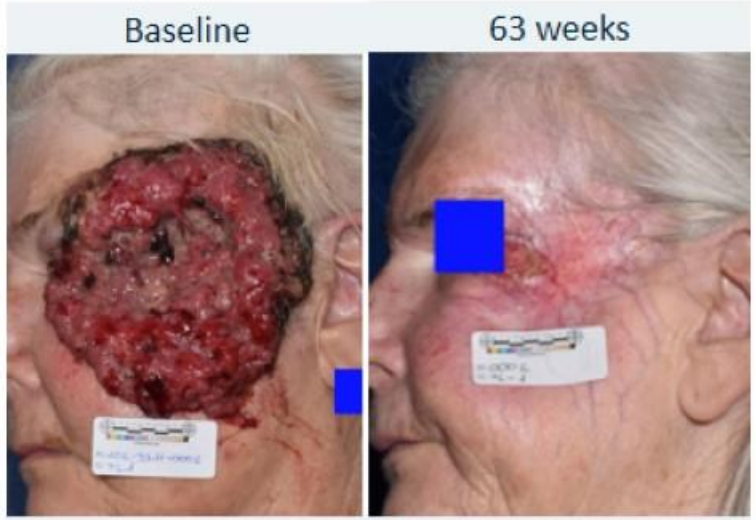
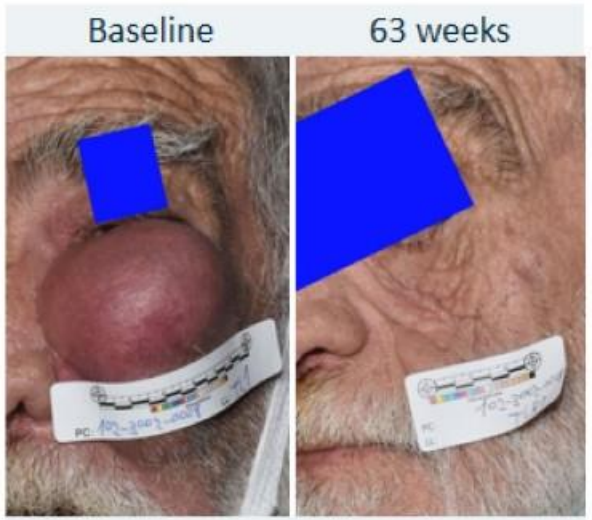
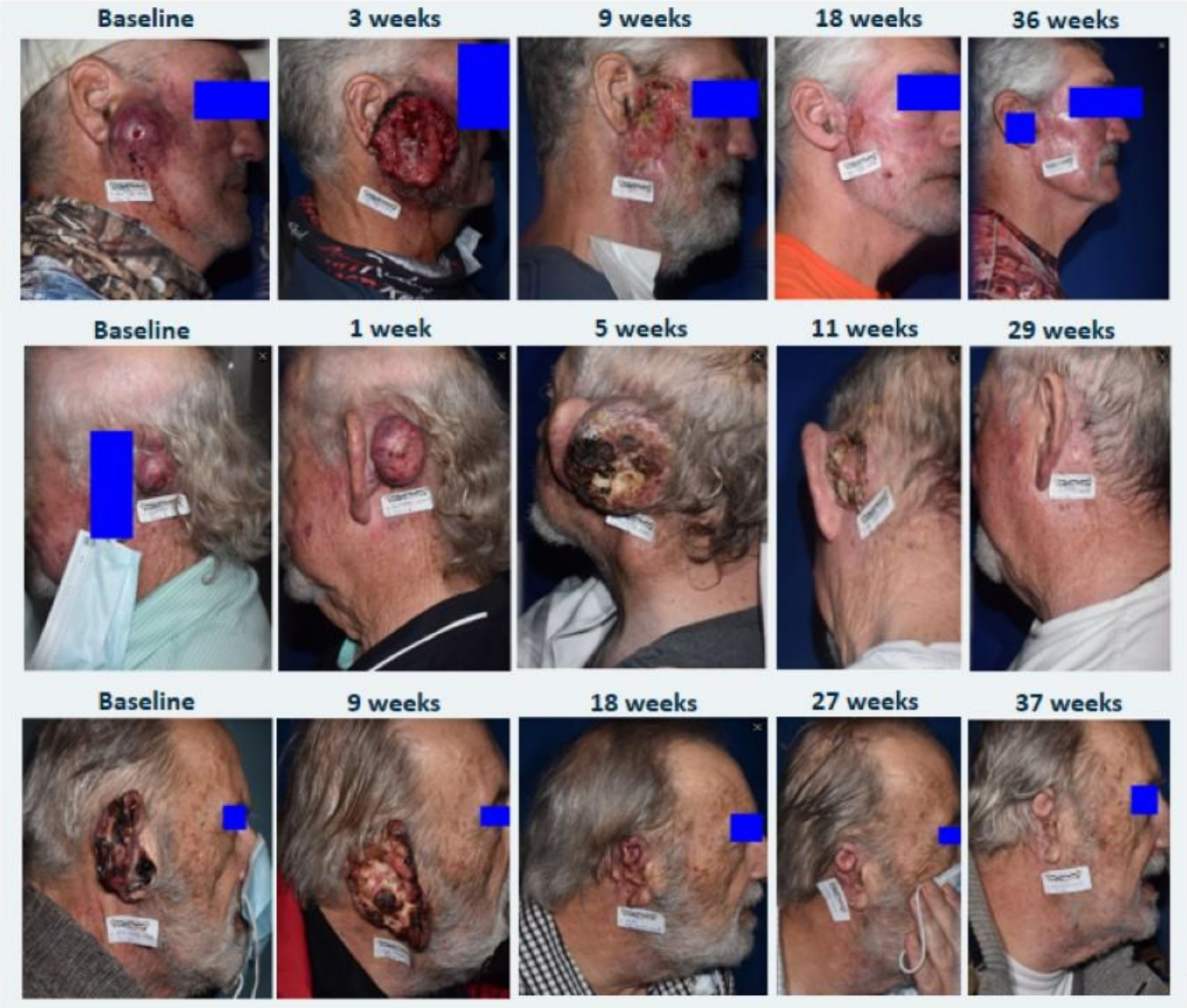


3311-0002



3002-0008

# Examples of pseudo-progression followed by durable CR in patients treated with RP1+cemiplimab




**Key Takeaway**

Pronounced pseudo-progression was seen with RP1+cemiplimab, which was only rarely seen with cemiplimab alone

# CERPASS summary & conclusions

- RP1+cemiplimab provides clinically meaningful benefit to patients with 1L CSCC, validating RP1+anti-PD1 therapy as an active combination in a randomized controlled setting
  - Depth, durability & clinical meaningfulness of responses are improved
  - RP1+cemiplimab addresses a key unmet need in patients with CSCC – treatment of patients with the type of disease which can have the most impact on a patient's quality of life
  - RP1+cemiplimab is a well tolerated regimen, with predominantly transient Grade 1-2 flu-like symptoms as compared to cemiplimab alone
  - High rate of CRs is also very promising for other settings e.g., neoadjuvant CSCC, where achieving CRs is key
- While a clear improvement in duration of response has already been seen, all time-based endpoints are currently immature, with longer follow up needed before conclusions can be fully drawn
  - Replimune intends to share CERPASS results with the FDA with all endpoints also being allowed to further mature before a further analysis is conducted to support the overall BLA filing strategy for RP1

# Acknowledgements

We thank the patients and their families and caregivers, the investigators and the investigational site staff of the CERPASS study across 83 sites and 10 countries

We would also like to extend our gratitude to the CERPASS study Steering Committee members: Michael Migden, Caroline Robert, Nikhil Khushalani, Anna Pavlick, Ana Arance, Paolo Ascierto, Helen Gogas, Andrew Haydon, Celeste Lebbe and Dirk Schadendorf

SECTION I

RP1: Exec Summary and Overview

SECTION II

RP1: 1L CSCC (CERPASS)

SECTION III

**RP1 IGNYTE and ARTACUS Skin Cancer Data and Anti-PD1 Failed Melanoma Update**

SECTION IV

RP1 Regulatory Update

SECTION V

Panel Q&A

# AGENDA

# New & updated IGNYTE data with RP1 combined with nivolumab in patients with skin cancer

# Treatment related AEs for skin cancer patients treated with RP1 combined with nivolumab (N=246)

*(related to either RP1 or nivolumab)*

| Preferred term, n (%) | TRAEs which occurred in >5% of patients (all Grade 3-5 are listed below) | | | | |
|---|---|---|---|---|---|
| | Grade 1-2 | Grade 3 | Grade 4 | Grade 5 | Total (n=246) |
| Fatigue | 76 (30.9) | 6 (2.4) | 0 | 0 | 80 (32.5) |
| Chills | 75 (30.5) | 0 | 0 | 0 | 75 (30.5) |
| Pyrexia | 69 (28.0) | 2 (0.8) | 0 | 0 | 69 (28.0) |
| Nausea | 46 (18.7) | 0 | 0 | 0 | 46 (18.7) |
| Influenza like illness | 40 (16.3) | 0 | 0 | 0 | 40 (16.3) |
| Pruritus | 37 (15.0) | 1 (0.4) | 0 | 0 | 37 (15.0) |
| Diarrhoea | 32 (13.0) | 3 (1.2) | 0 | 0 | 33 (13.4) |
| Injection site pain | 27 (11.0) | 0 | 0 | 0 | 27 (11.0) |
| Vomiting | 27 (11.0) | 0 | 0 | 0 | 27 (11.0) |
| Headache | 24 (9.8) | 0 | 0 | 0 | 24 (9.8) |
| Rash | 17 (6.9) | 1 (0.4) | 0 | 0 | 18 (7.3) |
| Myalgia | 16 (6.5) | 0 | 0 | 0 | 16 (6.5) |
| Asthenia | 14 (5.7) | 1 (0.4) | 0 | 0 | 15 (6.1) |
| Decreased appetite | 13 (5.3) | 2 (0.8) | 0 | 0 | 15 (6.1) |
| Injection site reaction | 14 (5.7) | 1 (0.4) | 0 | 0 | 14 (5.7) |

## Key Takeaway

- RP1 combined with nivolumab continues to be a generally well tolerated regimen with predominantly Grade 1/2 constitutional-type side effects and with a low incidence Grade 3-5 events seen

**Grade 3** events were five events of rash maculo-popular; two events each of eczema, hyponatremia, hypophysitis, immune-mediated hepatitis, one event each of arthralgia, lipase increased, dyspnoea, tumour pain, infusion related reaction, amylase increased, back pain, hypotension, abdominal pain, arthritis, dehydration, hypertension, immune-mediated enterocolitis, muscular weakness, paraesthesia, blood bilirubin increased, confusional state, delirium, dermatitis bullous, hyperglycaemia, acute left ventricular failure, cancer pain, dermatitis allergic, dysphagia, enterocolitis, extranodal marginal zone B-cell lymphoma (MALT type), glomerulonephritis, hypovolaemic shock, immune-mediated myocarditis, left ventricular dysfunction, liver function test increased, localized oedema, lymph node pain, memory impairment, meningitis aseptic, mental status changes, oedema, oral candidiasis, palmar-plantar erythrodysaesthesia syndrome, peripheral sensory neuropathy, radiculitis branchial, sinus arrhythmia, syncope, tricuspid valve incompetence, type 1 diabetes mellitus, uveitis, vaccine-induced seroconversion.

**Grade 4** events were one each of lipase increased, cytokine release syndrome, myocarditis and hepatic cytolysis.

**Grade 5** one event of immune mediated myocarditis

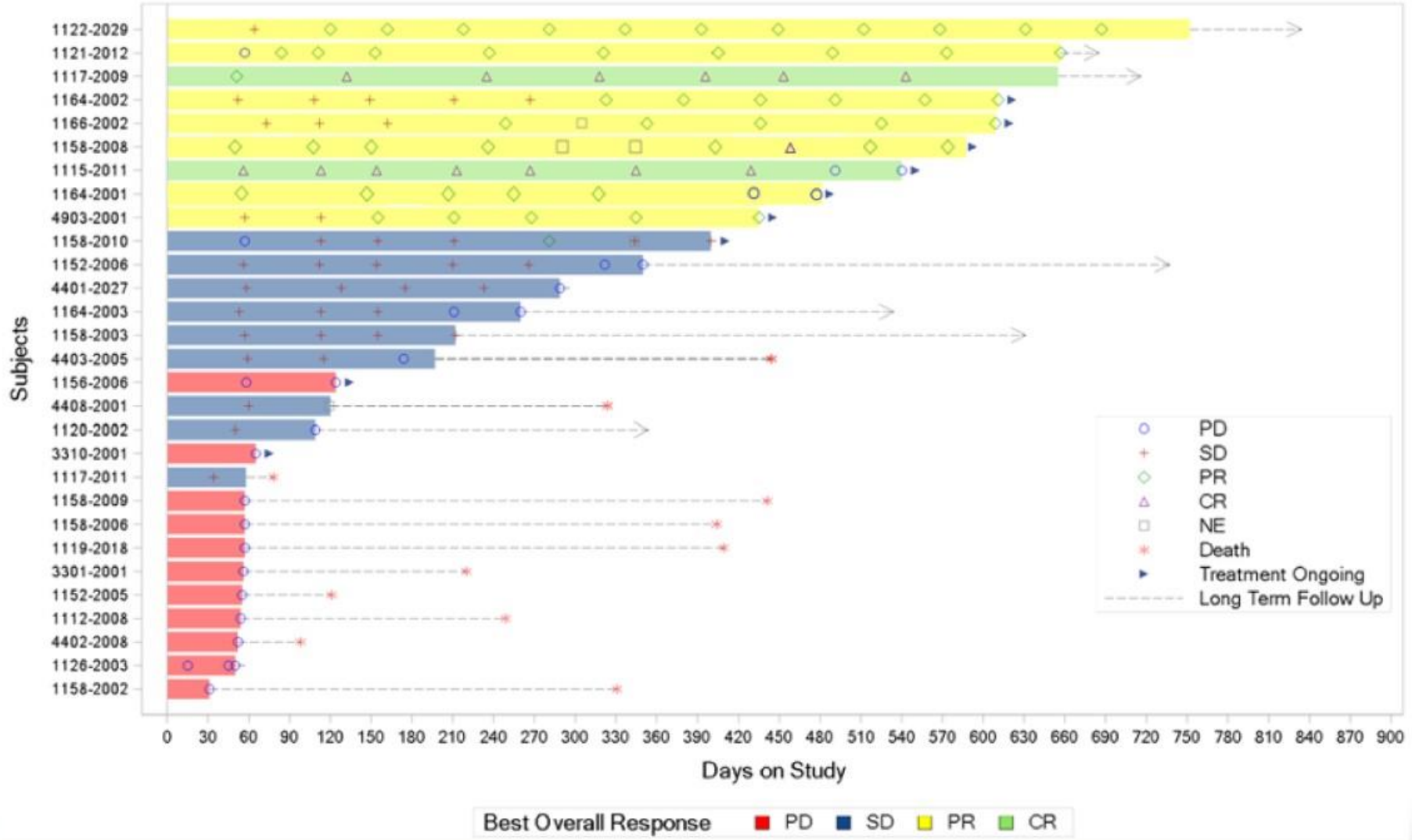
# RP1 combined with nivolumab in anti-PD1 failed non-melanoma skin cancers (NMSC)

# ORR subgroup analysis

## All patients (n=30)

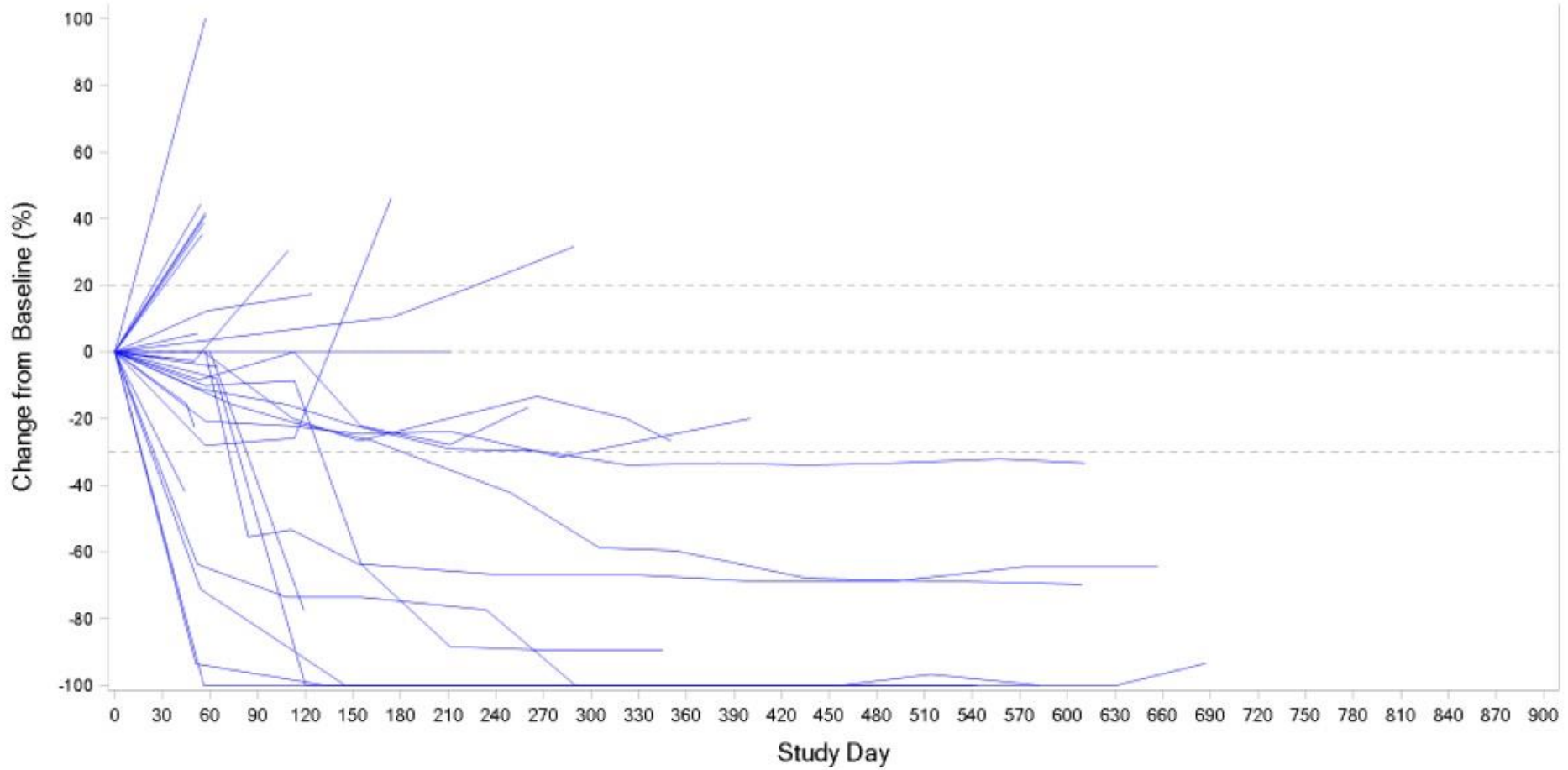
| BOR n (%) | All patients (n=30) | CSCC (n=17) | MCC (n=6) | BCC (n=2) | Angiosarcoma (n=3) | Other (n=2) |
|---|---|---|---|---|---|---|
| CR | 2 (6.7) | 1 (5.9) | 1 (16.7) | 0 | 0 | 0 |
| PR | 7 (23.3) | 2 (11.8) | 2 (33.3) | 2 (100.0) | 1 (33.3) | 0 |
| SD | 9 (30.0) | 7 (41.2) | 1 (16.7) | 0 | 1 (33.3) | 0 |
| PD | 12 (40.0) | 7 (41.2) | 2 (33.3) | 0 | 1 (33.3) | 2 (100.0) |
| ORR | 9 (30.0) | 3 (17.6) | 3 (50.0) | 2 (100.0) | 1 (33.3) | 0 |

# Duration of benefit n=30



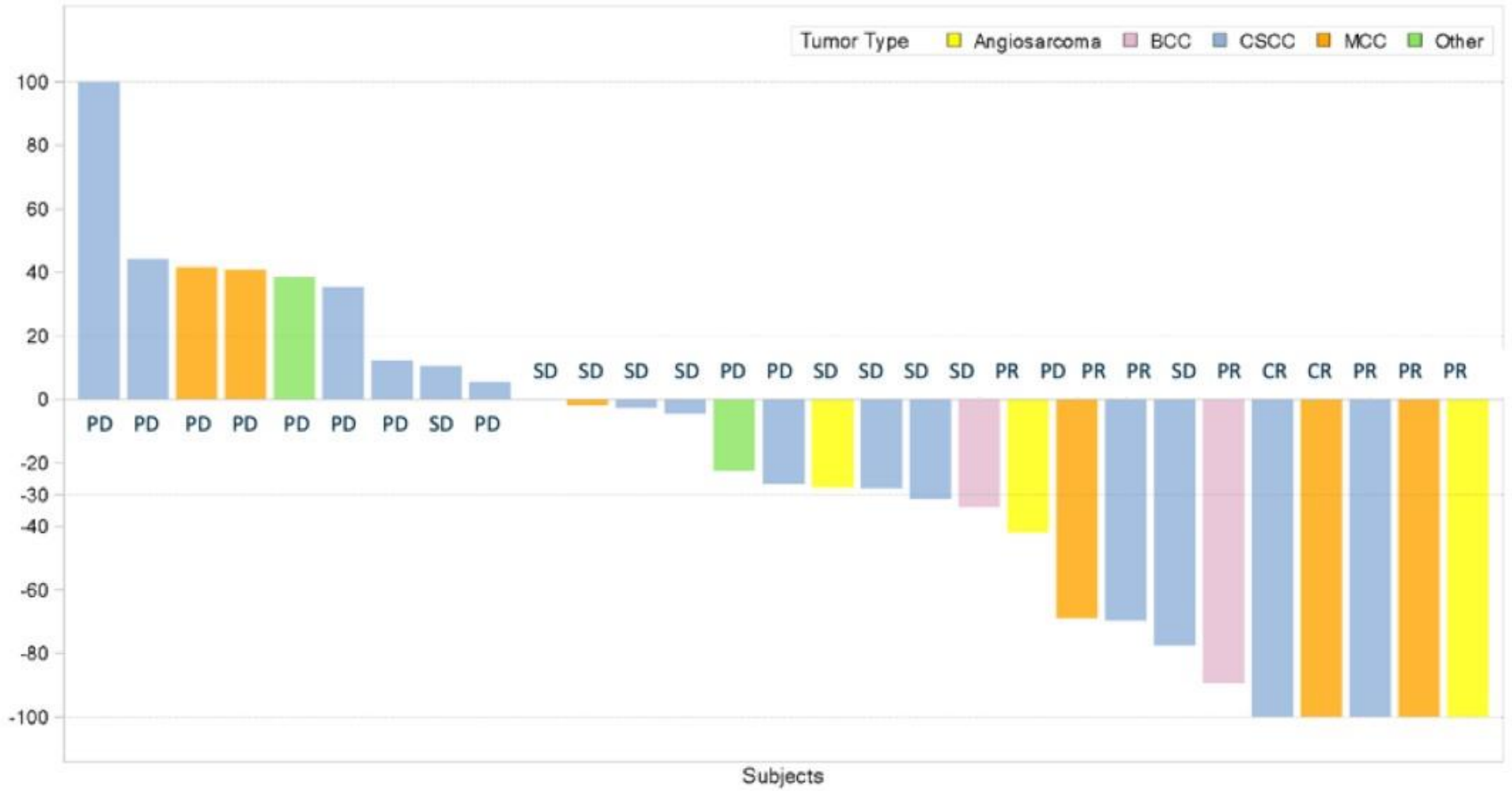
# Kinetics of response n=30

## 30 Patients with 6 month follow up - 30% Response Rate



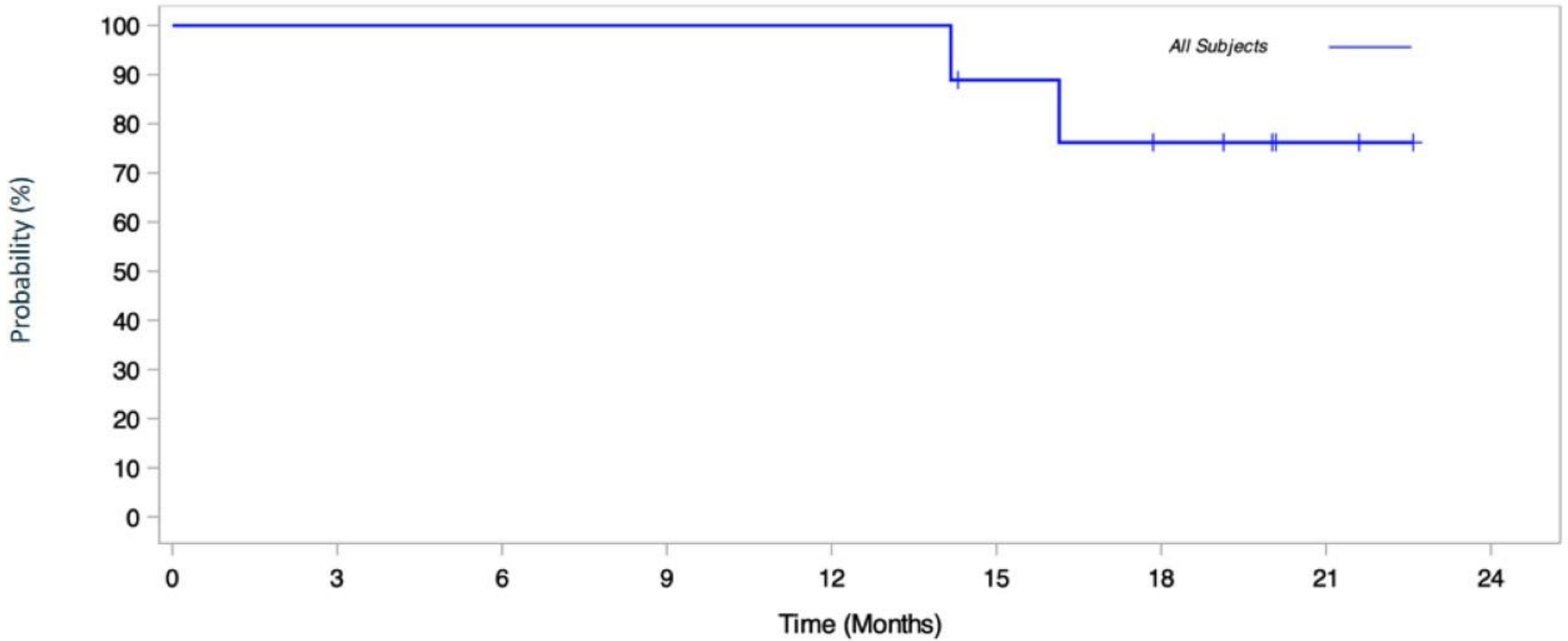

Patients with at least one post baseline assessment – target lesion response for each patient

# Depth of response n=30




Patients with at least one post baseline assessment – target lesion response for each patient

# Duration of response
## (time from baseline to end of response for responders)

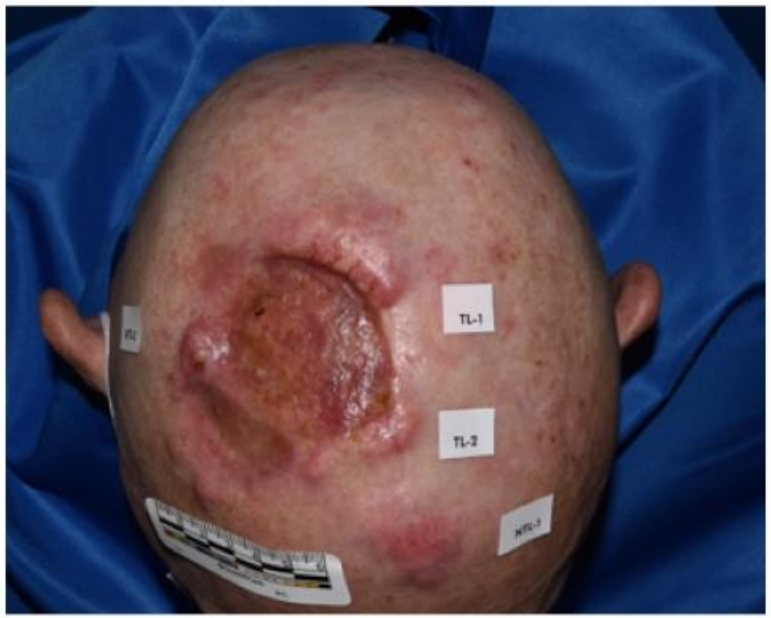


# Anti-PD1 failed non-melanoma skin cancer (NMSC) examples

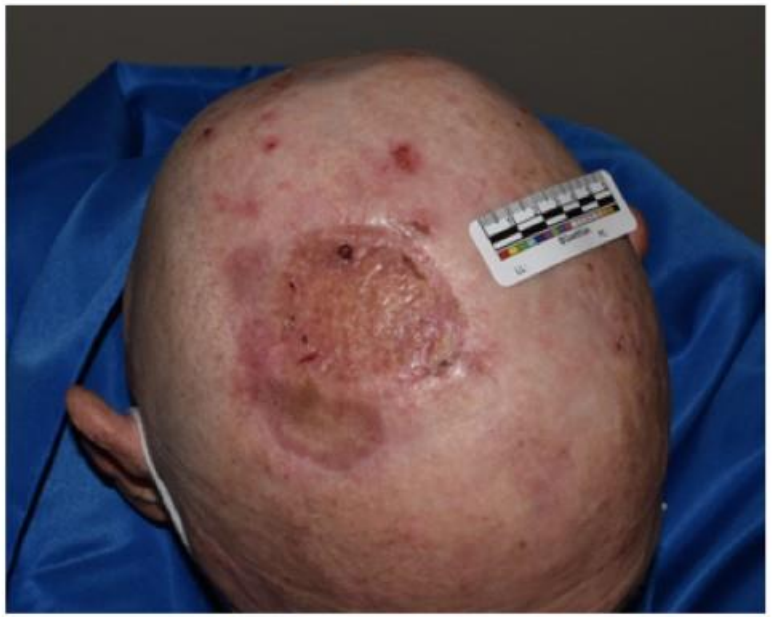
# Patient 1115-2011: CSCC

***BOR: CR***

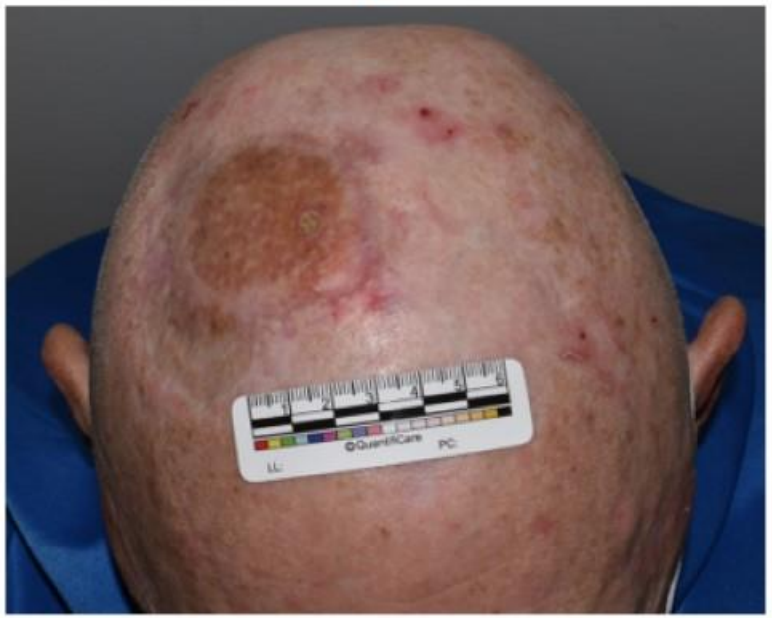
***Screening***




***Day 57***



***Day 211***



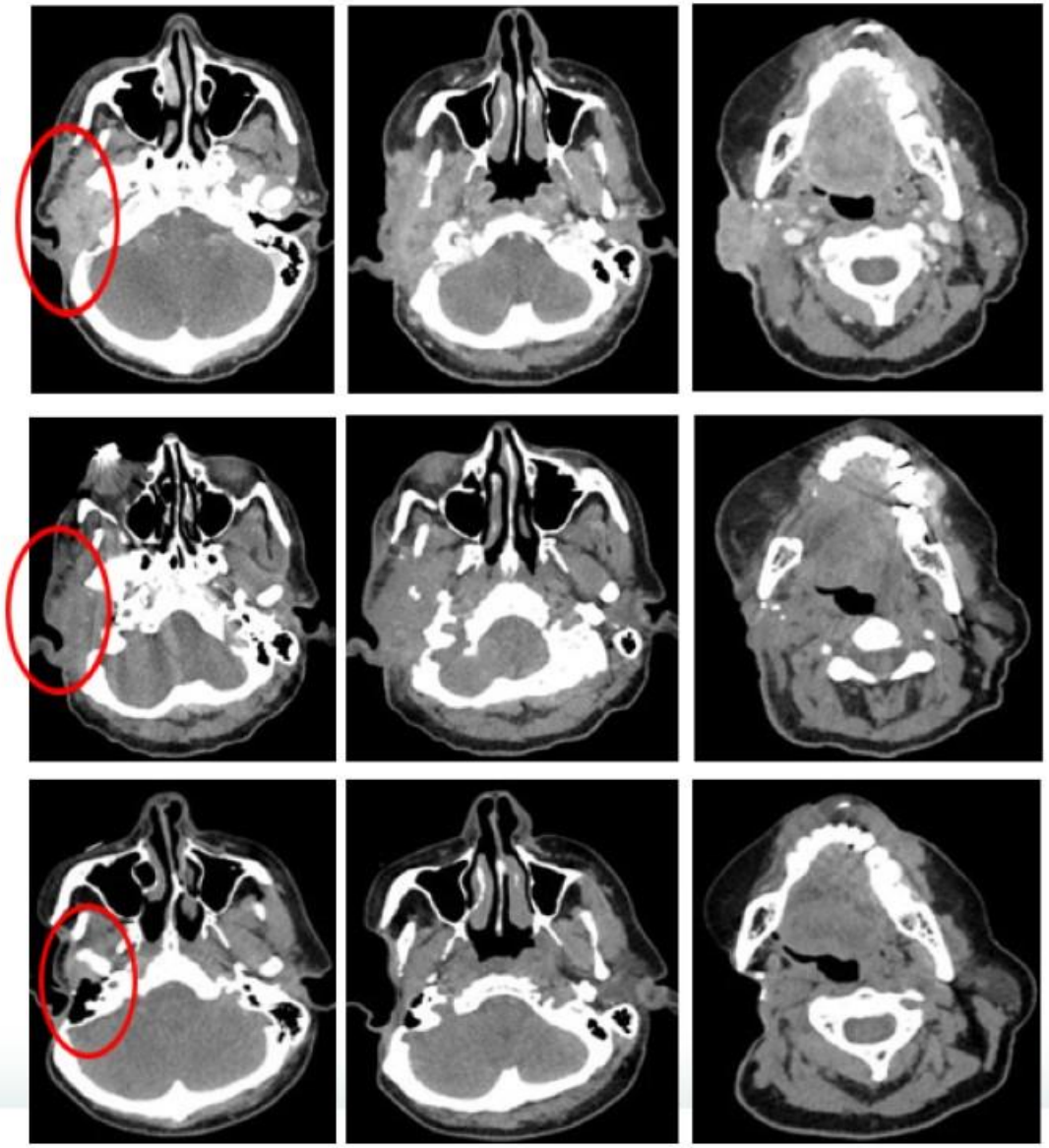
# Patient 1122-2029: CSCC

Replimune

Screening

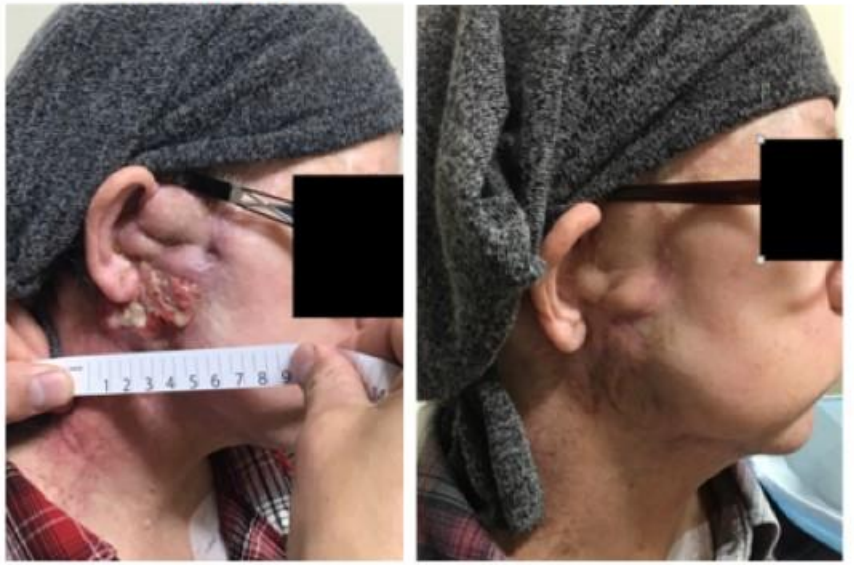
Day 57

Day 575



Screening

6 months

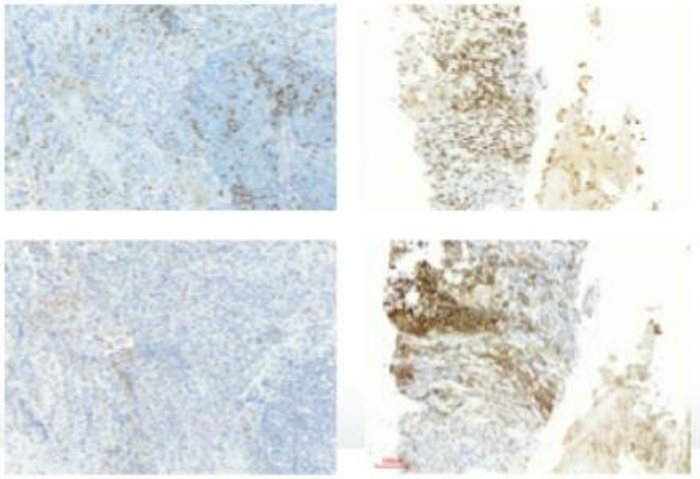


Screening

Day 43

CD8+
T cells

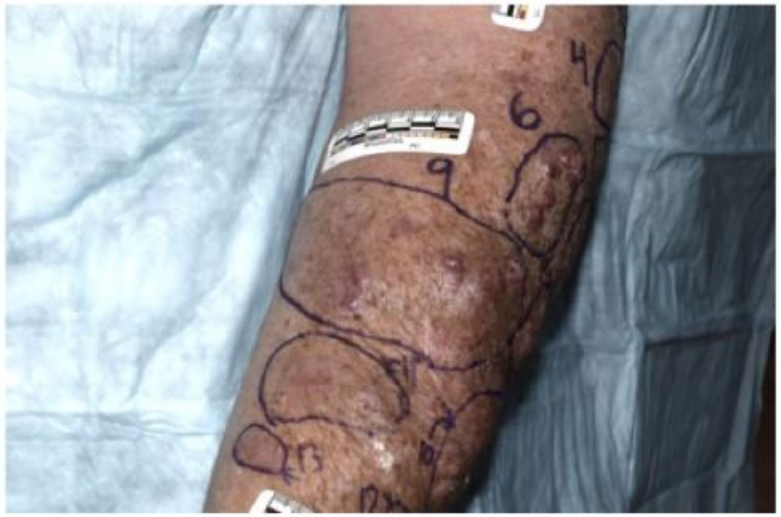
PD-L1

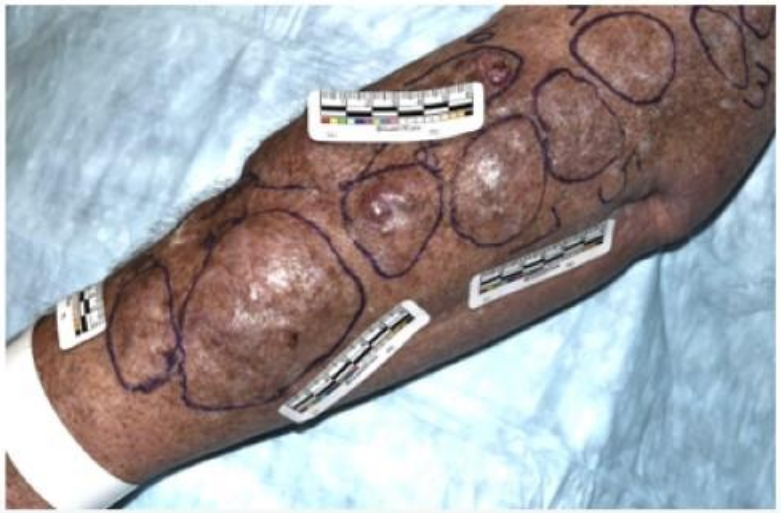


# Patient 1158-2008: MCC

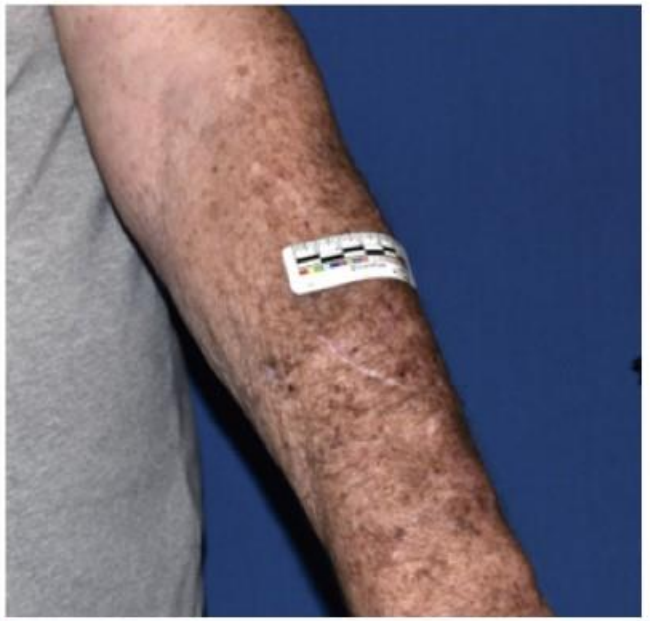
***BOR: PR***

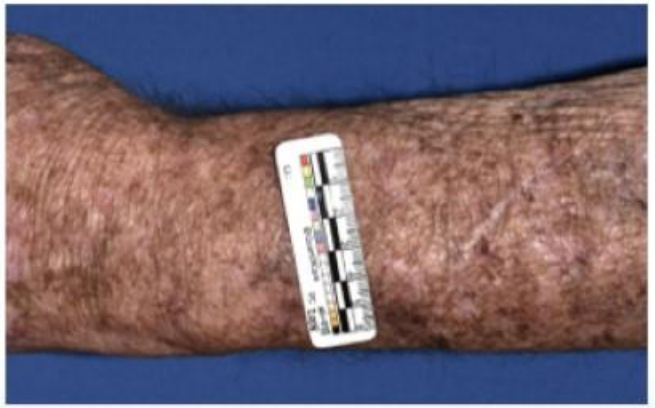
***Screening***





***Day 323***





# Anti-PD1 failed NMSC conclusions

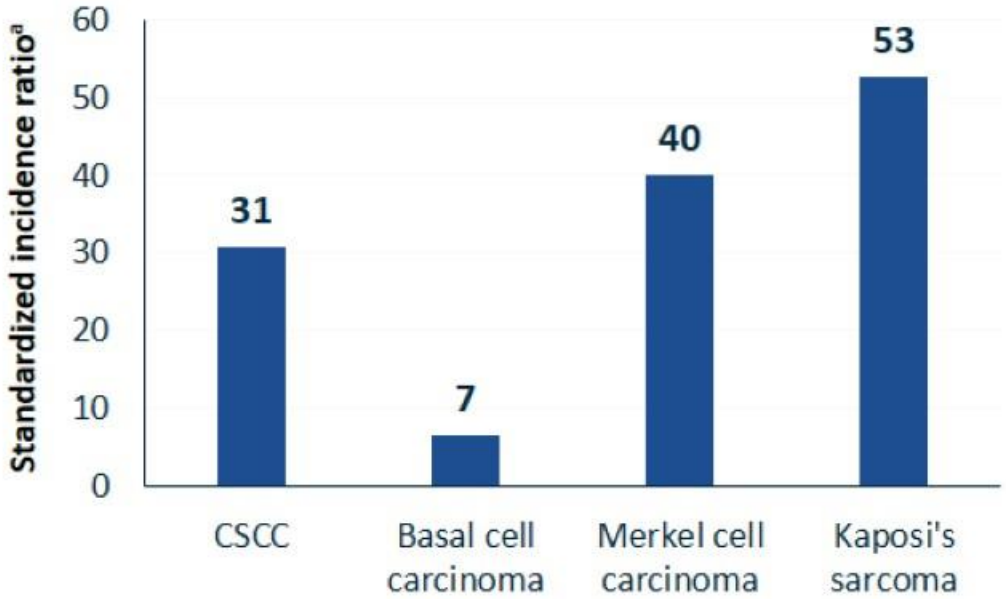
- **RP1+nivolumab provides clinically meaningful and durable benefit in patients with anti-PD1 failed NMSC**
  - ORR seen is consistent with data presented in anti-PD1 failed melanoma with approximately a third of patients responding and 60% demonstrating clinical benefit
- Treatment options are currently limited for anti-PD1 failed NMSC patients
- The combination of **RP1+nivolumab is well tolerated in anti-PD1 failed NMSC patients**, with safety consistent with the overall experience seen for RP1+nivolumab in patients with skin cancer

# RP1 monotherapy in solid organ transplant recipients with skin cancer – *ARTACUS data*

# Solid organ transplantation and non-melanoma skin cancer (NMSC)

- Non-melanoma skin cancer (NMSC) is the most common post-transplant malignancy in solid organ transplant (SOT) recipients and occurs at a 7-53x higher incidence vs the general population[1]
  - Cutaneous squamous cell carcinoma (CSCC) and basal cell carcinoma account for >90% of all cases of NMSC in SOT recipients[1,2]
  - Systemic immune checkpoint blockade is contra-indicated in the setting of SOT-associated NMSC given the documented risk of allograft rejection[3,4]

- Management of locally advanced and metastatic CSCC that has spread to other areas of the skin, soft tissue, or lymph nodes in SOT patients is not well established[3,4]
  - Withdrawal of immunosuppressive therapy may be required for the management of CSCC but may increase the risk of organ transplant rejection




[a]Standardized incidence ratios were calculated by dividing the observed number of NMSC cases by the expected number of cases based on the general population.
CSCC, cutaneous squamous cell carcinoma; NMSC, non-melanoma skin cancer; SOT, solid organ transplantation.
1. Friman T, et al. *Int J Cancer*. 2022;150(11):1779-91. 2. Garrett G, et al. *JAMA Dermatol*. 2017;153(3):296-303. 3. Mittal A and Colegio O. *Am J Transplant*. 2017;17(10):2509-30.
4. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Squamous Cell Skin Cancer. Version 1. 2023.

# Patient demographics and baseline characteristics

| Characteristic | All patients (N = 27) |
|---|---|
| **Age,** years, median (range) | 68.0 (48–86) |
| **Male,** n (%) | 21 (77.8) |
| **Race,** n (%) | |
| White | 26 (96.3) |
| Native Hawaiian/Pacific Islander | 1 (3.7) |
| **Allograft type,** n (%) | |
| Kidney | 22 (81.5) |
| Liver | 4 (14.8) |
| Lung | 1 (3.7) |
| Heart | 0 |

| Characteristic | All patients (N = 27) |
|---|---|
| **Cutaneous malignancies,** n (%) | |
| CSCC | 24 (88.9) |
| MCC | 3 (11.1) |
| **Stage at study baseline,** n (%) | |
| Locally advanced | 15 (55.6) |
| Metastatic[a] | 12 (44.4) |
| **Primary tumor location,** n (%) | |
| Skin | 26 (96.3) |
| Lymph node | 1 (3.7) |

**Data cutoff: June 18, 2023**

[a]Per protocol, metastatic to skin, soft tissue, or lymph nodes.
CSCC, cutaneous squamous cell carcinoma; MCC, Merkel cell carcinoma.

# ARTACUS: Safety

| All-grade TEAEs (>10% of patients), n (%) | All patients (N = 27) | | |
|---|---|---|---|
| | Grade 1/2 | Grade ≥3 | Total |
| Fatigue | 9 (33.3) | 0 | 9 (33.3) |
| Chills | 7 (25.9) | 0 | 7 (25.9) |
| Pyrexia | 7 (25.9) | 0 | 7 (25.9) |
| Anemia | 2 (7.4) | 3 (11.1) | 5 (18.5) |
| Blood creatinine increased | 5 (18.5) | 0 | 5 (18.5) |
| Nausea | 5 (18.5) | 0 | 5 (18.5) |
| Urinary tract infection | 3 (11.1) | 2 (7.4) | 5 (18.5) |
| Decreased appetite | 4 (14.8) | 0 | 4 (14.8) |
| Diarrhea | 4 (14.8) | 0 | 4 (14.8) |

| All-grade TEAEs (>10% of patients), n (%) | All patients (N = 27) | | |
|---|---|---|---|
| | Grade 1/2 | Grade ≥3 | Total |
| Headache | 4 (14.8) | 0 | 4 (14.8) |
| Injection-site pain | 4 (14.8) | 0 | 4 (14.8) |
| Cellulitis | 2 (7.4) | 1 (3.7) | 3 (11.1) |
| Confusional state | 3 (11.1) | 0 | 3 (11.1) |
| Constipation | 3 (11.1) | 0 | 3 (11.1) |
| Facial pain | 3 (11.1) | 0 | 3 (11.1) |
| Hypercalcemia | 3 (11.1) | 0 | 3 (11.1) |
| Hyperglycemia | 2 (7.4) | 1 (3.7) | 3 (11.1 |
| Sepsis | 0 | 3 (11.1) | 3 (11.1) |
| Tumor pain | 2 (7.4) | 1 (3.7) | 3 (11.1) |

- The most common TEAEs were fatigue (33.3%), chills (25.9%), and pyrexia (25.9%)
  - No evidence of allograft rejection
  - Seventeen patients had at least one grade ≥3 AE, all unrelated to RP1
  - Two immune-mediated grade 3 AEs of encephalopathy in patients who died of disease progression; neither were related to RP1
  - Eight deaths were reported: disease progression (n = 3); pneumonia (n = 2); sepsis, stroke, and pulmonary hypertension (each n = 1); none were related to RP1

AE, adverse event; TEAE, treatment-emergent AE.

# ARTACUS: Efficacy

| | Evaluable patients[a] (N = 23) |
|---|---|
| **Best overall response (RECIST 1.1)** | n (%) |
| CR | 5 (21.7)[b] |
| PR | 3 (13.0)[c] |
| SD | 1 (4.3) |
| PD | 14 (60.9) |
| **ORR (CR + PR)** | 8 (34.8) |
| **DCR (CR + PR + SD)** | 9 (39.1) |

| | Responders (n = 8) |
|---|---|
| **Characteristics of responders** | n |
| **Tumor type** | |
| CSCC | 6 |
| MCC | 2 |
| **Stage at study baseline** | |
| Locally advanced | 6 |
| Metastatic | 2 |

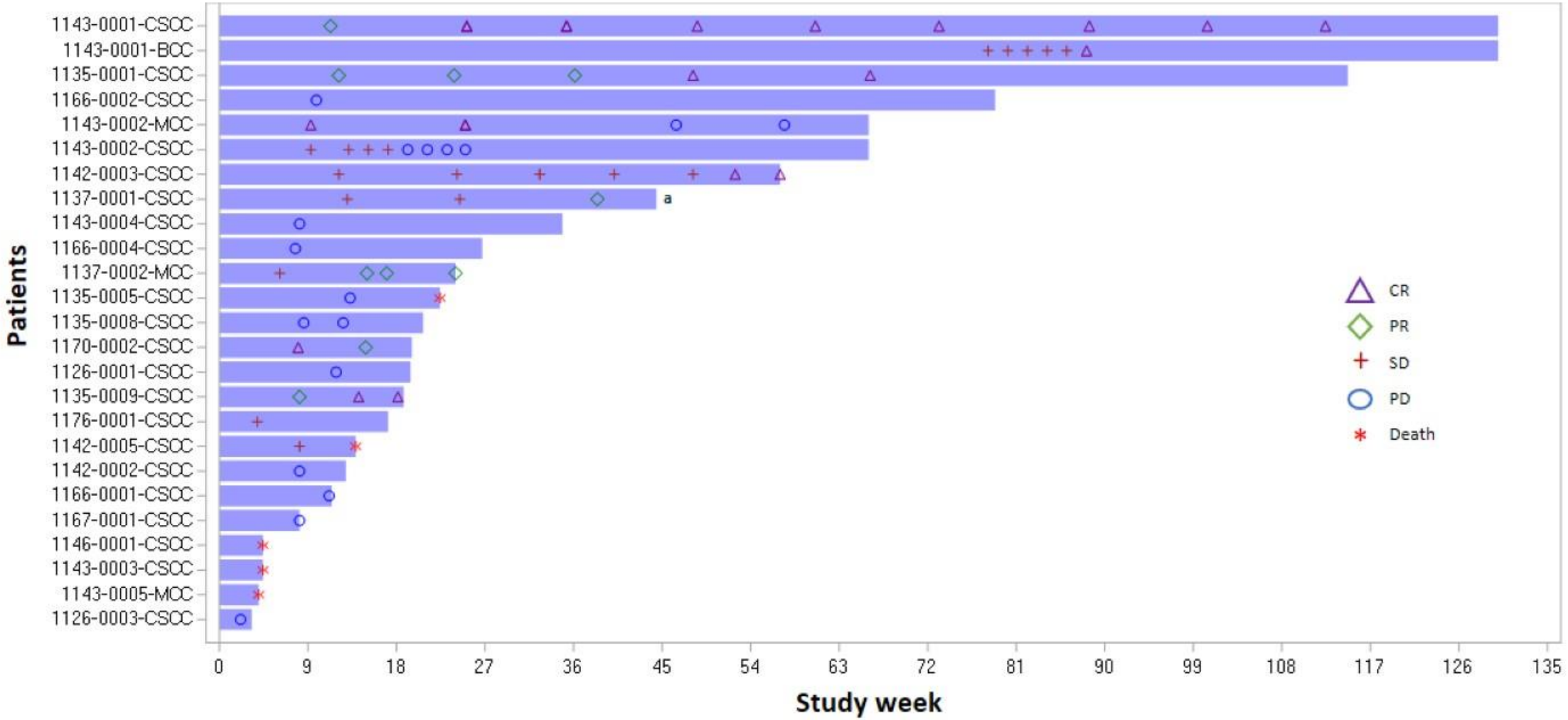
[a]Enrolled ≥3 months before the data cut; 4 patients who went off study for reasons unrelated to NMSC or RP1-related adverse events (1 death each from COVID-19, stroke, and pneumonia and 1 withdrawal because of injection pain) were excluded from the efficacy analysis.

[b]One patient with CSCC also had CR of a new primary BCC which appeared post baseline and was also treated with RP1.

[c]One PR could not be confirmed because the patient withdrew consent; all other responses are confirmed.

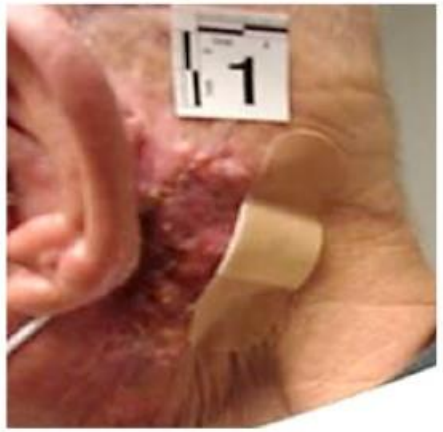
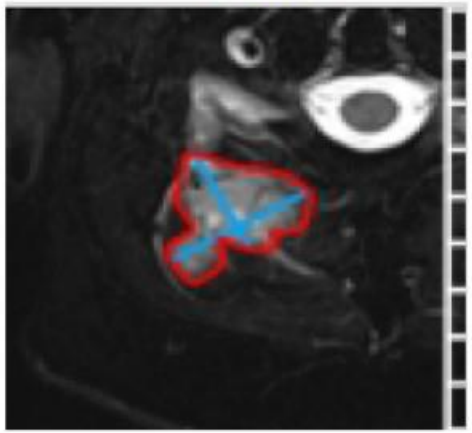
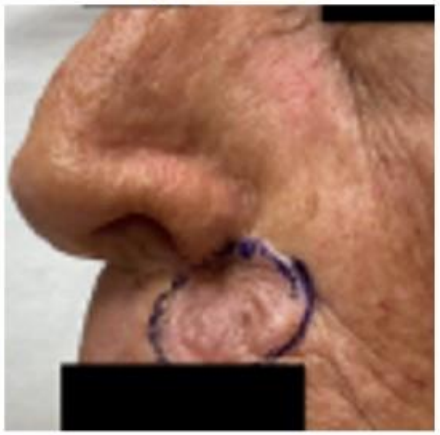
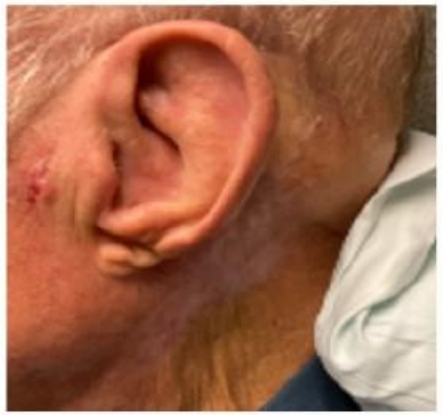
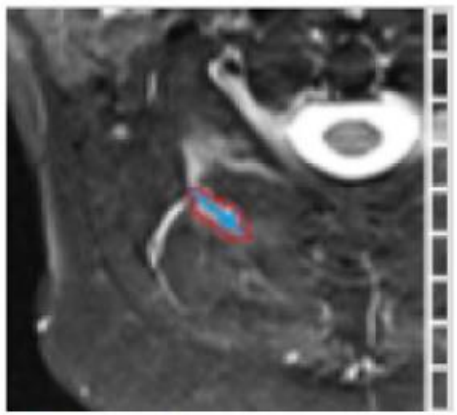
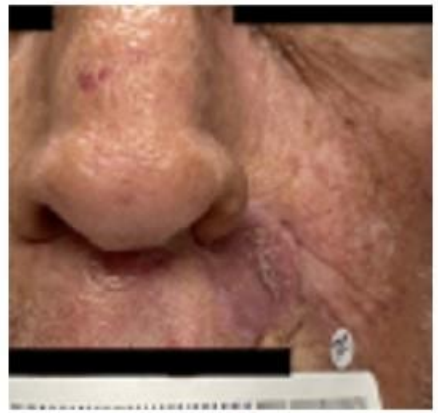
BCC, basal cell carcinoma; CSCC, cutaneous squamous cell carcinoma; COVID-19, coronavirus disease 2019; CR, complete response; DCR, disease control rate; MCC, Merkel cell carcinoma; ORR, objective response rate; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.

# ARTACUS: Duration of response



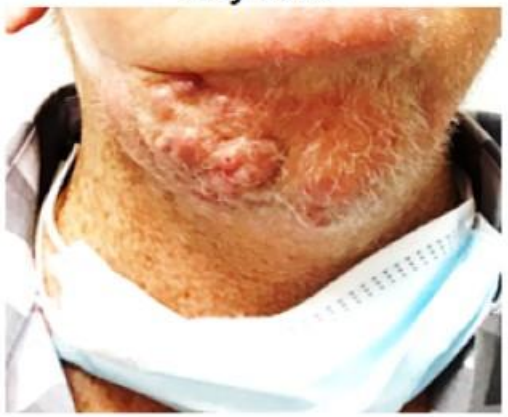
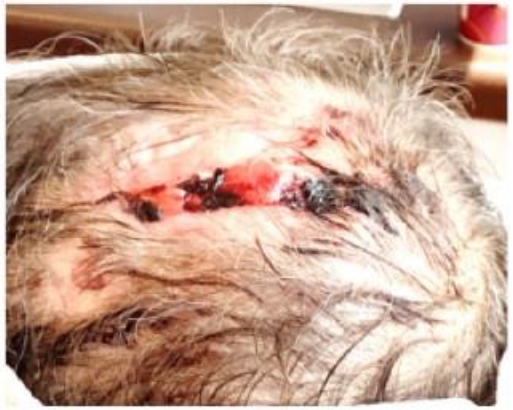
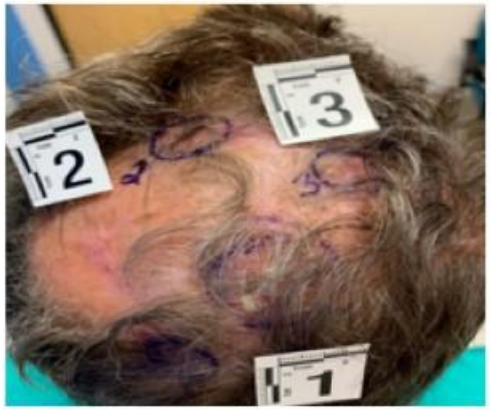
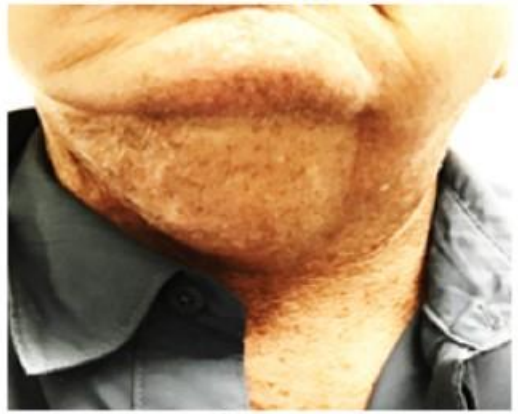
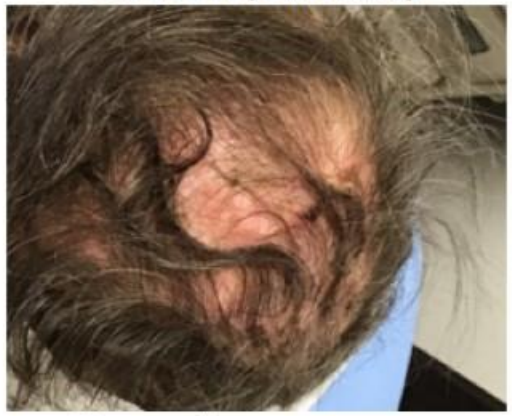
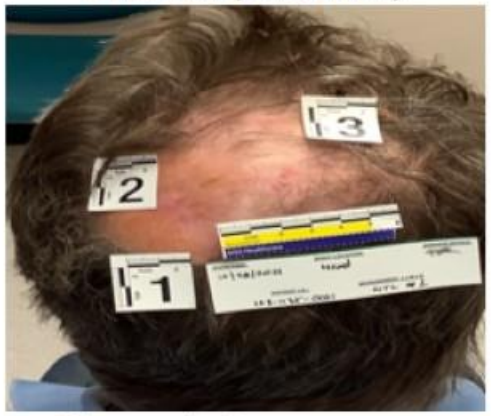

[a]Withdrew consent.
CR, complete response; BCC, basal cell carcinoma; CSCC, cutaneous squamous cell carcinoma; MCC, Merkel cell carcinoma; PD, progressive disease; PR, partial response; SD, stable disease.

# ARTACUS: Examples of confirmed response

| | 1142-0003<br>August 2022 | 1137-0002[a]<br>March 2023 | 1135-0009<br>April 2023 |
|---|---|---|---|
| Baseline |  |  |  |
| On-treatment | September 2023 (13 months)<br>  | September 2023 (6 months)<br>  | June 2023 (2 months)<br>  |
| | Complete response | Partial response | Complete response |

[a]Paraspinal muscle lesion at C1-C2 vertebrae.

# ARTACUS: Examples of confirmed response (cont'd)

| | 1143-0002 May 2022 | 1143-0001 Jun 2021 | 1135-0001 Jul 2021 |
|---|---|---|---|
| Baseline |  |  |  |
| On-treatment | Aug 2022 (3 months)<br>  | Dec 2021 (6 months)<br>  | Oct 2021 (3 months)<br>  |
| | Complete response | Complete response | Complete response |

# ARTACUS summary & conclusions

- This is the **first clinical trial** assessing **single-agent RP1** in **solid organ/hematopoietic cell transplant patients on chronic immunosuppressive treatment with advanced skin cancer** in whom systemic immunotherapy is typically contra-indicated
- **RP1 monotherapy showed clear anti-tumor activity, with an ORR of 34.8%** (5 of 23 confirmed CR [21.7%]) in evaluable patients, with most responses ongoing as of the data cutoff[a]
- **No evidence of allograft rejection was observed** as of the data cutoff[a] **including in hepatic and lung allografts**
- **RP1 monotherapy was well tolerated**, and the safety profile was similar to the profile in non-immunocompromised patients with advanced skin cancers (IGNYTE study)

[a]June 18, 2023.
CR, confirmed response; ORR, objective response rate.

# RP1 combined with nivolumab in anti-PD1 failed melanoma

# Overview of the current 2nd line melanoma landscape

- There are **limited options for melanoma patients having progressed on anti-PD1 therapy** (including patients who progressed on adjuvant anti-PD1 therapy)
- For patients who have not already received anti-CTLA-4 therapy, **single agent ipilimumab or ipilimumab +nivolumab or relatinib (Opdualag) is an option**
  - *Expected response rate in patients who have not received prior anti-CTLA-4, approx. 10% to 30% for ipilimumab or ipilimumab+nivolumab combination, depending on the setting, but with high toxicity**
  - *For patients who have received prior anti-CTLA-4 therapy, limited options remain*
- To date, while approved in the **1L setting adding anti-LAG3 to anti-PD1 has not demonstrated meaningful efficacy in anti-PD1 failed melanoma patients** (BMS & Regeneron data)
- For BRAF mutant patients, if not already BRAF/MEK experienced, **BRAF targeted therapy is an option, but in general responses are transient**
- **TIL therapy** (Iovance & others) has shown response rates in the 30% range, and may become FDA approved, but the **treatment comes with considerable toxicity** (nearly all patients experience grade 3/4 toxicity) and **practicality considerations**

*1. Pires da Silva I, et al. Lancet Oncol. 2021;22(6):836-847. 2. Olson DJ, et al. J Clin Oncol. 2021;39(24):2647-2655. 3. Vanderwalde AM, et al. Presented at AACR 2022. New Orleans

# IGNYTE – Phase 2 study design (anti-PD1 failed cutaneous melanoma cohort; intended for registration)

IGNYTE

**Tumor response assessment**
Radiographic imaging (CT) at baseline and every 8 weeks from first dose and every 12 weeks after confirmation of response

**Anti-PD1 Failed Cutaneous Melanoma (N=140)**

**Screening** → *28 days* → **First Dose** RP11X10^6 → *2 Weeks* → **RP1+Opdivo** 1X10^7, 240 mg → *2 Weeks* → **Opdivo** 240 mg → *2 Weeks* → **Opdivo** 480 mg (Q4W)

**Cycle 1** | **Cycle 2-8** | **Cycle 9** | **Cycles 10-30***

**3-year follow-up post last patient enrolled**

**100 Day Safety Follow-Up**

## Primary Objectives
- To assess the safety and tolerability of RP1 in combination with nivolumab
- To assess the efficacy of RP1 in combination with nivolumab as determined by ORR using modified RECIST 1.1 criteria

## Secondary Objectives
To assess the efficacy of RP1 in combination with nivolumab as determined by DOR, CR rate, DCR, PFS, and 1-year and 2-year OS

## Key Eligibility
Advanced or metastatic non-neurological solid tumors without treatment options; at least 1 measurable and injectable lesion (≥ 1cm LD); adequate organ function; no prior treatment with oncolytic therapy. ECOG performance status (PS) 0-1.

## Criteria for CPI-failed:
At least 8 weeks of prior anti-PD1, confirmed progression while on anti-PD1, anti-PD1 must be the last therapy before the clinical trial. Patients on prior adjuvant therapy must have progressed while on prior adjuvant treatment (confirmed by biopsy).

Note: Dosing with Opdivo begins at Dose 2 of RP1 (C2D15)
*Option to reinitiate RP1 for 8 cycles if criteria are met
Data shown is a snapshot from the ongoing study, with a data cut off date of 6th Nov 2023

# Demographics (n=156)

| | N=16 n (%) | N=140 n (%) | n=156 n (%) |
|---|---|---|---|
| **Stage** | | | |
| IIIb/IIIc/IVM1a | 3 (18.8) | 73 (52.1) | 76 (48.7) |
| IVM1b/c /d | 13 (81.2) | 67 (47.9) | 80 (51.3) |
| **Prior therapy** | | | |
| Anti-PD1 only as adjuvant therapy | 2 (12.5) | 43 (30.7) | 45 (28.8) |
| Anti-PD1 not as adjuvant therapy | 14 (87.5) | 97 (69.3) | 111 (71.2) |
| Anti-PD1 combined with anti-CTLA-4* | 9 (56.3) | 63 (45.0) | 72 46.2) |
| Prior single agent anti-CTLA-4, including as adjuvant | 0 | 3 (2.1) | 3 (1.9) |
| Received BRAF directed therapy | 0 | 16 (11.4) | 16 (10.3) |
| BRAF wt & received combination anti-PD1 & anti-CTLA-4 | 9 (56.3) | 39 (27.9) | 48 (30.8) |
| **Other disease characteristics^** | | | |
| Primary resistance to prior anti-PD1 * | 9 (56.3) | 82 (58.6) | 91 (58.3) |
| Secondary resistance to prior anti-PD1 | 6 (37.5) | 57 (40.7) | 63 (40.4) |
| UNK resistance to prior anti-PD1 | 1 (6.3) | 1 (0.7) | 2 (1.3) |
| BRAF wild-type | 16 (100.0) | 87 (62.1) | 103 (66.0) |
| BRAF mutant | 0 | 53 (37.9) | 53 (34.0) |
| LDH ≤ULN | 13 (81.2) | 92 (65.7) | 105 (67.3) |
| LDH >ULN | 3 (18.8 ) | 47 (33.6) | 50 (32.1) |
| LDH UNK | 0 | 1 (0.7) | 1 (0.6) |

*N=16 are the anti-PD1 failed melanoma patients from the initial IGNYTE melanoma cohort (enrolled 30 patients with treatment naïve and previously treated cutaneous, uveal & mucosal melanoma*

*N=140 are the full 140 patients enrolled into the IGNYTE anti-PD1 failed cutaneous melanoma cohort*

*N=156 are all IGNYTE patients treated with RP1+nivolumab with anti-PD1 failed cutaneous melanoma (ie both groups added together)*

*Primary resistance = Best response of PD, or SD for <6 months on the prior course of anti-PD13; for prior adjuvant patients, progressed within 6 months of starting anti-PD1

Secondary resistance = Best response of PR, CR, or SD >6months on the prior course of anti-PD13; for adjuvant patients, progressed after 6 months of starting anti-PD1.

^PD-L1 status in progress and not currently available

# ORR analysis confirms a consistent benefit across all subgroups

## All patients (n=156)

| BOR n (%) | Prior cohort (n=16) | Anti-PD1 failed cohort (n=140) | All patients (n=156) | Prior single agent anti-PD1 (n=84) | Prior combination anti–PD-1 & anti–CTLA-4* (n=72) | Stage IIIb/IIIc/IVa (n=76) | Stage IVb/c/d (n=80) | Primary resistance to anti-PD1 (n=91) | Secondary resistance to anti-PD1 (n=63) |
|---|---|---|---|---|---|---|---|---|---|
| | All patients (n=156) | | | | | | | | |
| CR | 2 (12.5) | 17 (12.1) | 19 (12.2) | 14 (16.7) | 5 (6.9) | 15 (19.7) | 4 (5.0) | 12 (13.2) | 6 (9.5) |
| PR | 4 (25.0) | 26 (18.6) | 30 (19.2) | 16 (19.0) | 14 (19.4) | 14 (18.4) | 16 (20.0) | 19 (20.9) | 11 (17.5) |
| SD | 2 (12.5) | 29 (20.7) | 31 (19.9)^ | 21 (25.0) | 10 (13.9) | 18 (23.7)^ | 13 (16.3) | 15 (16.5)^ | 16 (25.4) |
| PD | 8 (50.0) | 68 (48.6) | 76 (48.7) | 33 (39.3) | 43 (59.7) | 29 (38.2) | 47 (58.8) | 45 (49.5) | 30 (47.6) |
| ORR | 6 (37.5) | 43 (30.7) | 49 (31.4) | 30 (35.7) | 19 (26.4) | 29 (38.2) | 20 (25.0) | 31 (34.1) | 17 (27.0) |

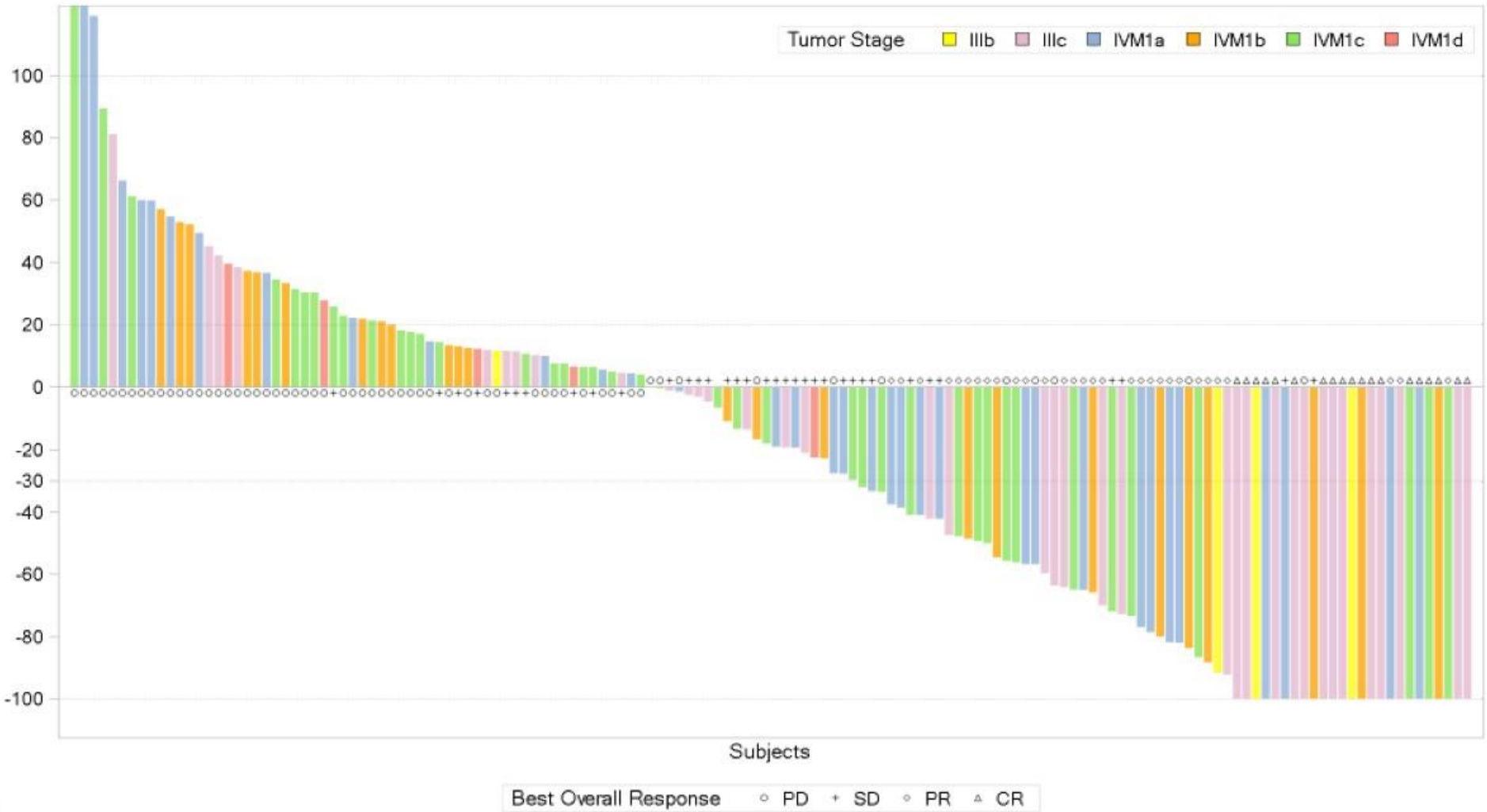
^Includes 1 patient with a unconfirmed PR (uPR)

**There are 5 patients still on study with the opportunity for response.**

BOR=best overall response

# Depth of response n=156

## Maximum change in target lesions; patients with at least one follow up assessment

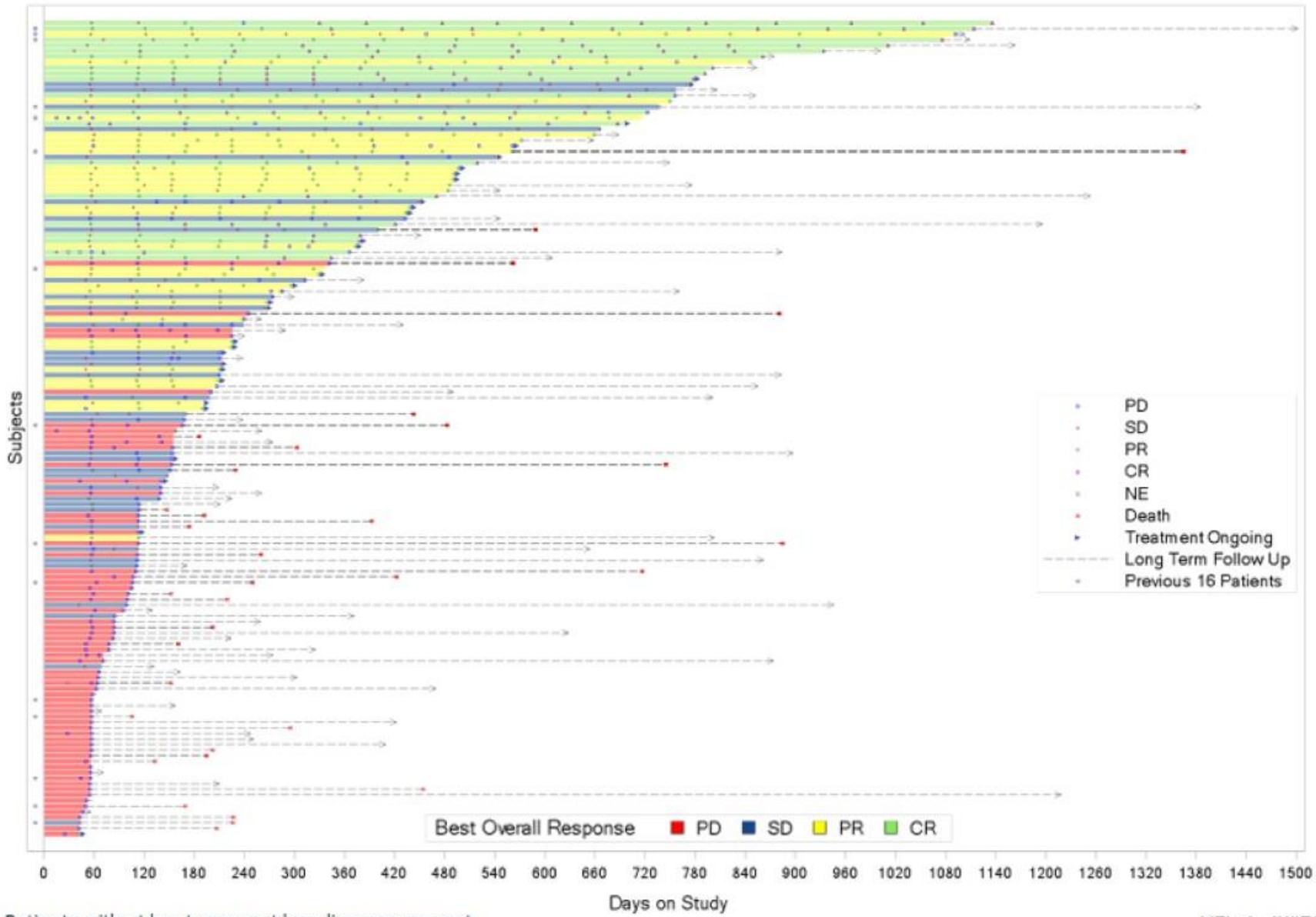



### Key Takeaways

- Target tumor reduction is seen in >50% of patients
- Responses were seen across disease stages, including complete responses in patients with stage IVM1b/c disease

Patients with at least one post baseline assessment – target lesion response for each patient

# Duration of benefit n=156

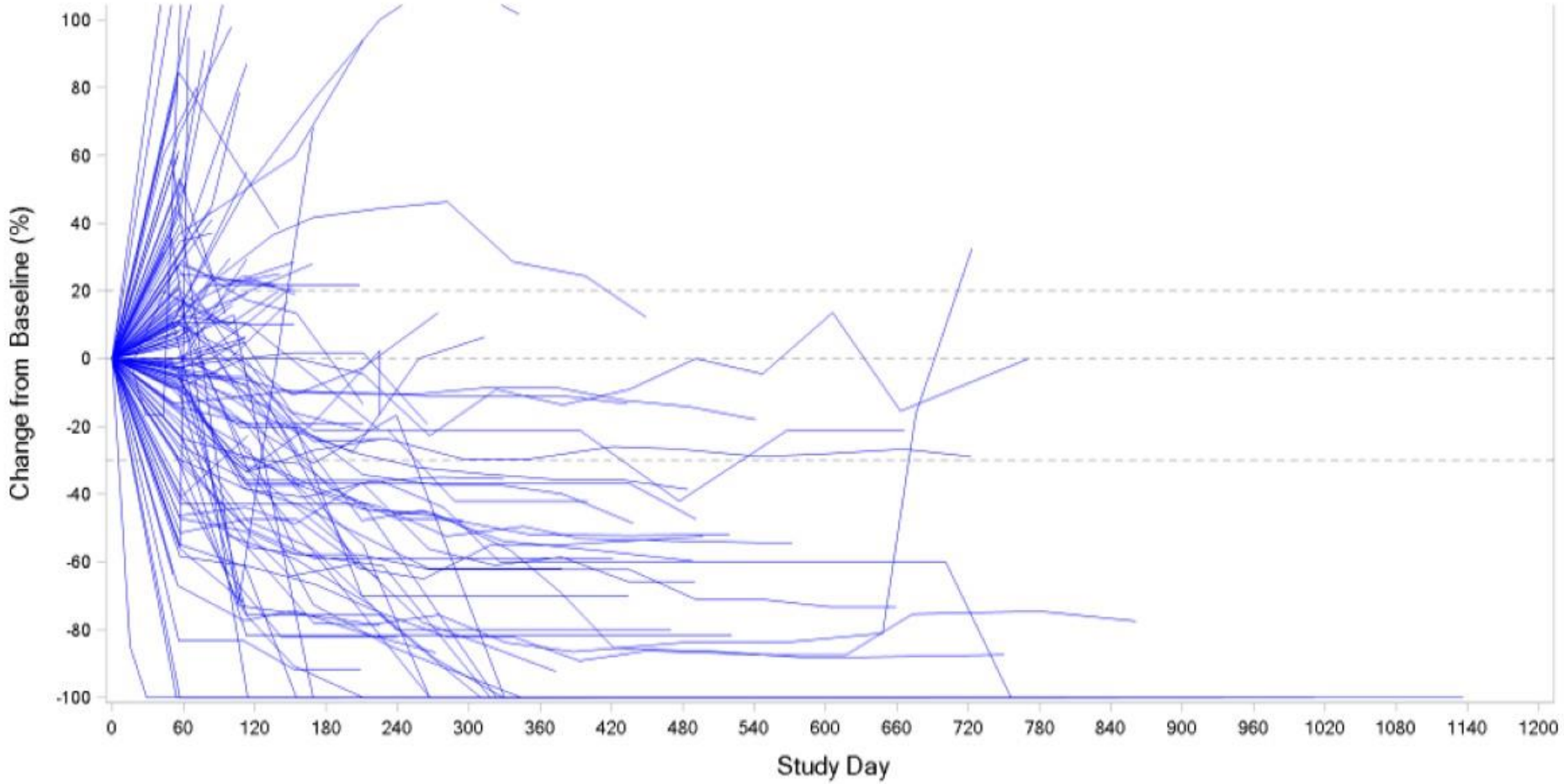



Patients with at least one post baseline assessment

## Key Takeaways

- A substantial proportion of patients achieve durable clinical benefit, including those with SD
- 78% of responses are ongoing

# Kinetics of response n=156



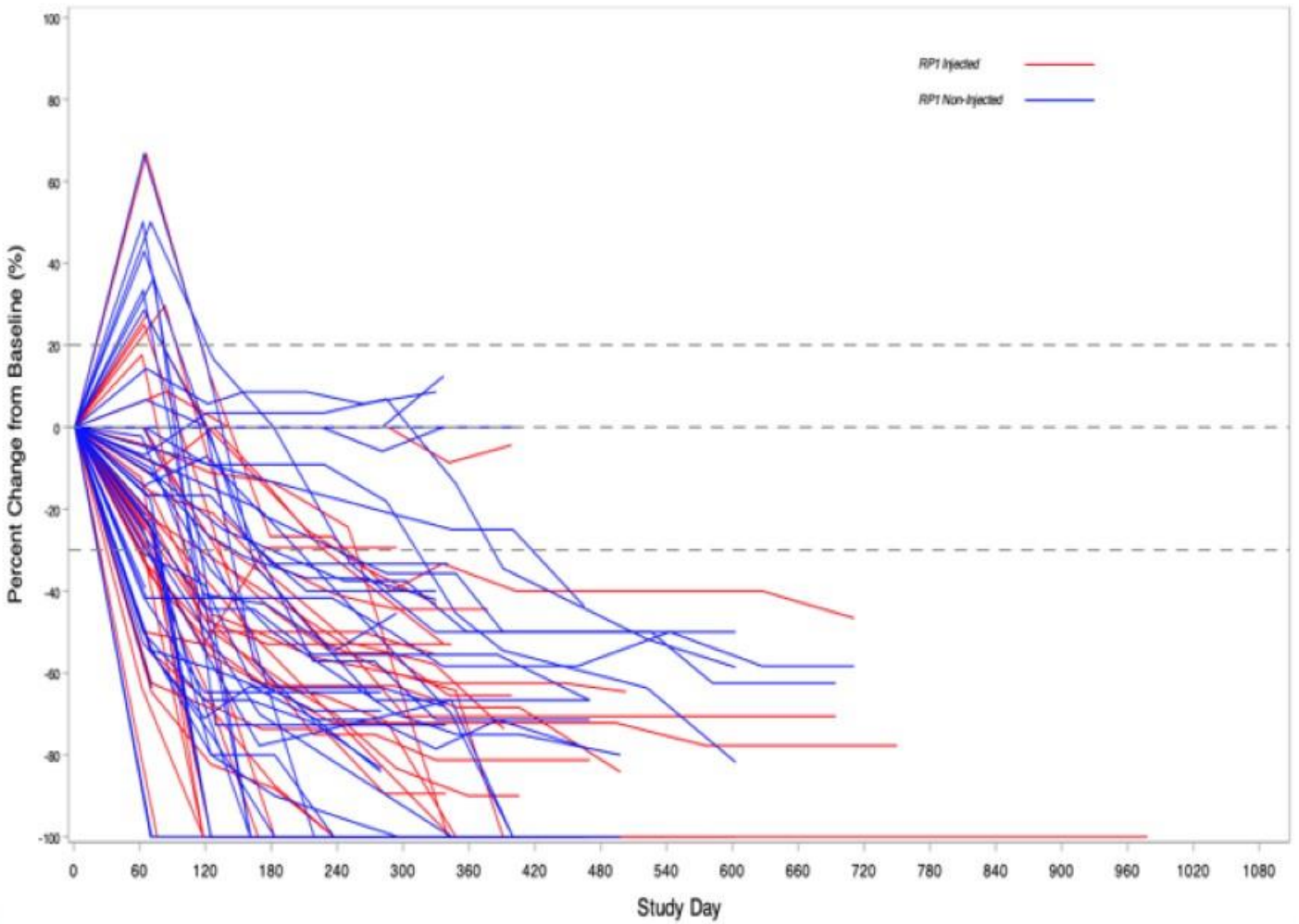

**Key Takeaway**

Responses are generally durable, and often deepen over time

Patients with at least one post baseline assessment – target lesion response for each patient

# IGNYTE kinetics of response (from earlier ASCO data) n=75

## Change in size of individual injected and uninjected lesions

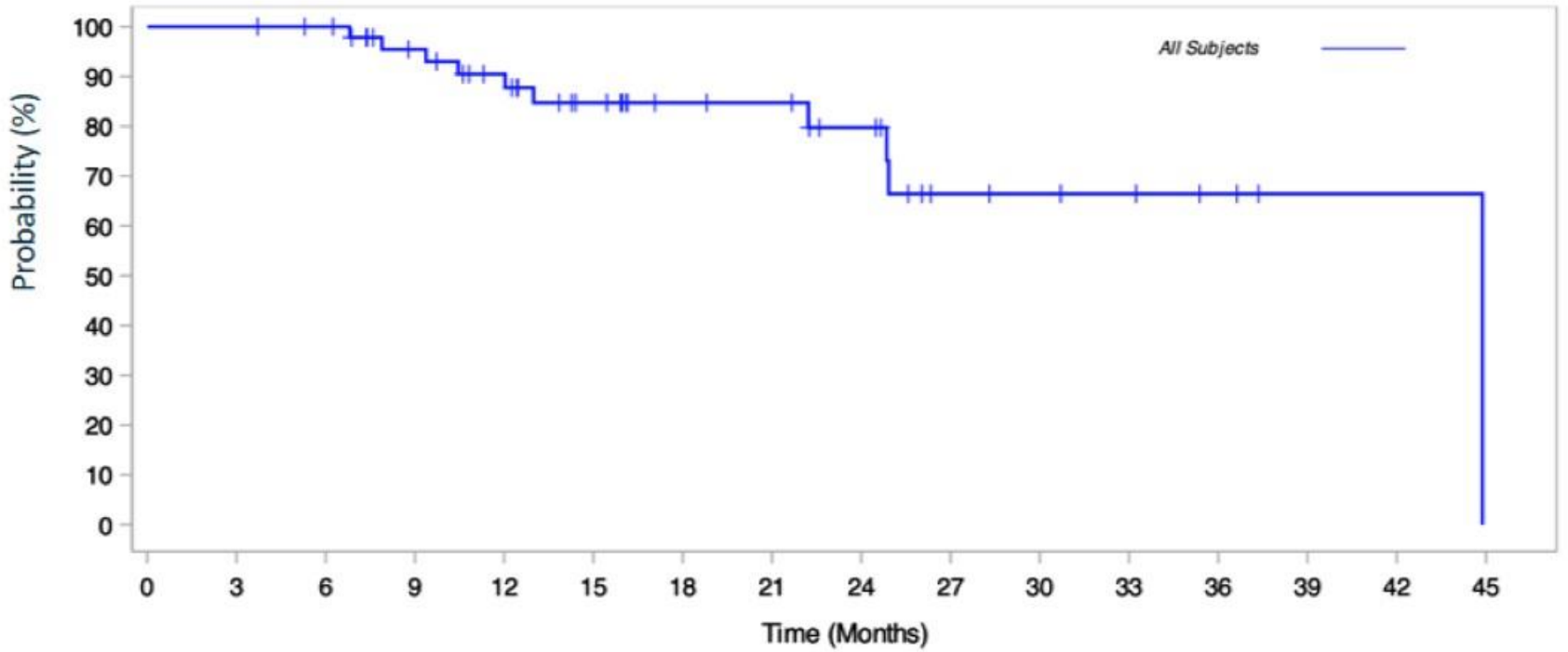



### Key Takeaways

- Systemic effects including in patients with:
  - Visceral lesions, after both deep and superficial injection
  - Bulky lesions
  - Up to >20cm of total tumor burden and up to >10cm of uninjected disease
- 70.4% of responding patients had uninjected lesions
  - Responders include patients with minority of lesions injected
- Large number of uninjected lesions respond supporting systemic benefit
- Injected and uninjected lesions respond with similar durability and kinetics
  - Depth of response independent whether injected

Includes both target and non-target lesions for RECIST assessment, measured from CT/MRI scans for radiologically assessable lesions (n=75 group). 58/75 patients had at ≥ 1 uninjected lesion, of whom 15 achieved a response based on those lesions (excludes possible response in injected lesions); ORR of 25.9% on the basis of uninjected lesions only

# Duration of response
## (time from baseline to end of response for responders)



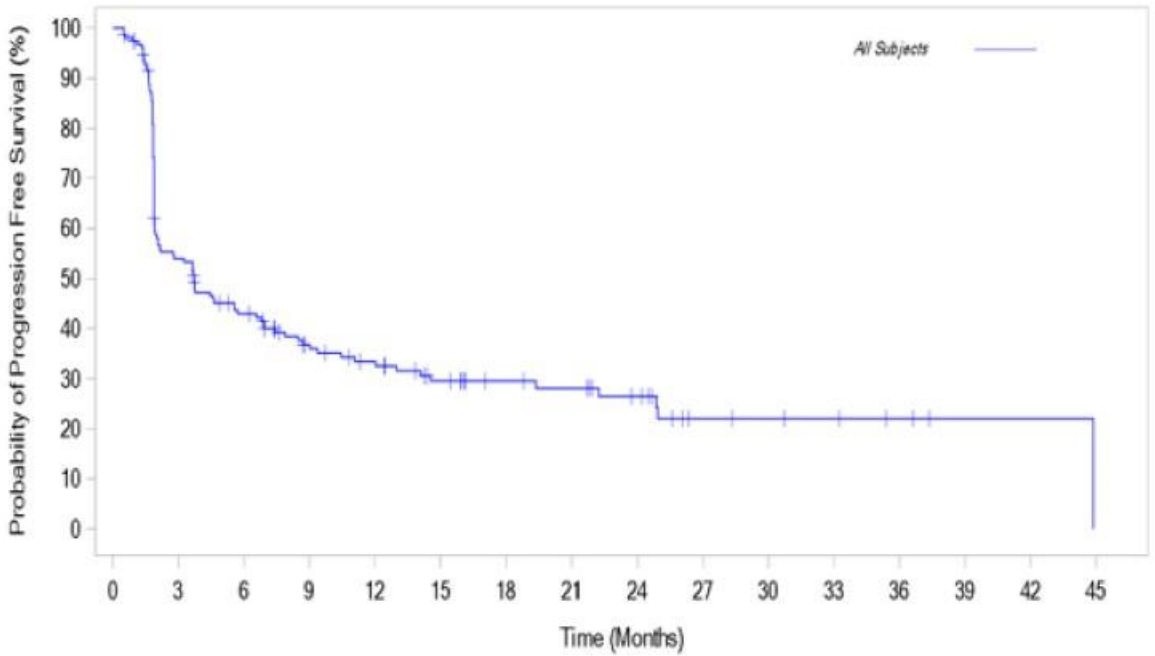

| >6 months | >12 months | >18 months | >24 months |
|---|---|---|---|
| 100% | 90.5% | 84.7% | 79.7% |

**Key Takeaway**

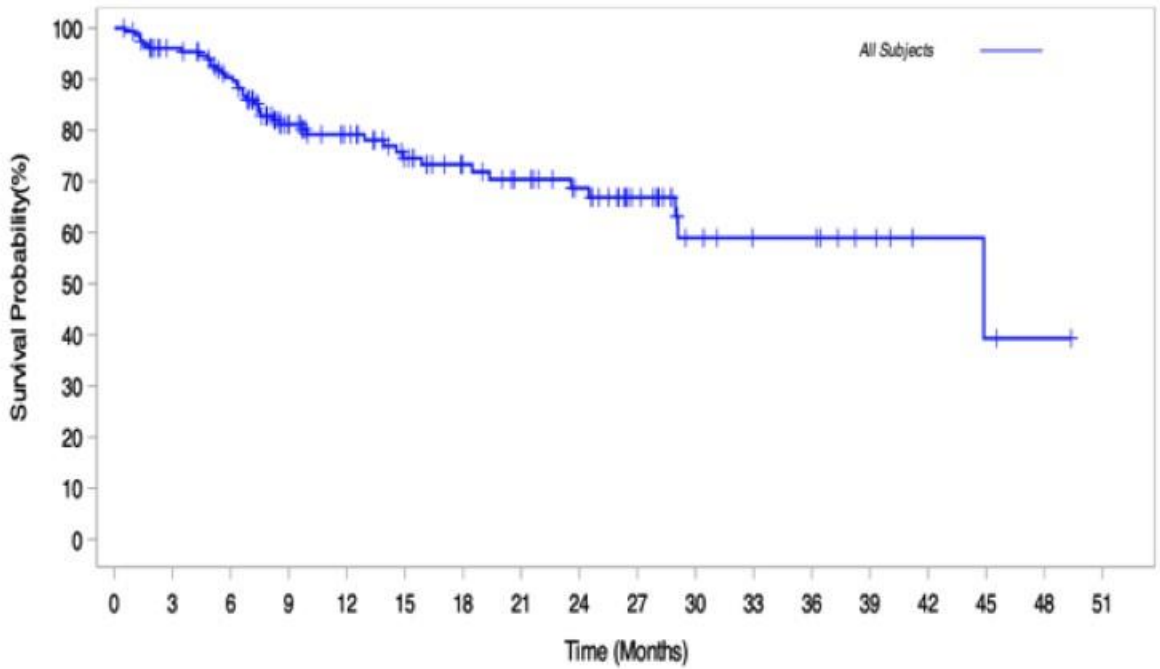
Responses are highly durable, with median DOR >24 months

# PFS and OS – all patients

PFS (all patients)

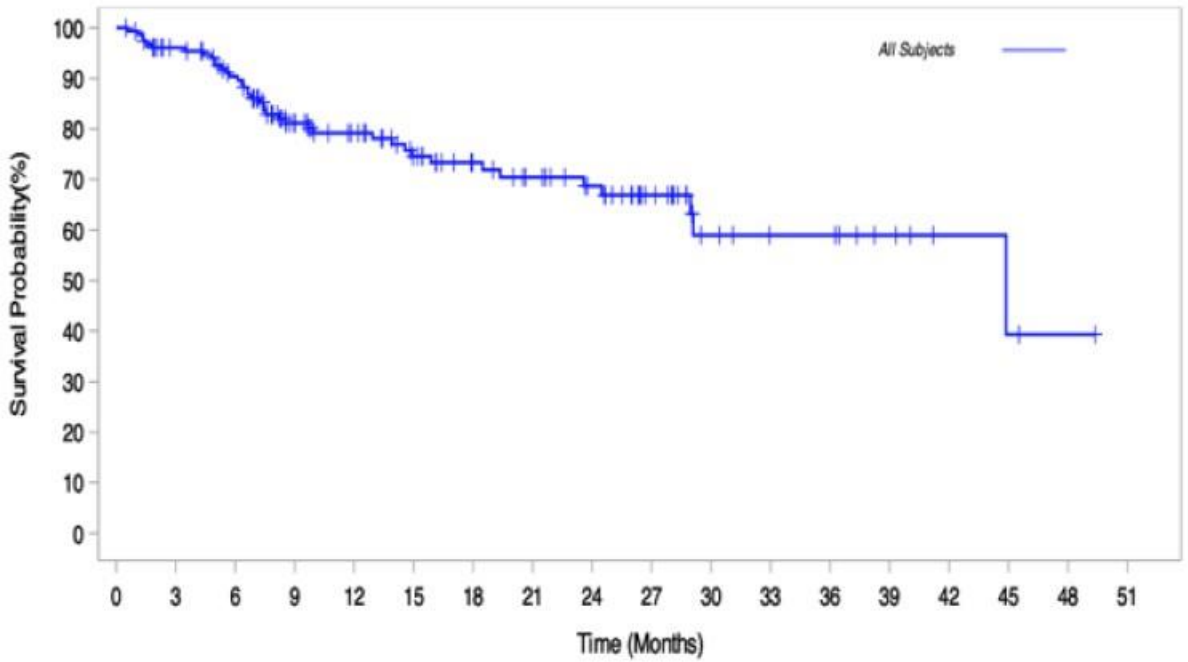



OS (all patients)

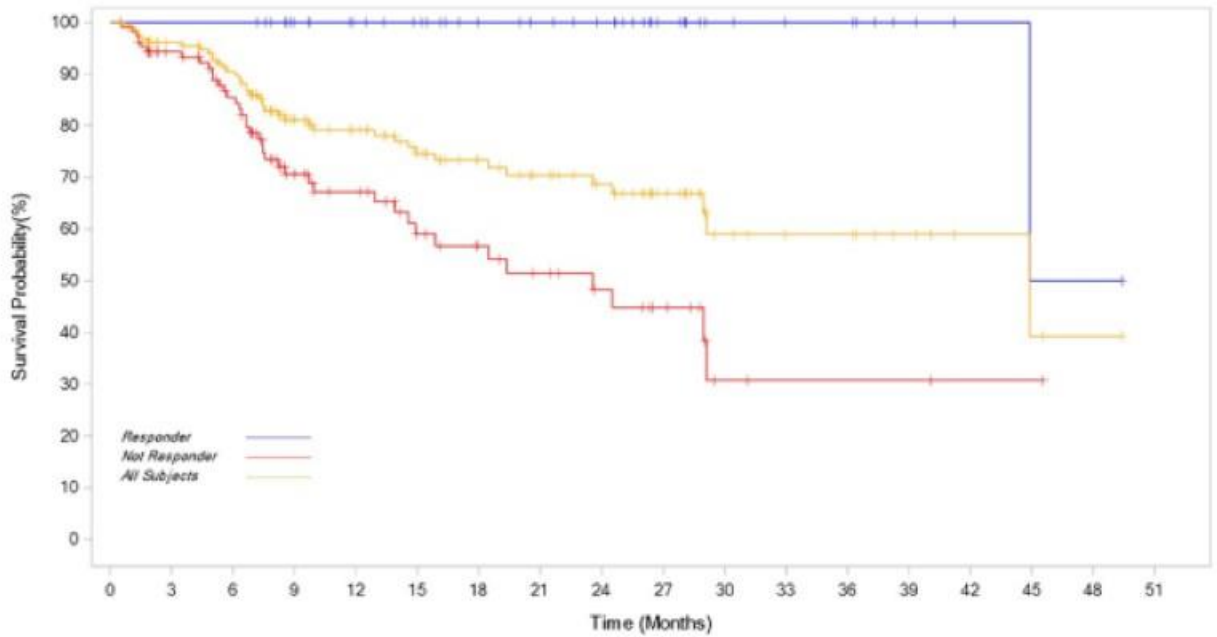


# OS for all patients & responding vs. non-responding patients

OS (all patients)



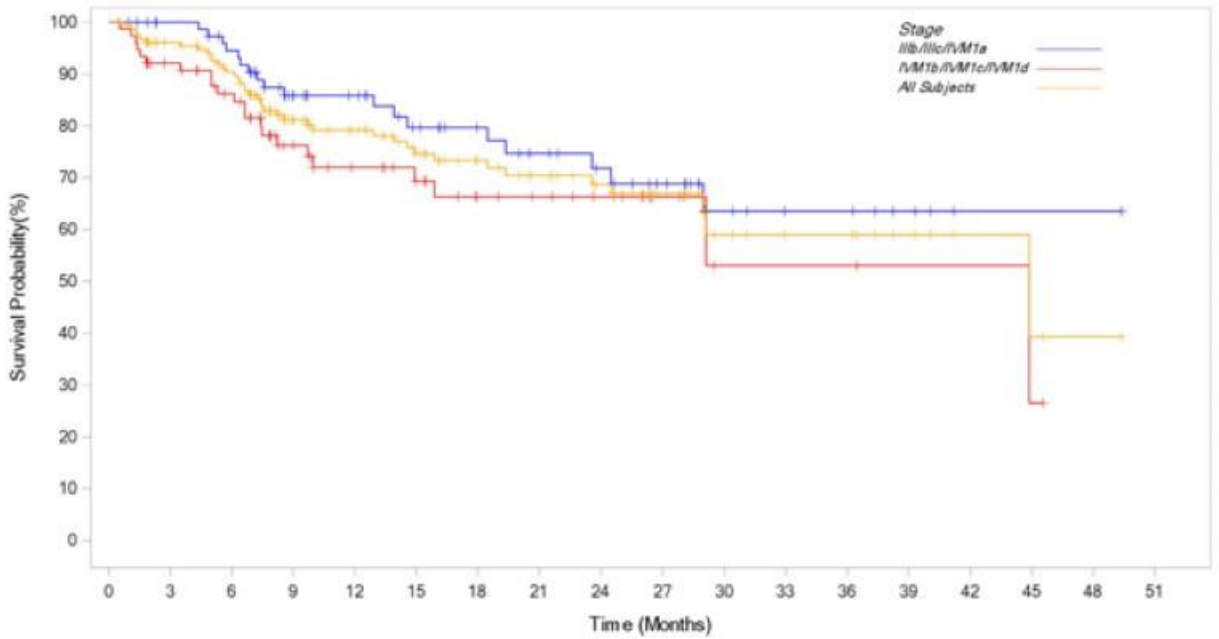

OS (by response type)



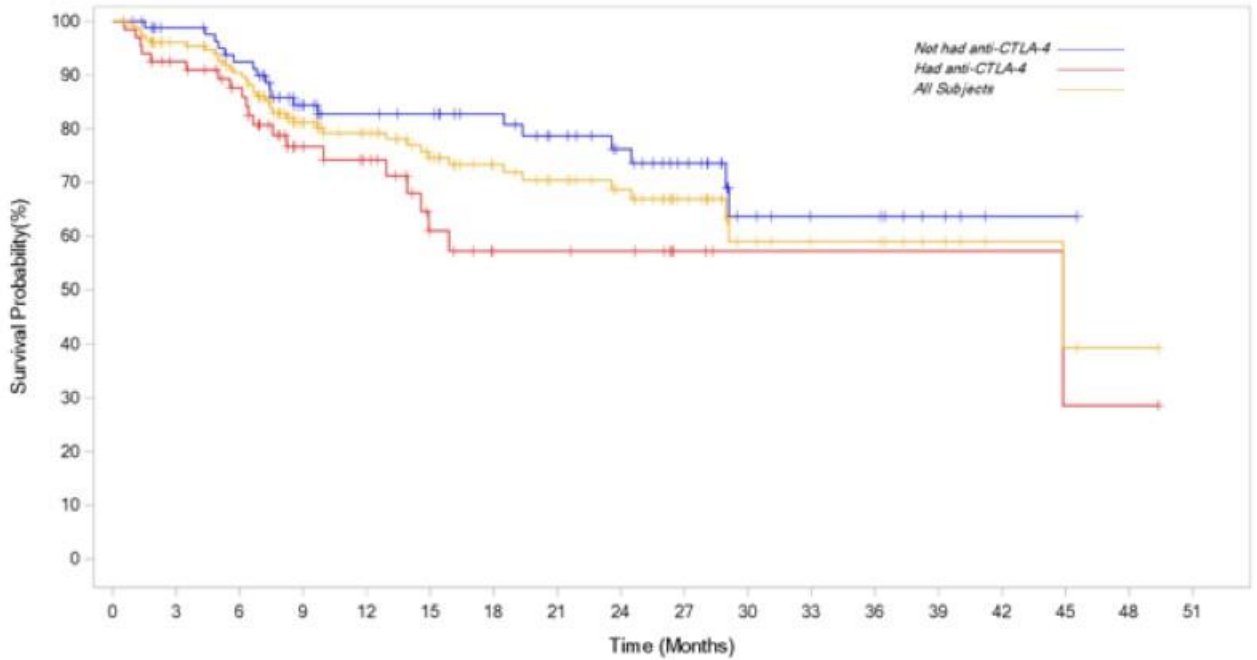
# Promising OS is seen across disease subsets, including those with the greatest unmet need

Replimune

Stage IIIb/IIIc/IVM1a vs Stage IV M1b/c/d




Prior anti-CTLA-4+anti-PD1 vs prior anti-PD1 alone



# IGNYTE summary & conclusions

- RP1 combined with nivolumab **continues to have an attractive safety profile**, with generally 'on target' and transient Grade 1-2 side effects, i.e. indicative of systemic immune activation
- The **snapshot from the full 156 melanoma patient cohort continues to show consistent, meaningful, and durable clinical benefit**
- **1 in 3 patients experienced a response**
    - 26.4% ORR in Ipi+Nivo failed patients (approx. 50% of the overall study population)
    - 100% of responses lasted >6 months, with median DOR >24 months
    - Clinically meaningful activity across all subgroups enrolled
- Approx. 50% of patients experienced clinical benefit (CR+PR+SD)
- **PFS/OS data are promising**
- The primary analysis for the study will be triggered once all patients have had at least 12 months follow up in March 2024
- **RP1 combined with nivolumab provides an attractive risk:benefit profile particularly compared with other therapies which might be considered for these patients**

*All patients have at least 6 months follow up, median follow up is 88.21 weeks.*

SECTION I

RP1: Exec Summary and Overview

SECTION II

RP1: 1L CSCC (CERPASS)

SECTION III

RP1: IGNYTE and ARTACUS Skin Cancer Data and Anti-PD1 Failed Melanoma

SECTION IV

**RP1: Regulatory Update/Summary & Next Steps**

SECTION V

Panel Q&A

# AGENDA

# Regulatory summary/next steps

CERPASS/IGNYTE

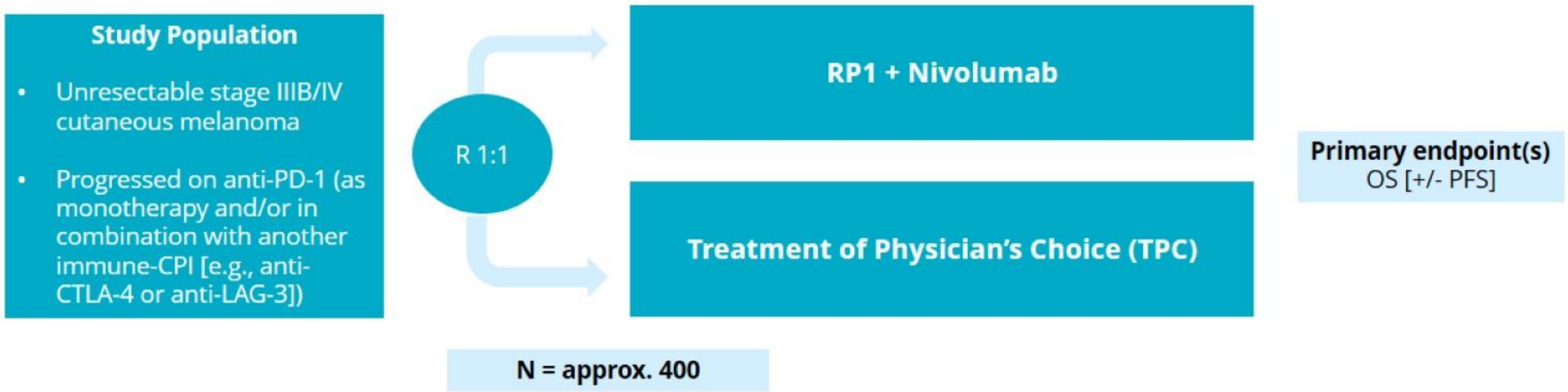
**CERPASS**

- Replimune plans to share the CERPASS data with the FDA & provide updates with more mature data as it becomes available
- The more matured data will determine next steps & the potential pathway forward in CSCC

**IGNYTE FDA Type C meeting on anti-PD1 failed melanoma**

- The FDA acknowledged that the IGNYTE population is one of unmet need
- The FDA agreed with a 2-arm randomized trial design in anti-PD1 failed melanoma with physician's choice as a comparator arm in the study population (full protocol development underway) as the confirmatory study to support potential accelerated approval in anti-PD1 failed melanoma
  - The study should be underway at time of BLA submission
- A BLA submission for anti-PD1 failed melanoma is planned for 2H 2024 to include:
  - Centrally reviewed data by RECIST v 1.1
  - All patients followed for at least 12 months (which is the per protocol primary analysis timepoint)
  - All responding patients followed for at least 6 months from response initiation

# Confirmatory study design concept in anti-PD1 failed melanoma agreed with FDA*




*Full protocol development is underway

# RP1 Summary and Next Steps

# Next steps

Replimune

## *RP1 in Skin Cancer*

- While CERPASSS missed its primary endpoints, a clinically meaningful benefit in CRR and DOR in CSCC was demonstrated
- Other skin cancer data including in hard-to-treat settings such as solid organ transplant and anti-PD1 failed melanoma & NMSC demonstrate compelling efficacy with an attractive safety profile
- The initial snapshot of data from all 156 anti-PD1 failed melanoma patients demonstrate that RP1+nivolumab maintains transformative potential in this high unmet need setting with limited treatment options
    - Assuming supported by positive IGNYTE primary analysis data, a BLA filing planned for 2H 2024

## *RP2 and RP3 mid-stage pipeline*

- Strong data with RP2 in uveal melanoma (plenary presentation at SMR Nov 2023)
    - Planning for a randomized controlled study in 2L uveal melanoma underway
    - Plan to investigate other rare cancer opportunities for rare disease indications
- RP3 development and phase 2 program discontinued
    - RP2 to replace RP3 in 2L HCC
    - H&N & CRC studies discontinued

## *Strong cash position to execute on our vision*

- Cash & investments of $496.8M as of 30 September 2023
- Cash Runway extended into early 2026

SECTION I

## RP1: Exec Summary and Overview

SECTION II

## RP1: 1L CSCC (CERPASS)

SECZTION III

## RP1: IGNYTE and ARTACUS Skin Cancer Data and Anti-PD1 Failed Melanoma

SECTION IV

## RP1 Regulatory Update/Overall Summary

SECTION V

## Panel Q&A

# AGENDA

# THANK YOU

## MISSION

To enable tumor directed oncolytic immunotherapy (TDOI) to become a cornerstone in the treatment of cancer

## VISION

To deliver **transformational** results for patients **across cancers** using tumor directed oncolytic immunotherapy to induce a powerful and durable systemic anti-tumor immune response resulting in **quality survival** and a **chance for a cure**

Replimune®

APPENDIX

# Additional Data Including Patient Examples

AGENDA

# All cemiplimab patients with externally visible disease & overall CR

***Cemiplimab patients with CR generally had a low-modest burden of external disease***

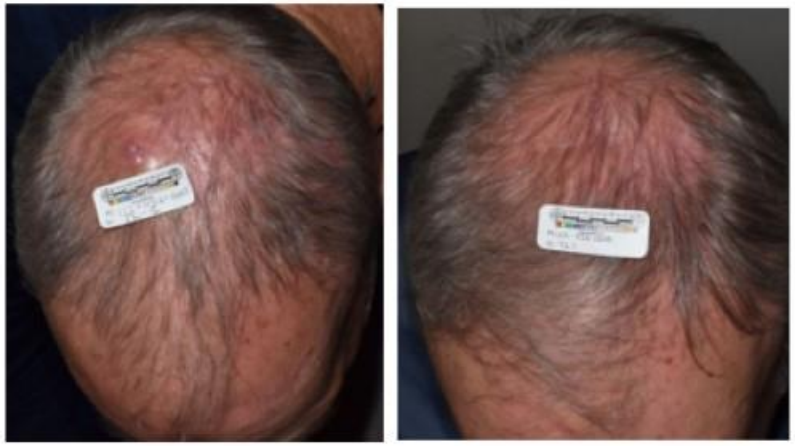
***(Patients with PR are shown in the Appendix)***

*External disease only shown – patients may have also had non-visible disease*
*Time on study is approximate*

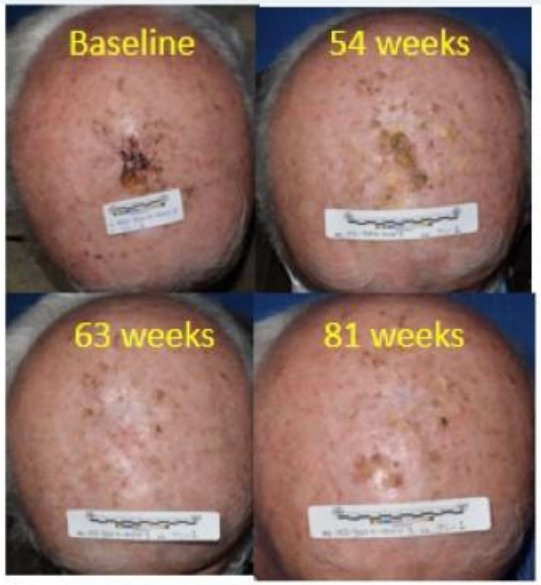
# All cemiplimab patients with CR & externally visible disease

Replimune

Baseline 75 weeks

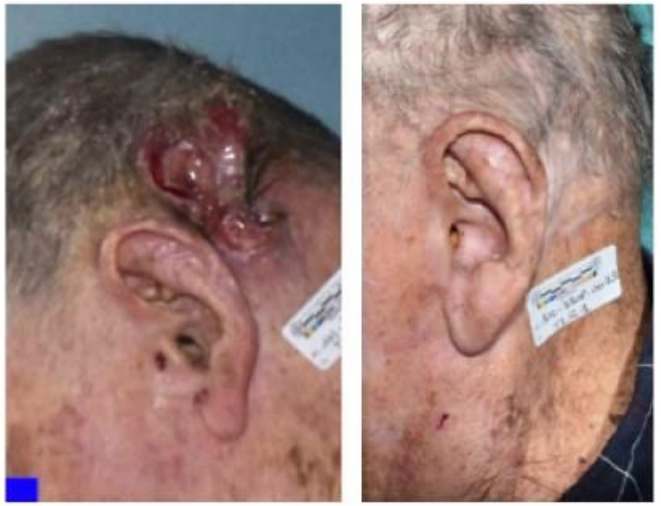


1126-0003



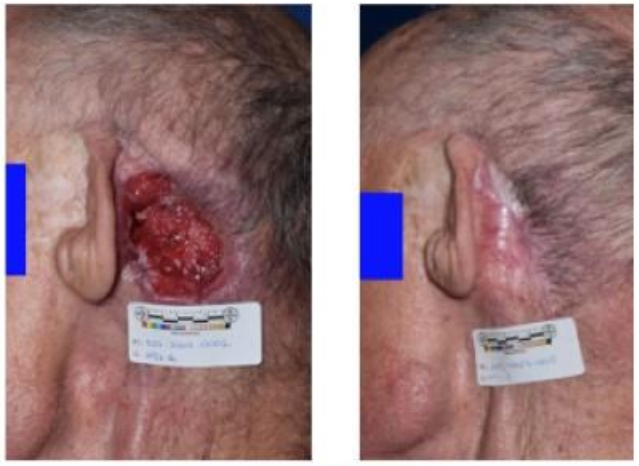

3004-0003

Baseline 68 weeks



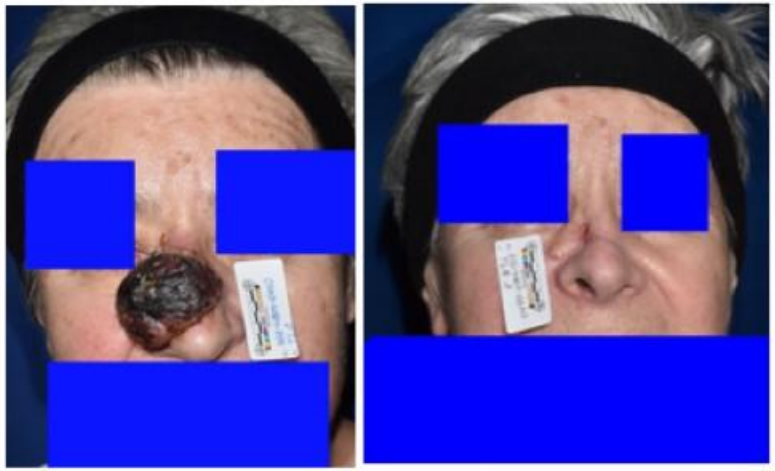
3308-0013

Baseline 45 weeks



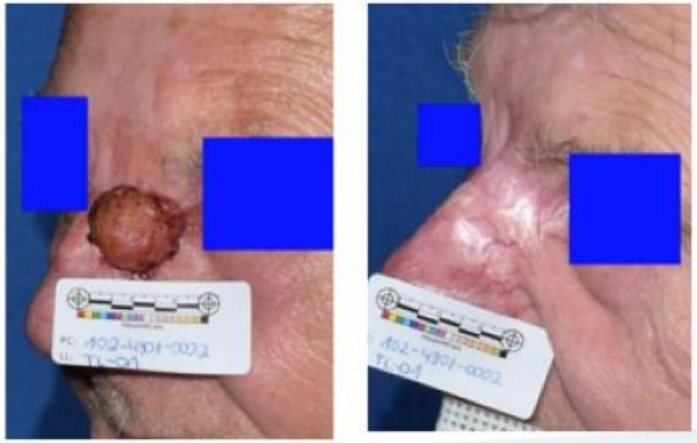
3407-0002

Baseline 54 weeks



4801-0010

Baseline 27 weeks

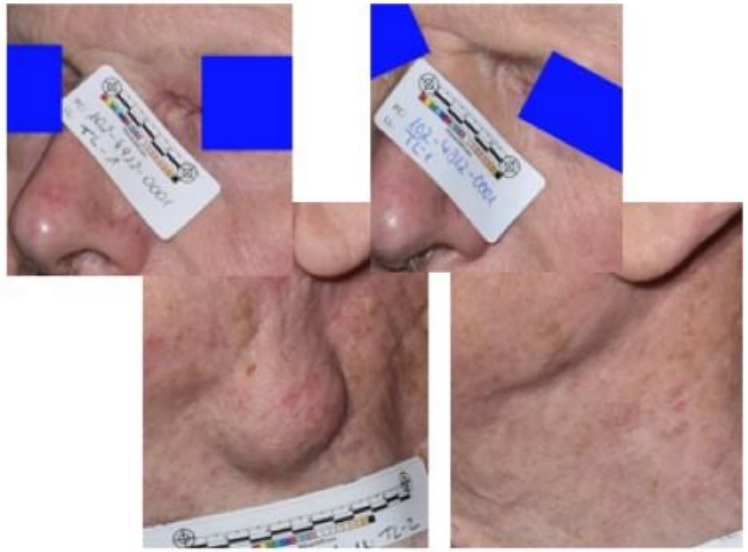


4901-0002

# All cemiplimab patients with CR & externally visible disease

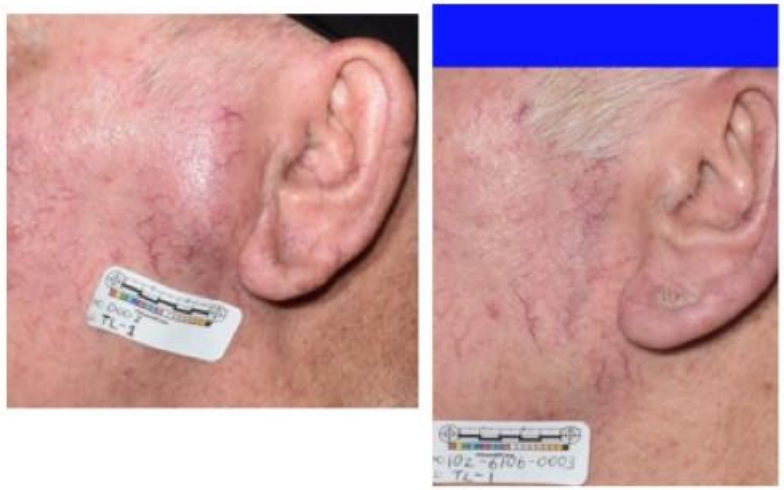
Replimune

Baseline 42 weeks



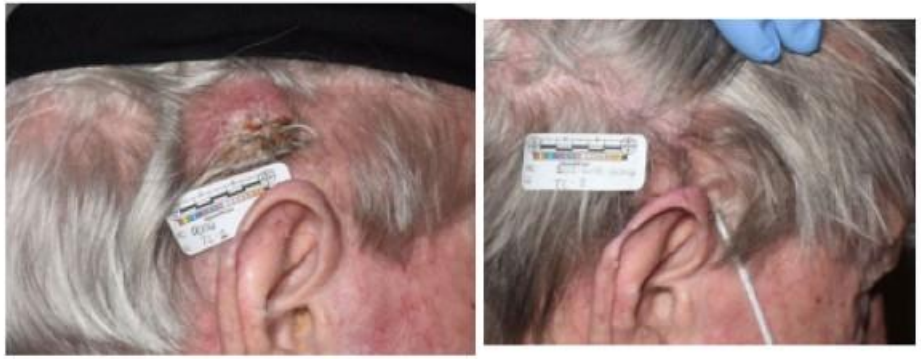
4912-0001

Baseline 108 weeks



6106-0003

Baseline 27 weeks



6106-0004

# All RP1+cemiplimab patients with externally visible disease & overall CR

***RP1+emiplimab patients with CR generally had higher burden/more 'nasty' disease than cemiplimab patients with an overall CR***

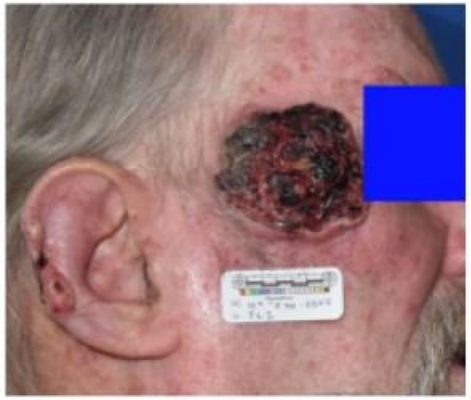
***(Patients with PR are shown in the Appendix)***

*External disease only shown – patients may have also had non-visible disease*
*Time on study is approximate*

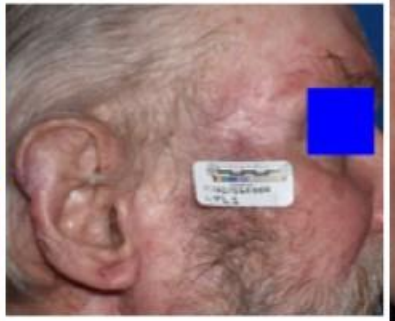
# All RP1+cemiplimab patients with CR & externally visible disease

Replimune

Baseline

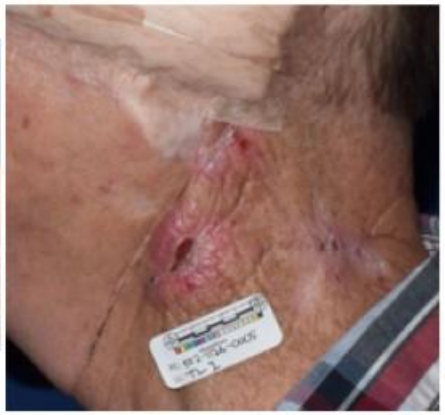


72 weeks

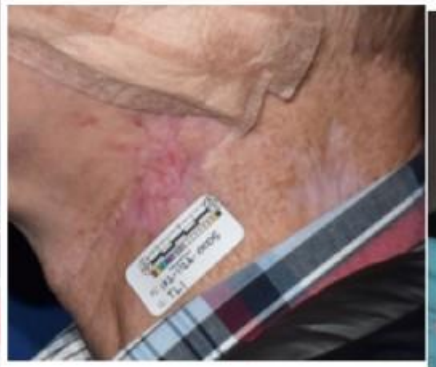


1126-0004

Baseline

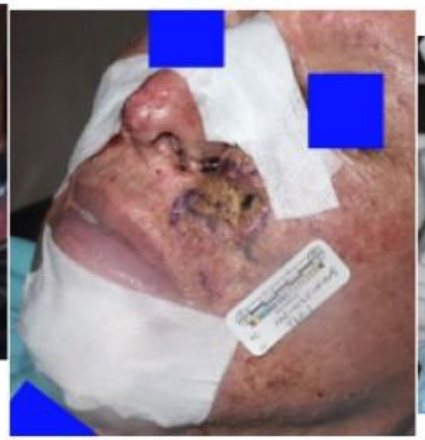


62 weeks

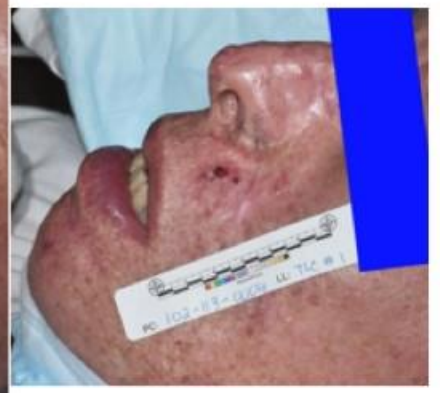


1126-0005

Baseline

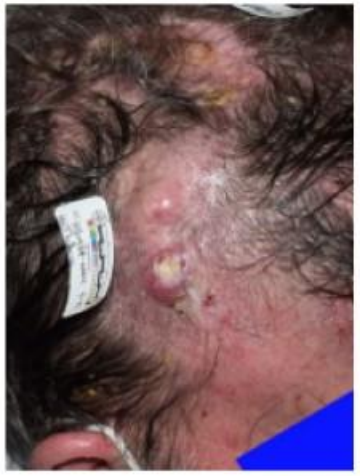


53 weeks

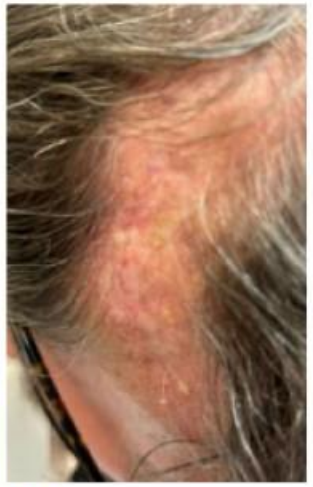


1135-0009

Baseline

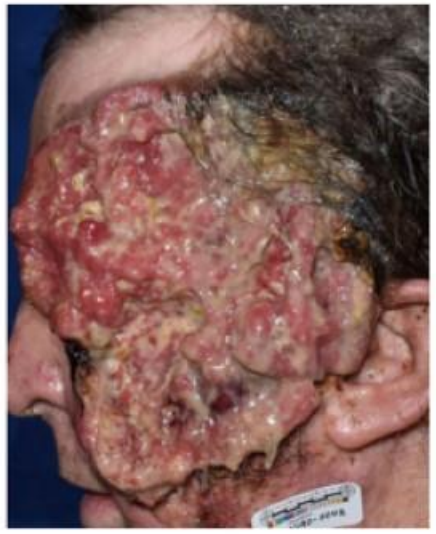


39 weeks

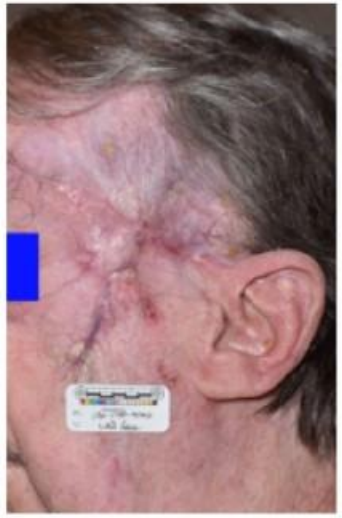


1139-0004

Baseline

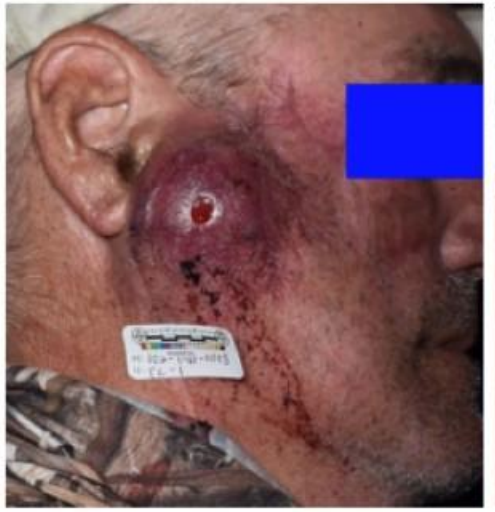


81 weeks

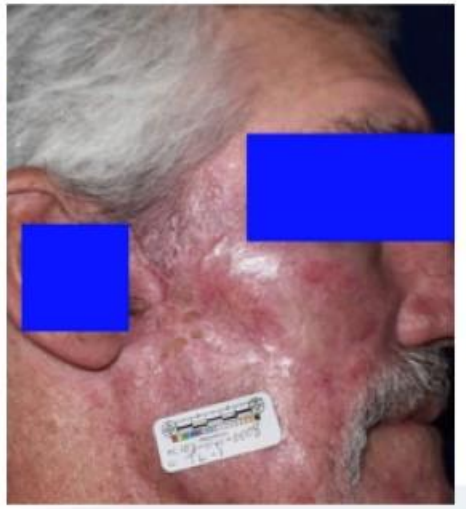


1140-0002

Baseline



45 weeks

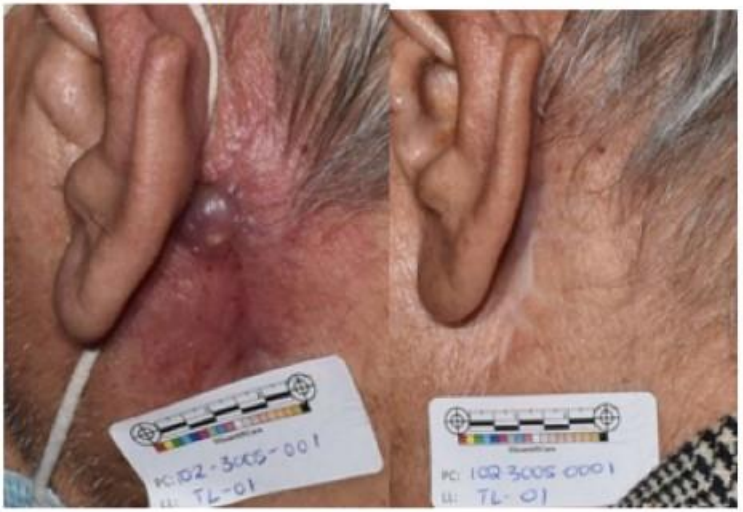


1141-0008

# All RP1+cemiplimab patients with CR & externally visible disease

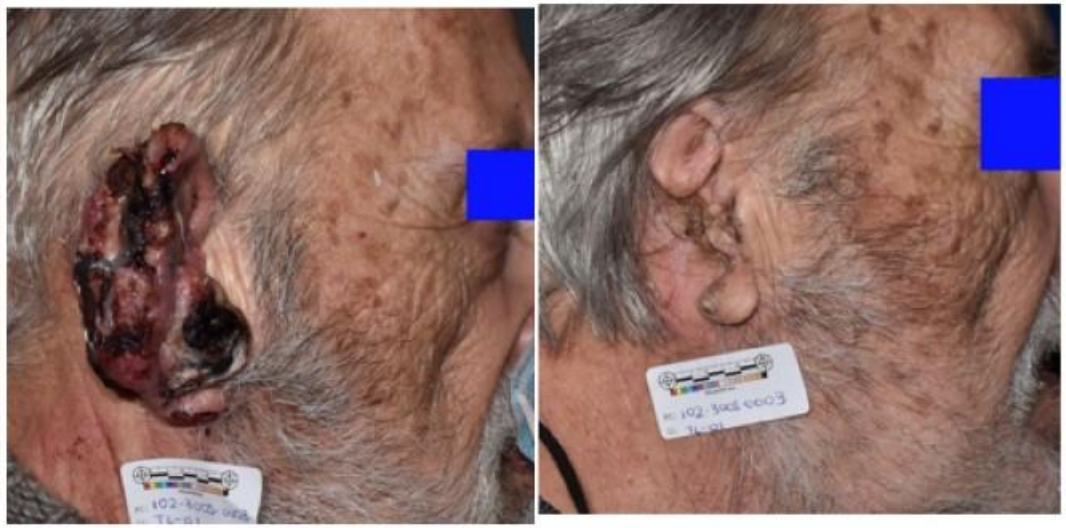
Replimune

Baseline 90 weeks



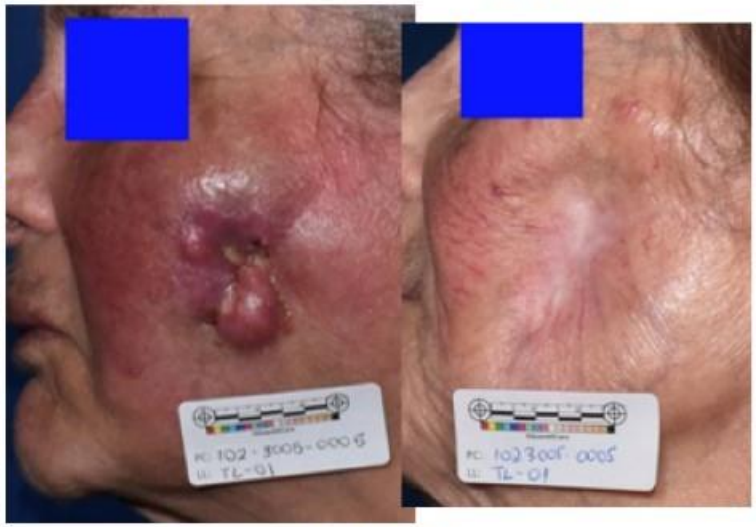
3005-0001

Baseline 54 weeks



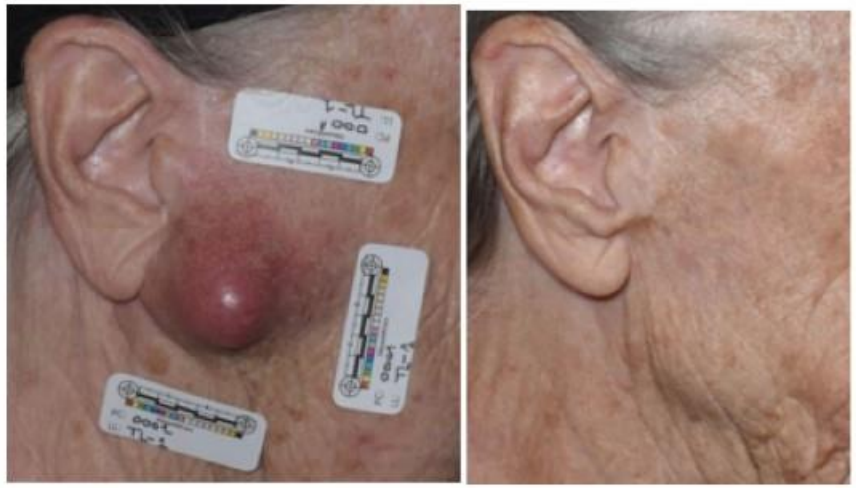
3005-0003

Baseline 72 weeks



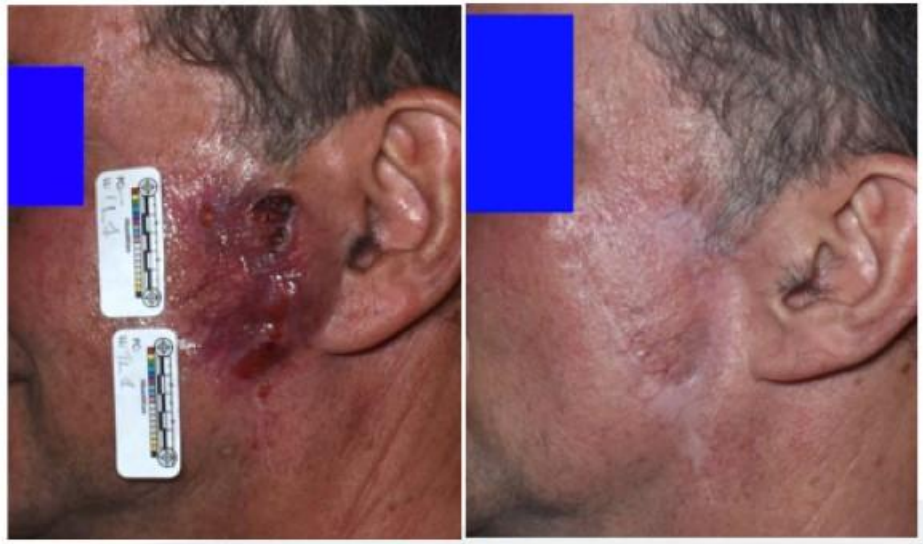
3005-0005

Baseline 105 weeks



3301-0001

Baseline 54 weeks

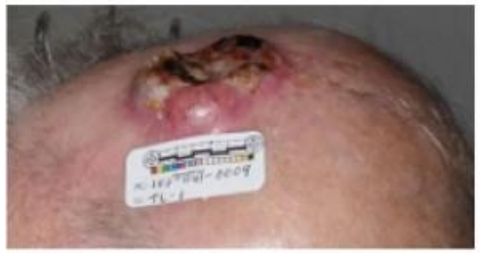


3301-0012

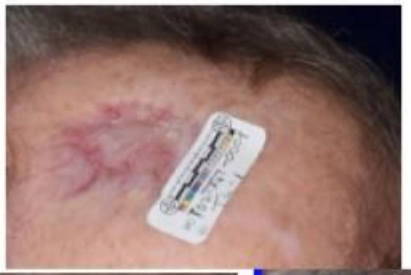
# All RP1+cemiplimab patients with CR & externally visible disease

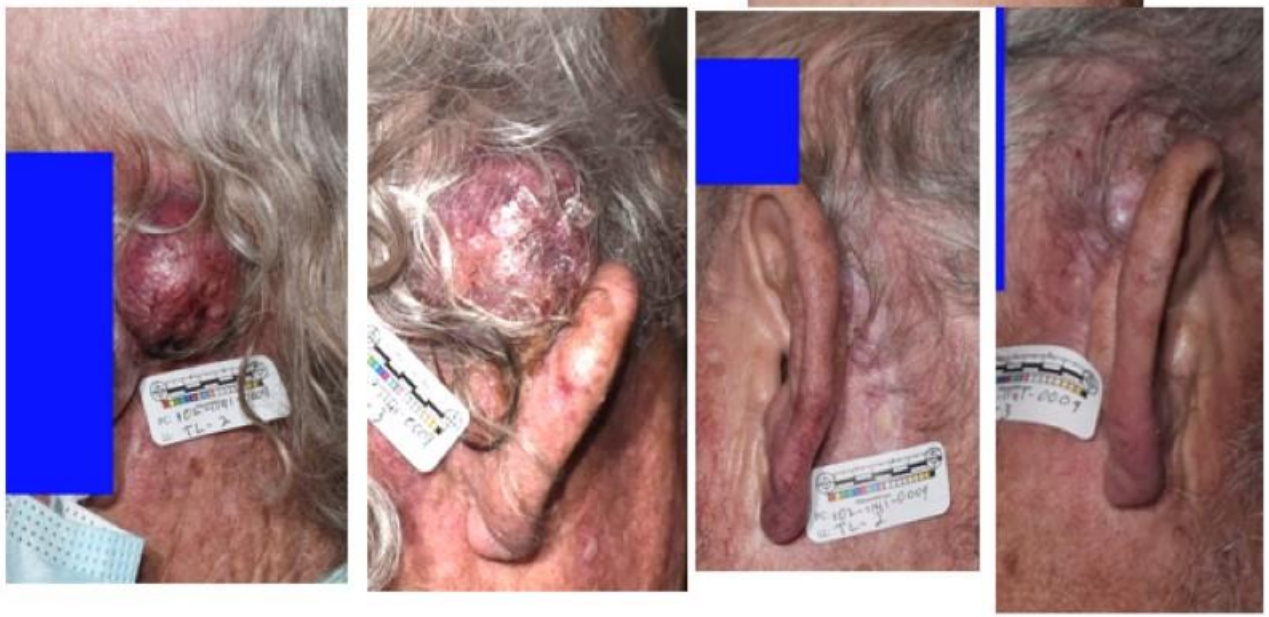
Replimune

Baseline



54 weeks

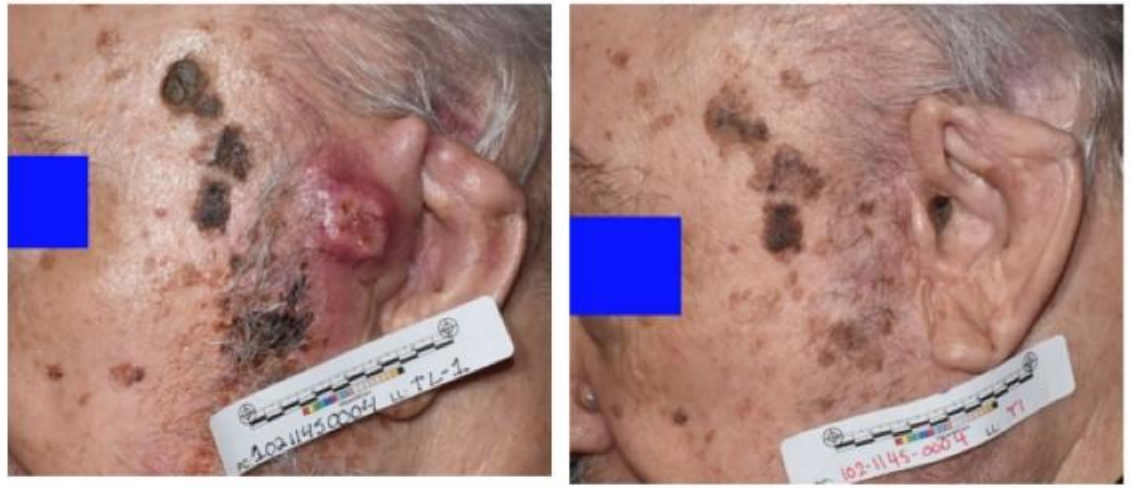




1141-0009

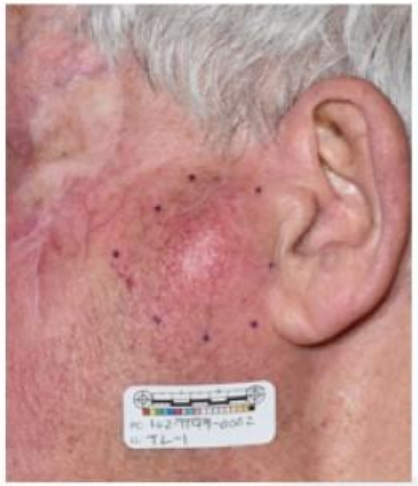
Baseline

50 weeks

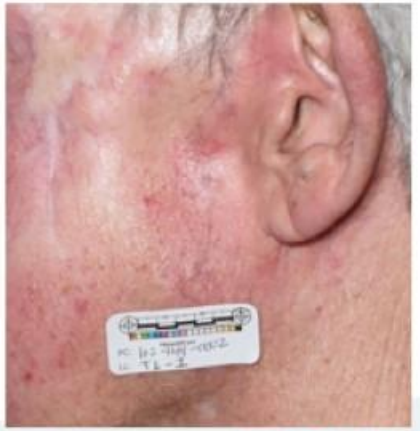


1145-0004

Baseline



120 weeks

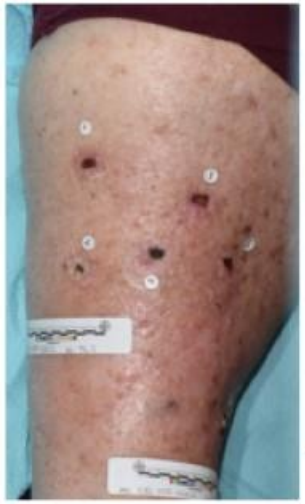


1149-0002

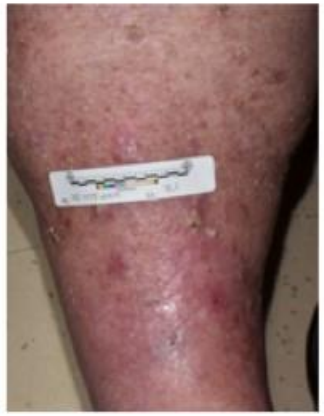
# All RP1+cemiplimab patients with CR & externally visible disease

Replimune

Baseline

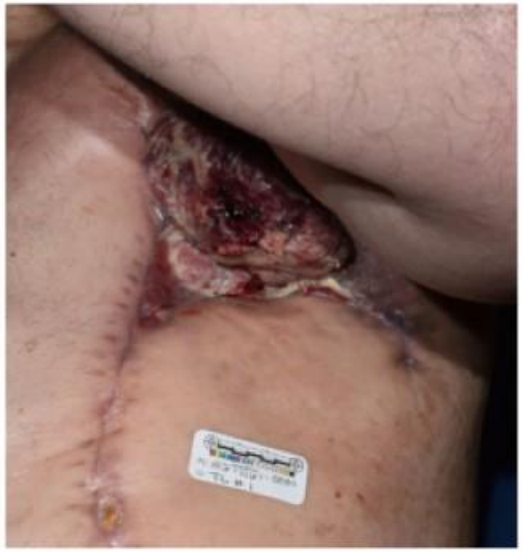


75 weeks

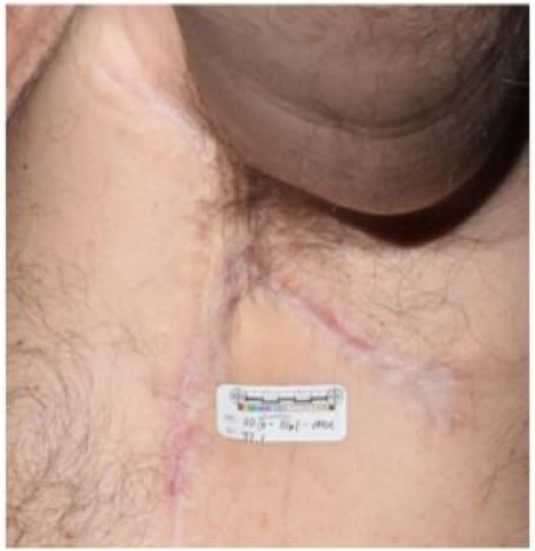


1159-0002

Baseline

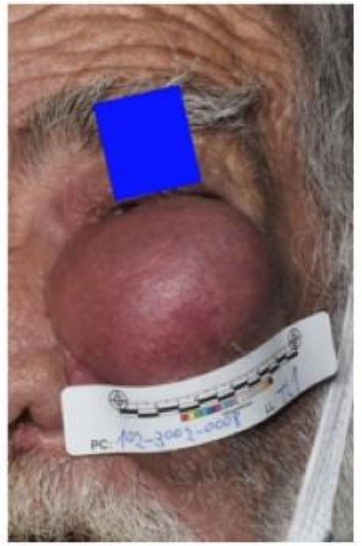


56 weeks

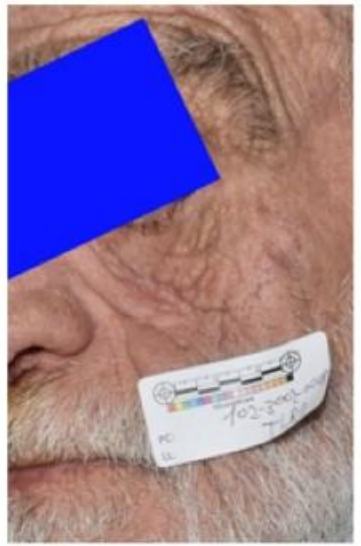


1161-0001

Baseline

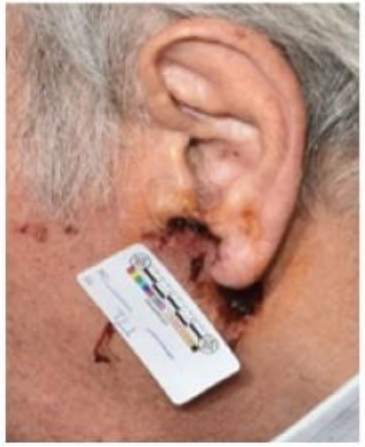


63 weeks



3002-0008

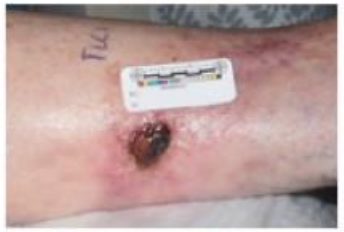
Baseline



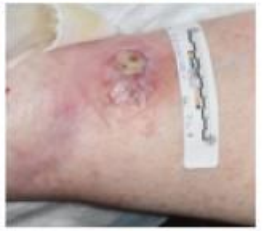
57 weeks

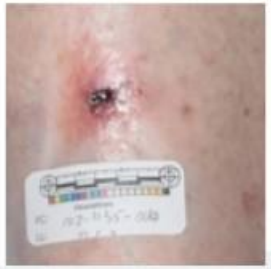
3001-0002

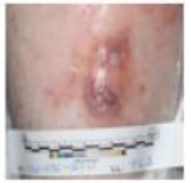
Baseline



54 weeks

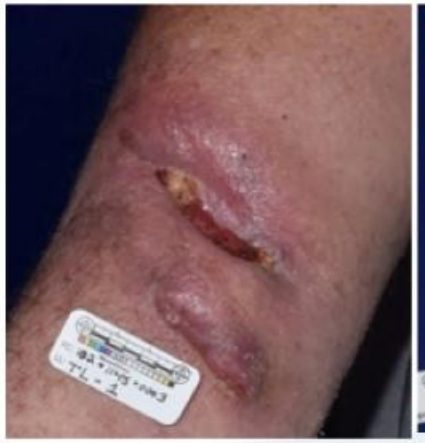




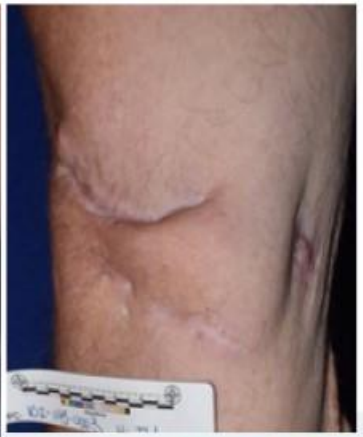


1135-0010 (all lesions tumor free by biopsy)

Baseline



54 weeks

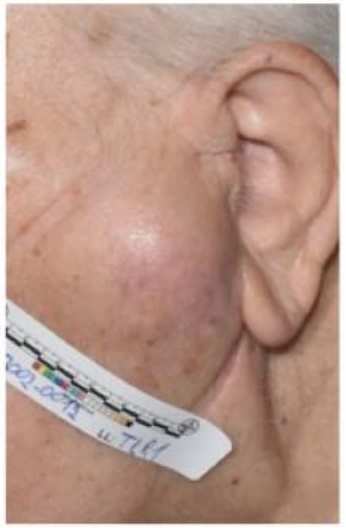


1145-0003

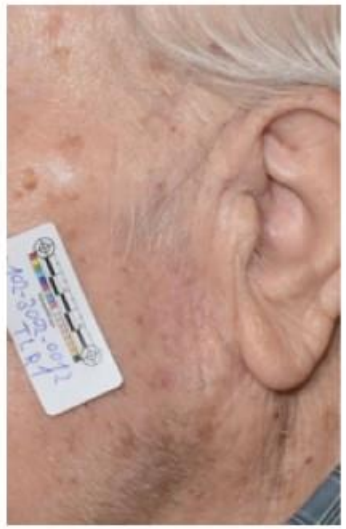
# All RP1+cemiplimab patients with CR & externally visible disease

Replimune

Baseline

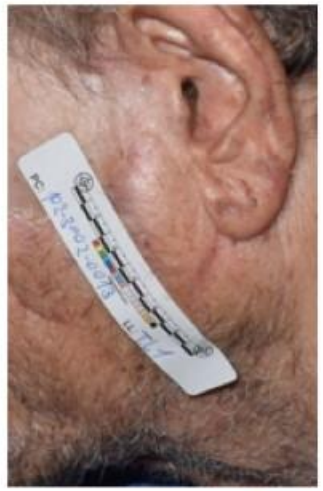


54 weeks

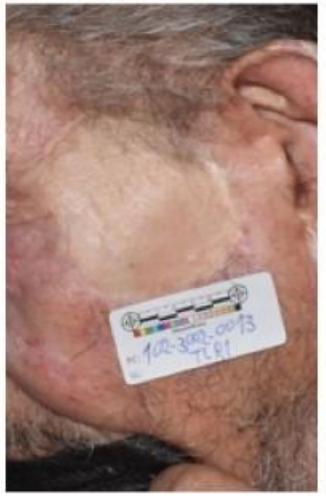


3002-0012

Baseline

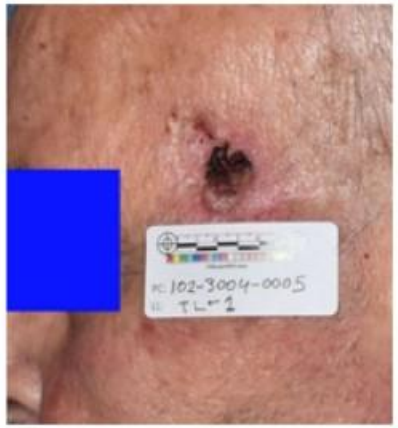


45 weeks

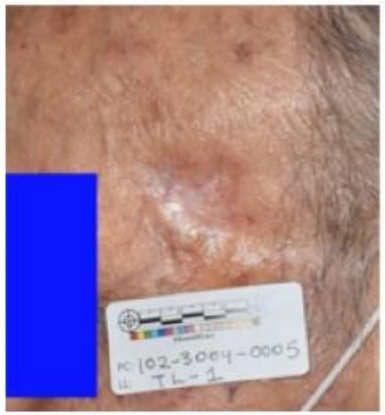


3002-0013

Baseline

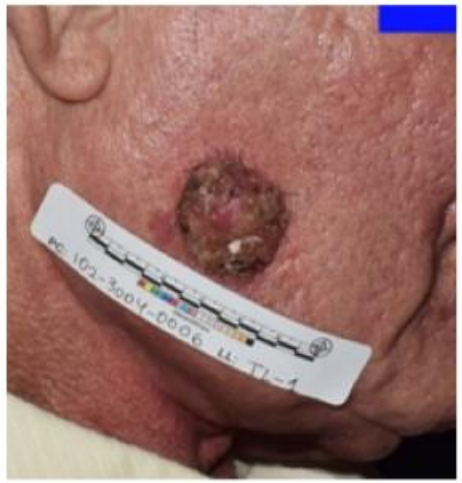


54 weeks



3004-0005

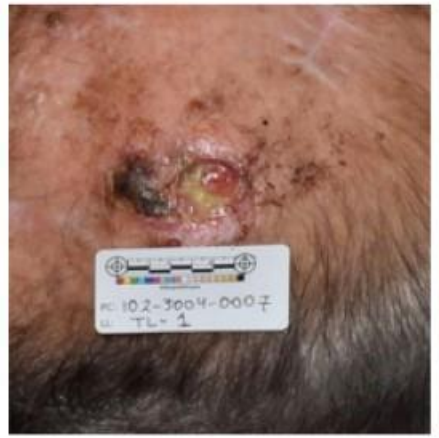
Baseline



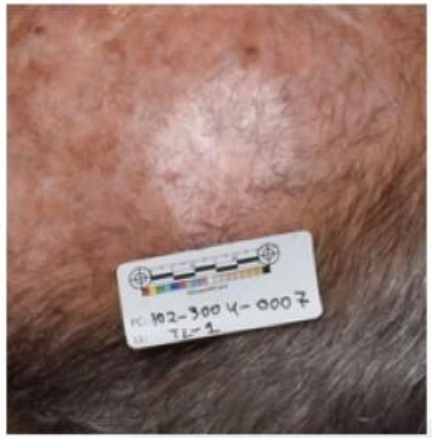
9 weeks

3004-0006

Baseline



63 weeks

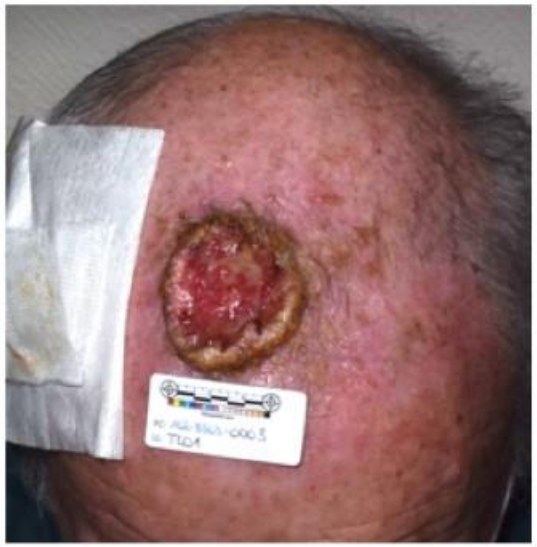


3004-0007

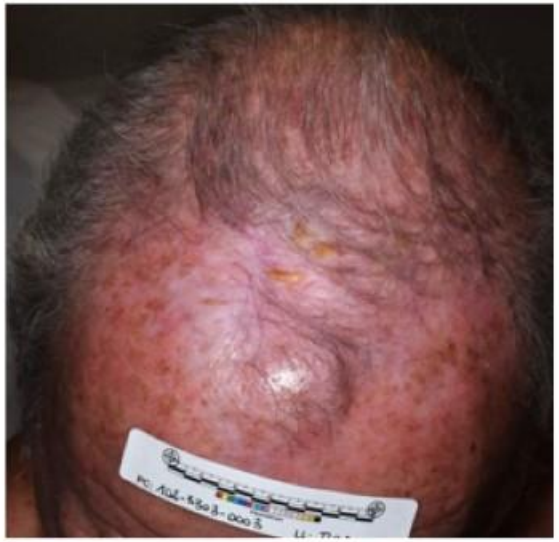
# All RP1+cemiplimab patients with CR & externally visible disease

Replimune

Baseline

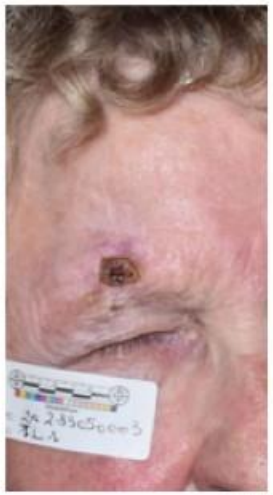


104 weeks

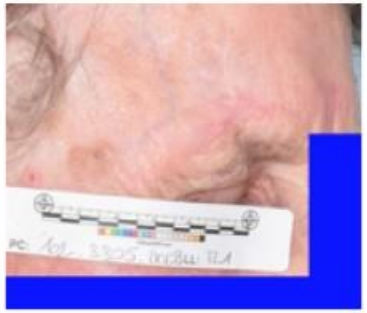


3303-0003

Baseline

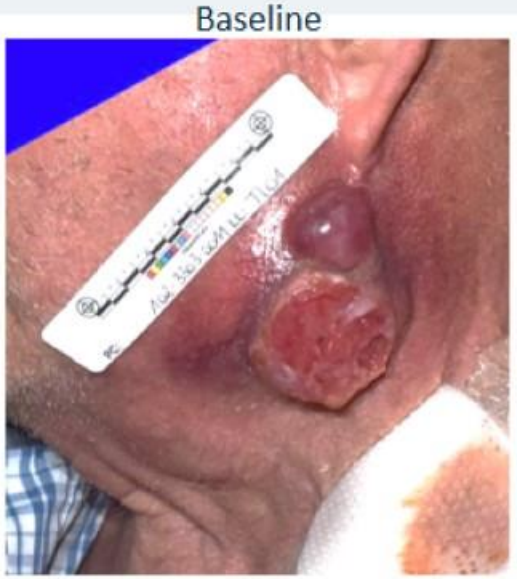


85 weeks

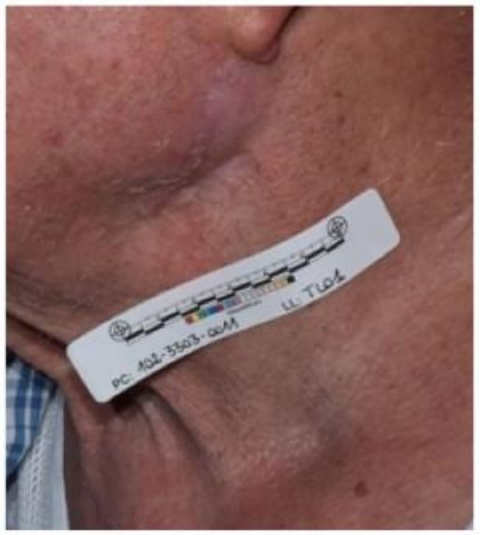


3305-0003

Baseline

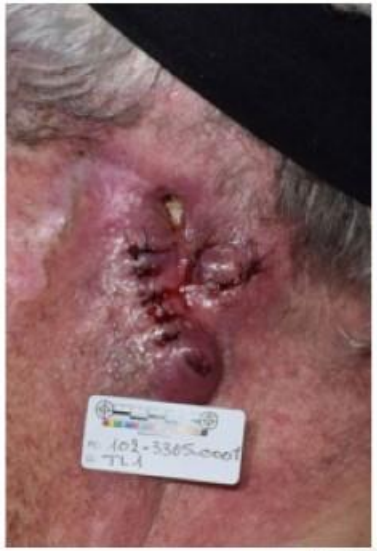


54 weeks

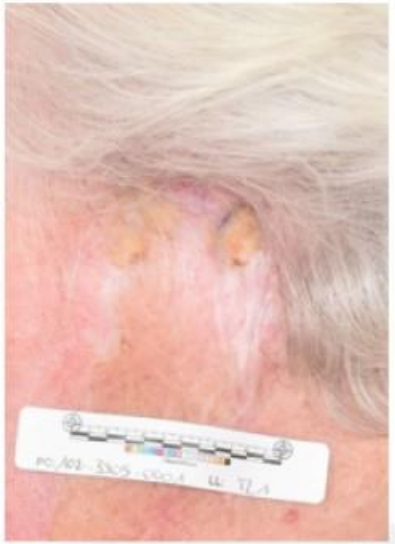


3303-0011

Baseline

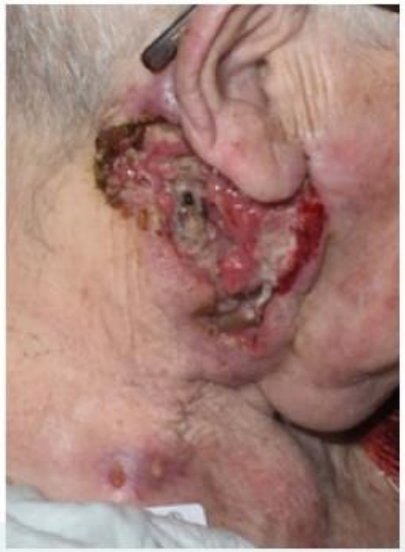


114 weeks

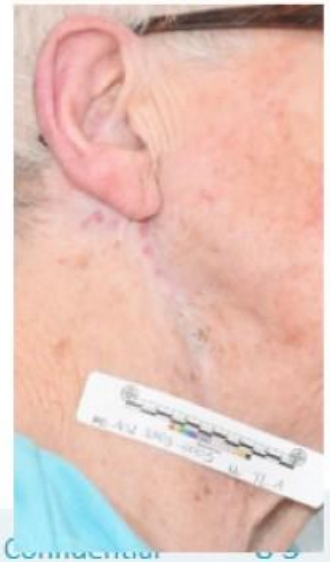


3305-0001

Baseline



54 weeks

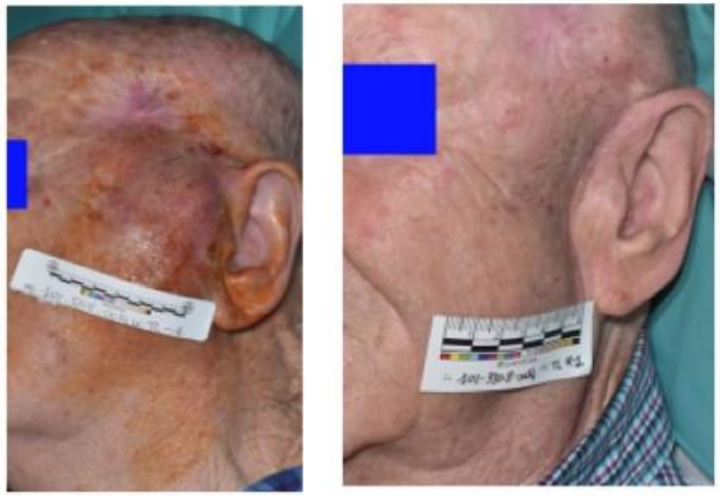


3305-0009

# All RP1+cemiplimab patients with CR & externally visible disease

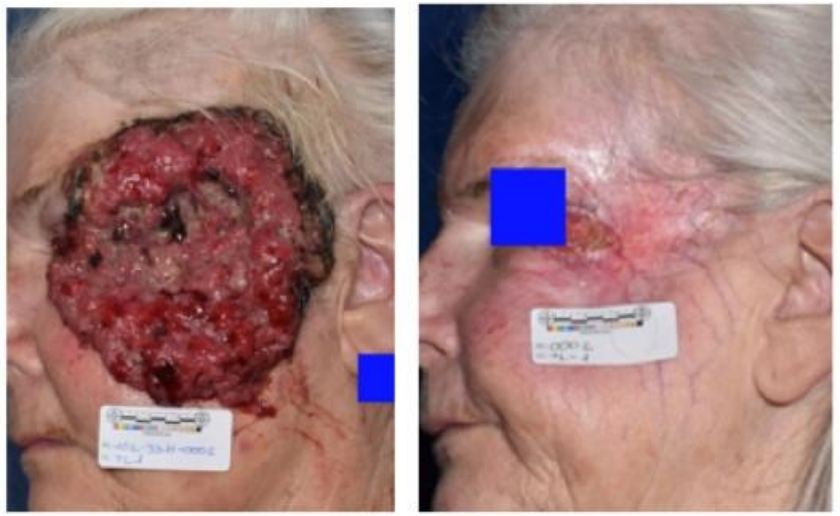
Replimune

Baseline 72 weeks



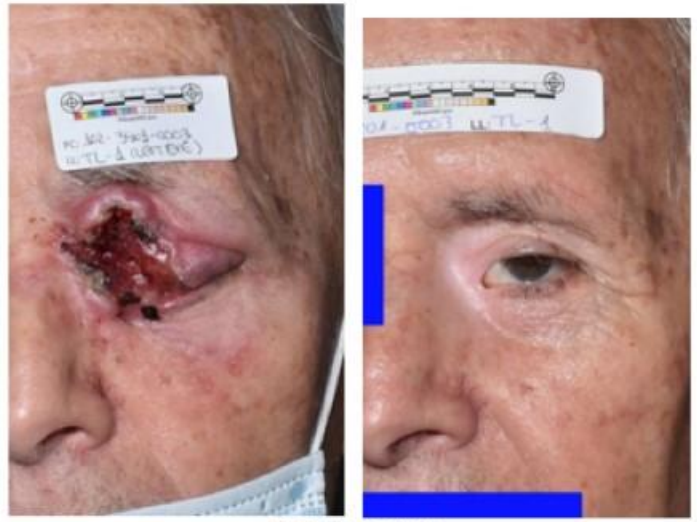
3308-0014

Baseline 63 weeks



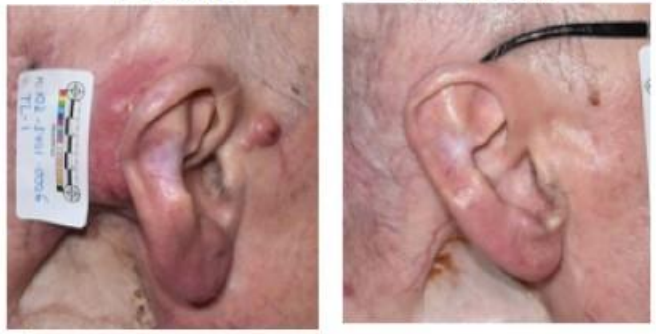
3311-0002

Baseline 82 weeks



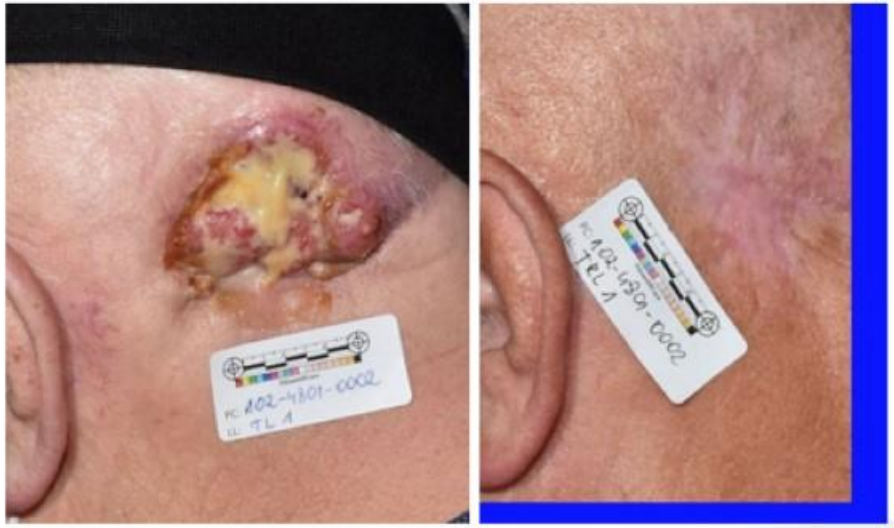
3401-0003

Baseline 63 weeks



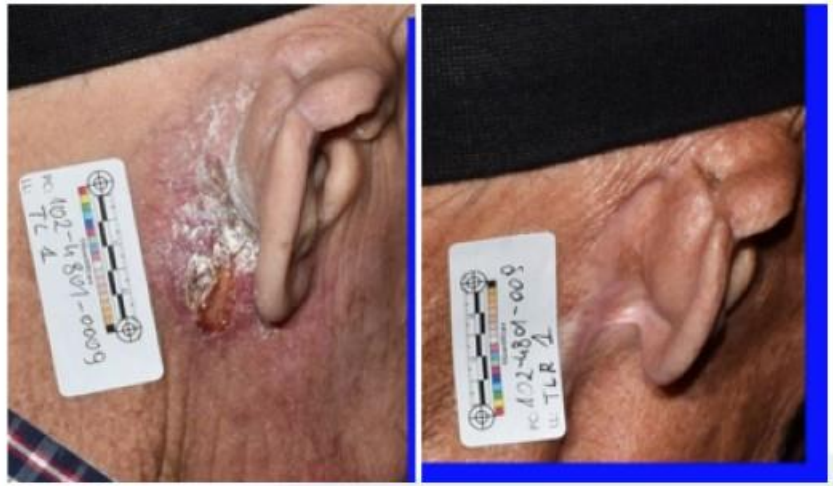
3401-0006

Baseline 87 weeks



4801-0002

Baseline 63 weeks

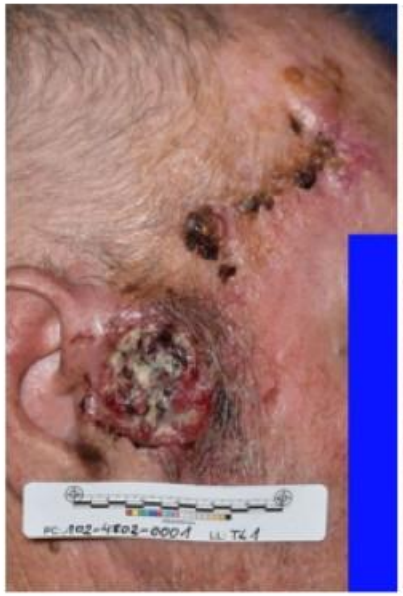


4801-0009

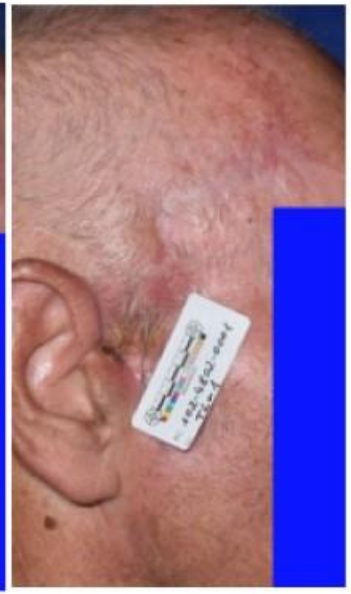
# All RP1+cemiplimab patients with CR & externally visible disease

Replimune

Baseline

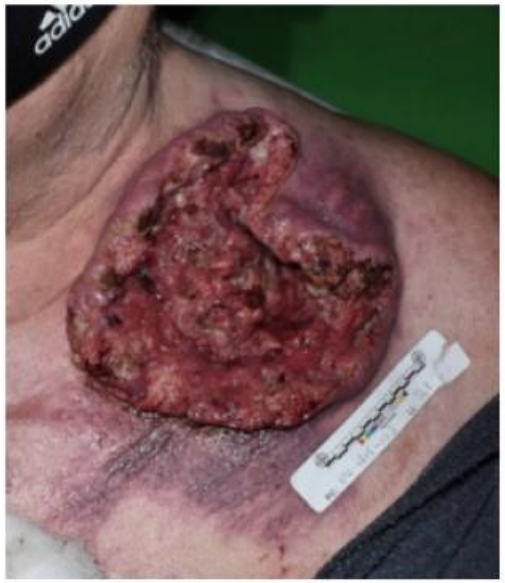


90 weeks

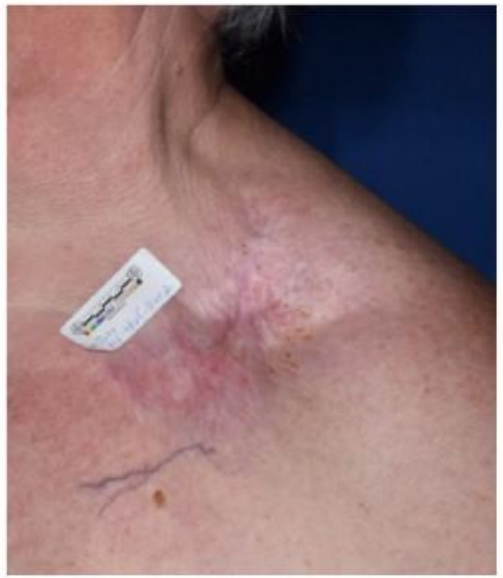


4802-0001

Baseline

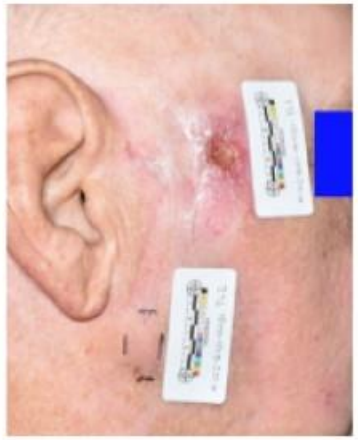


81 weeks

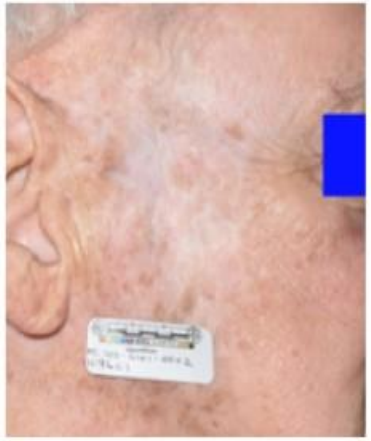


4805-0002

Baseline

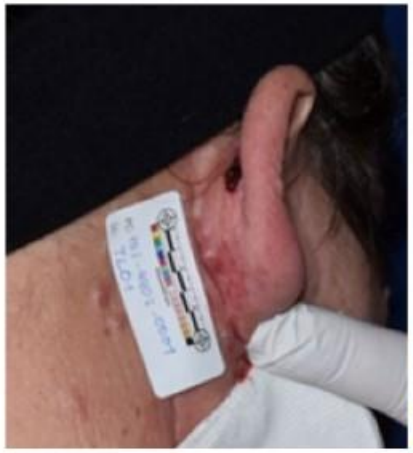


193 weeks

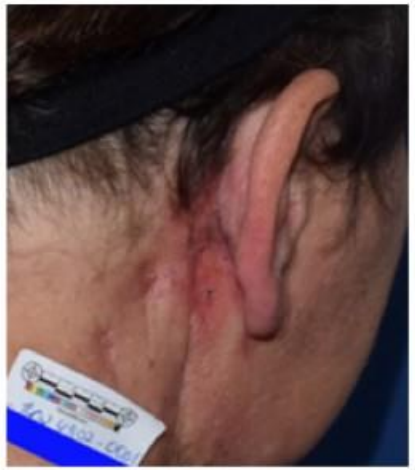


6101-0002

Baseline

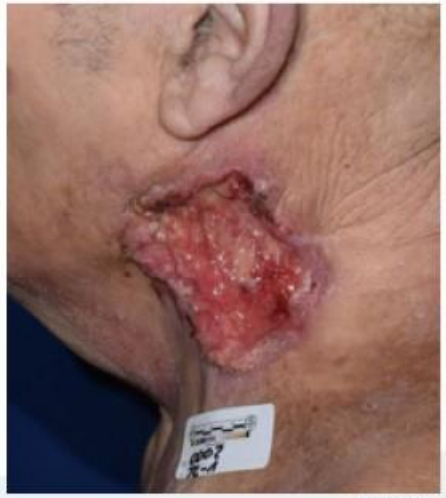


27 weeks

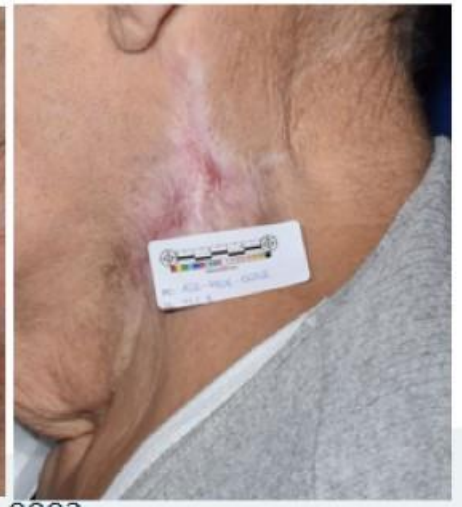


4902-0001

Baseline



45 weeks

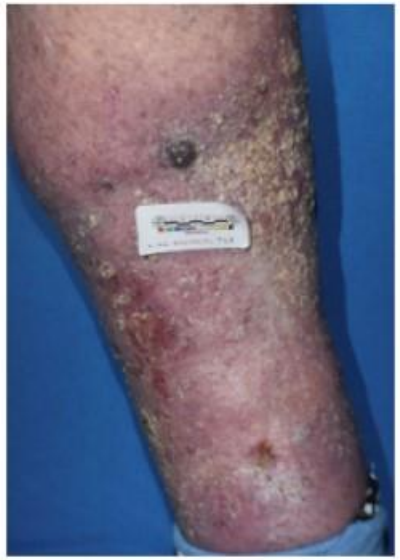


4806-0002

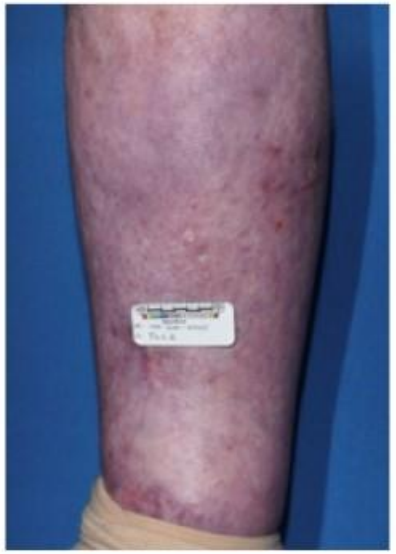
# All RP1+cemiplimab patients with CR & externally visible disease

Replimune

Baseline

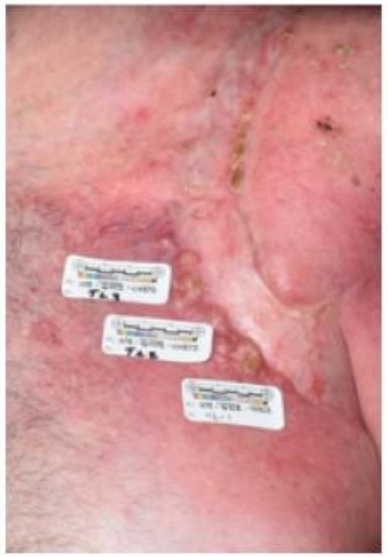


123 weeks

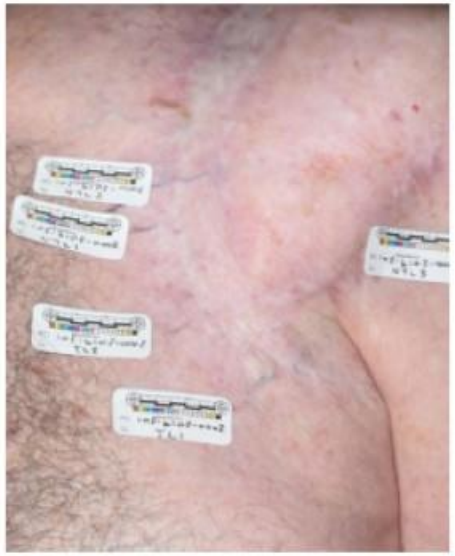


6101-0005

Baseline

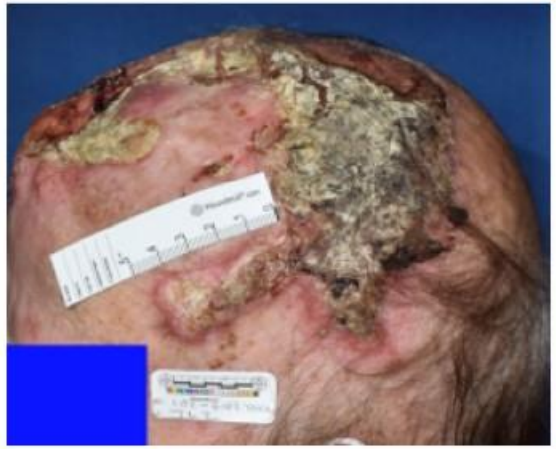


178 weeks

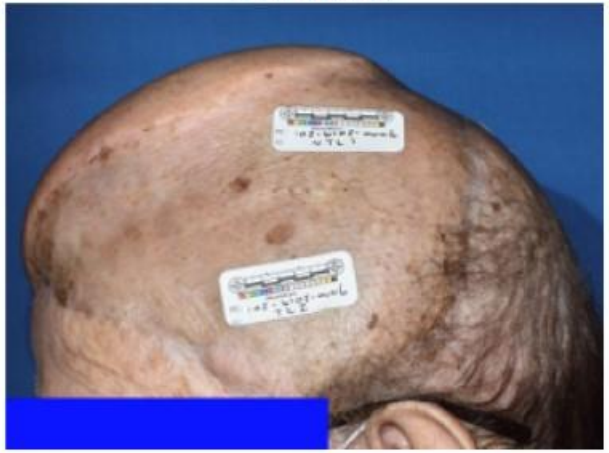


6102-0002

Baseline

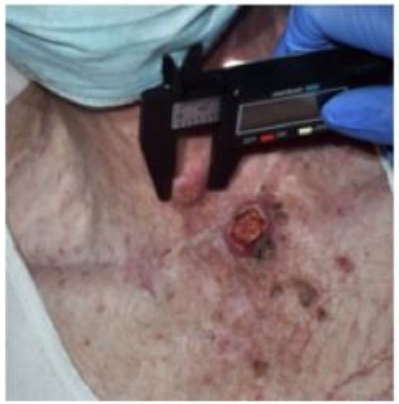


128 weeks

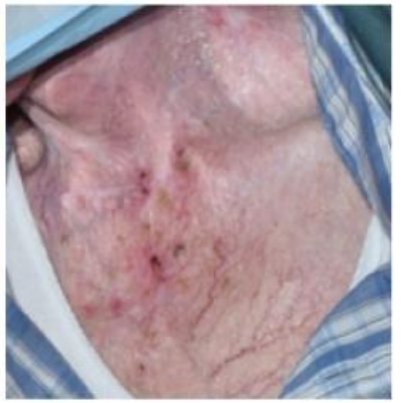


6102-0006

Baseline

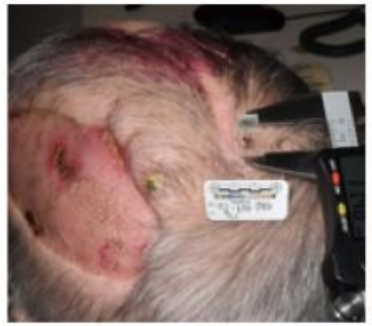


70 weeks

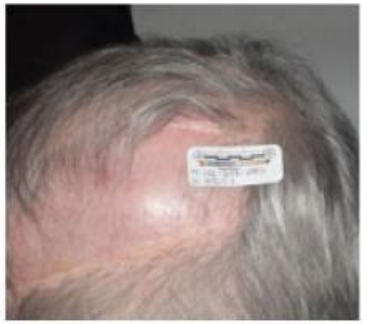


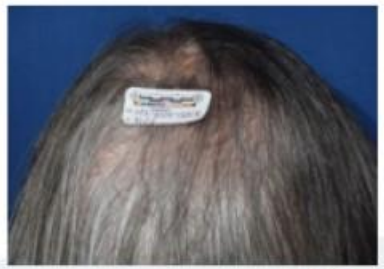
6105-0009

Baseline



18 weeks





105 weeks

6106-0006