IMO-2125
Clinical Data Update
September 11, 2017

Forward Looking Statements and Other Important Cautions

This presentation contains 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. All statements, other than statements of historical fact, included or incorporated in this presentation, including statements regarding the Company's strategy, future operations, collaborations, intellectual property, cash resources, financial position, future revenues, projected costs, prospects, plans, and objectives of management, are forward-looking statements. The words "believes," "anticipates," "estimates," "plans," "expects," "intends," "may," "could," "should," "potential," "likely," "projects," "continue," "will," and "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Idera cannot guarantee that it will actually achieve the plans, intentions or expectations disclosed in its forward-looking statements and you should not place undue reliance on the Company's forward-looking statements. There are a number of important factors that could cause Idera's actual results to differ materially from those indicated or implied by its forward-looking statements. Factors that may cause such a difference include: whether interim results from a clinical trial will be predictive of the final results of the trial, whether results obtained in preclinical studies and clinical trials will be indicative of the results that will be generated in future clinical trials, including in clinical trials in different disease indications; whether products based on Idera's technology will advance into or through the clinical trial process on a timely basis or at all and receive approval from the United States Food and Drug Administration or equivalent foreign regulatory agencies; whether, if the Company's products receive approval, they will be successfully distributed and marketed; and such other important factors as are set forth under the caption "Risk Factors" in the Company's Annual Report and on Form 10-K for the period ended December 31, 2016 and on Form 10-Q for the period ended June 30, 2017. Although Idera may elect to do so at some point in the future, the Company does not assume any obligation to update any forward-looking statements and it disclaims any intention or obligation to update or revise any forward-looking statement, whether as a result of new information, future events or otherwise.

Featured Speakers

Vincent Milano – Idera CEO

Mark Cornfeld, M.D. M.P.H. – Idera, Medical Lead, Oncology

Joanna Horobin, M.B., Ch.B. – Idera CMO

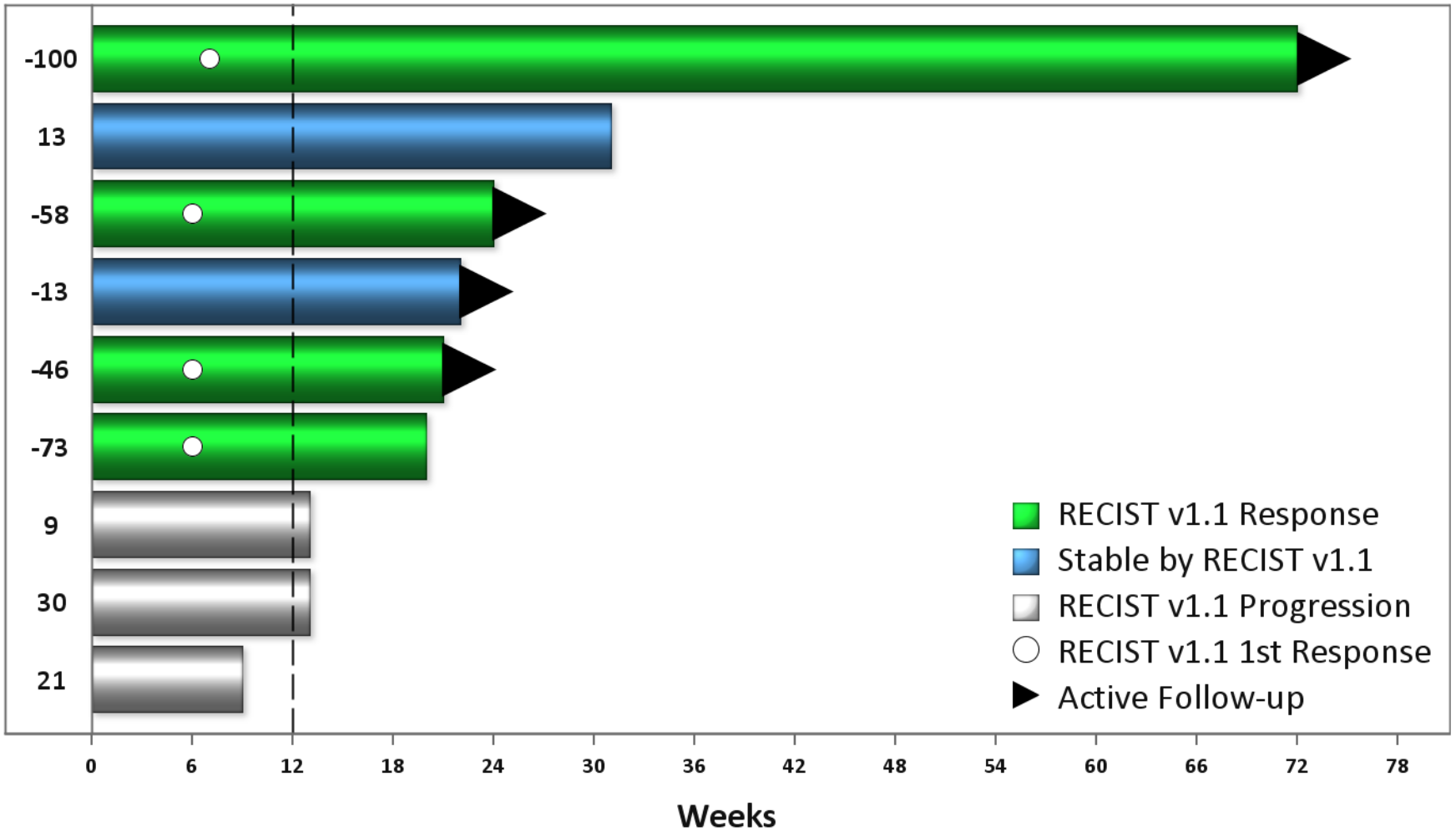
Adi Diab, M.D. – Lead Trial Investigator, Assistant Professor, Department of Melanoma Medical Oncology, Division of Cancer Medicine, University of Texas, MD Anderson Cancer Center

Call Agenda

- Opening Remarks – Vin Milano, Idera CEO
- Data Review and Responding Patient Profile Case Studies – Mark Cornfeld, M.D., M.P.H., Idera Oncology Lead
- IMO-2125 Development Next Steps - Joanna Horobin, M.B., Ch.B., Idera CMO
- Q&A – Vin Milano, Joanna Horobin, Mark Cornfeld, Adi Diab, M.D., MD Anderson Cancer Center

IMO-2125 Clinical Data Update
European Society for Medical Oncology (ESMO)

Time on Study with Best RECIST v1.1 Response and Largest Percent Decrease in Target Lesions as of 07AUG2017



Time on study ends at RECIST v1.1 PD (including death & start of new anti-cancer therapy) or study withdrawal for any reason.
Subjects treated with IMO-2125 8mg + Ipilimumab with at least 1 post-baseline disease evaluation.
Data cut-off date: 07AUG2017

Produced on 15AUG2017

Background

Treatment options following failure of first line anti-PD-1 therapy in melanoma are limited. The overall response rate (ORR) to ipilimumab following progression on pembrolizumab is only 13%, and not all responses are durable (Long, 2016). PD-1 inhibition is also less effective when liver metastases are present (Tumeh, 2017).

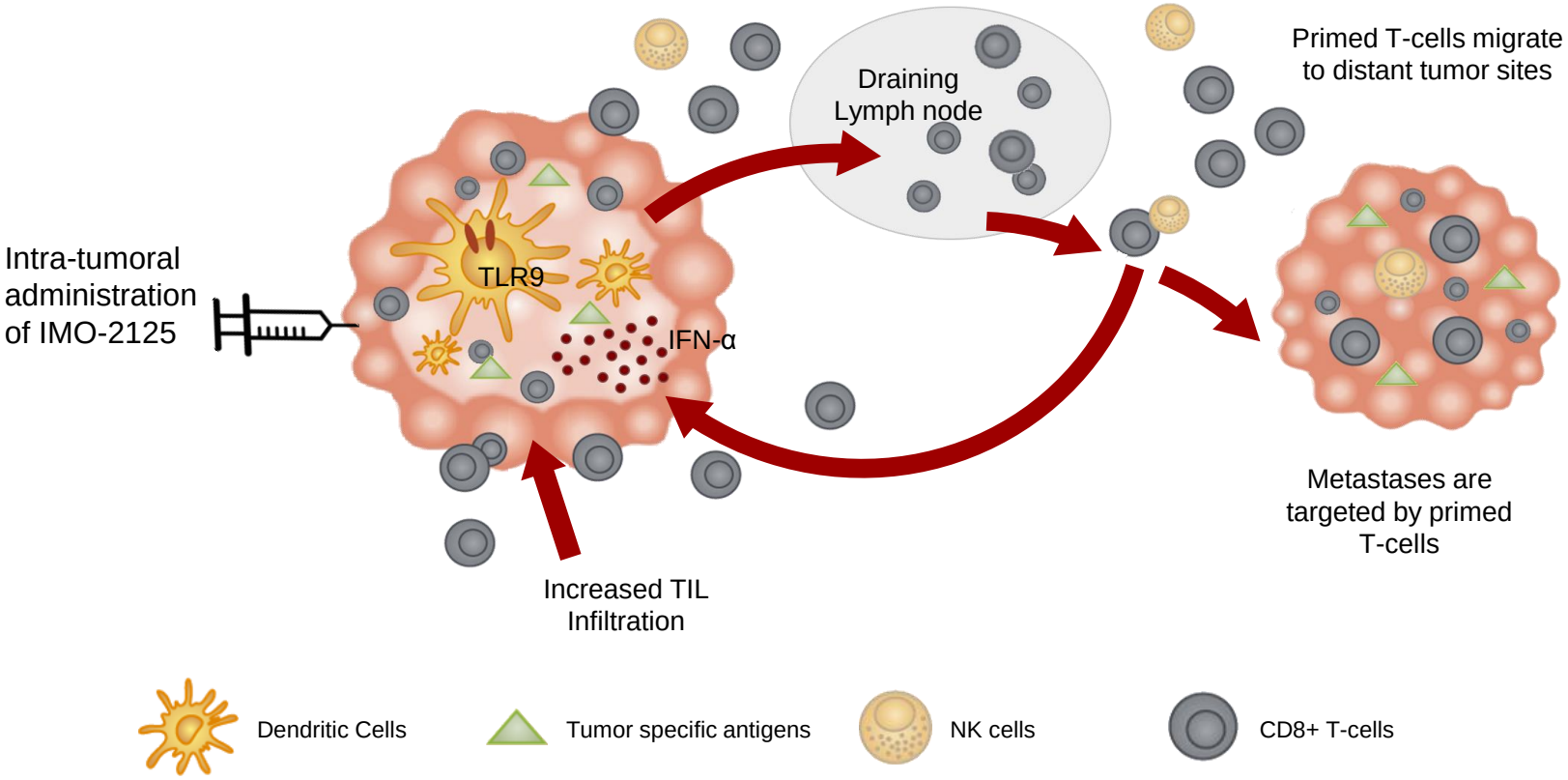
IMO-2125 is a synthetic phosphorothioate oligonucleotide that acts as a direct agonist of TLR9 to stimulate the innate and adaptive immune systems. Activation of TLR9 by IMO-2125 induces high levels of IFN-α from dendritic cells (DCs) along with B-cell proliferation and differentiation (Yu, 2008; Rodriguez Torres, 2010).

Preclinical data show that intratumoral IMO-2125 can produce durable and specific cytotoxic T cell responses against tumor antigens, leading to shrinkage of both the injected and distant tumors (Jiang, 2015).

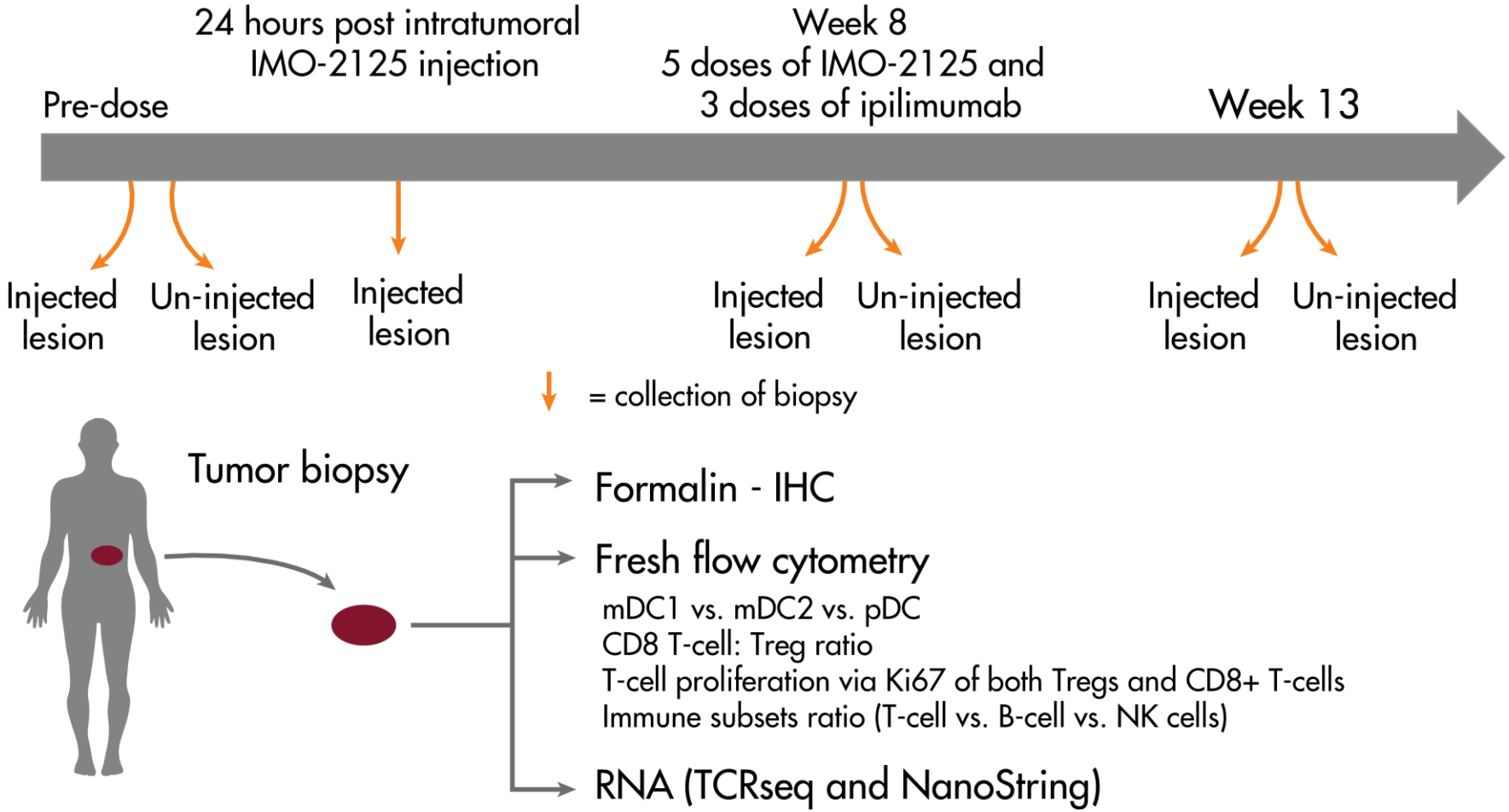
The combination of intratumoral IMO-2125 with a CTLA-4, PD-1, or IDO inhibitor in pre-clinical models results in improved tumor control compared to what can be produced by monotherapy with these agents (Wang, 2015 and 2016).

Based on these data, we initiated a Phase 1/2 clinical trial of intratumoral IMO-2125 in combination with ipilimumab or pembrolizumab in subjects refractory to PD-(L)1 inhibitors. Here, we describe results of the dose-finding Phase 1 portion of the trial for the IMO-2125-ipilimumab combination.

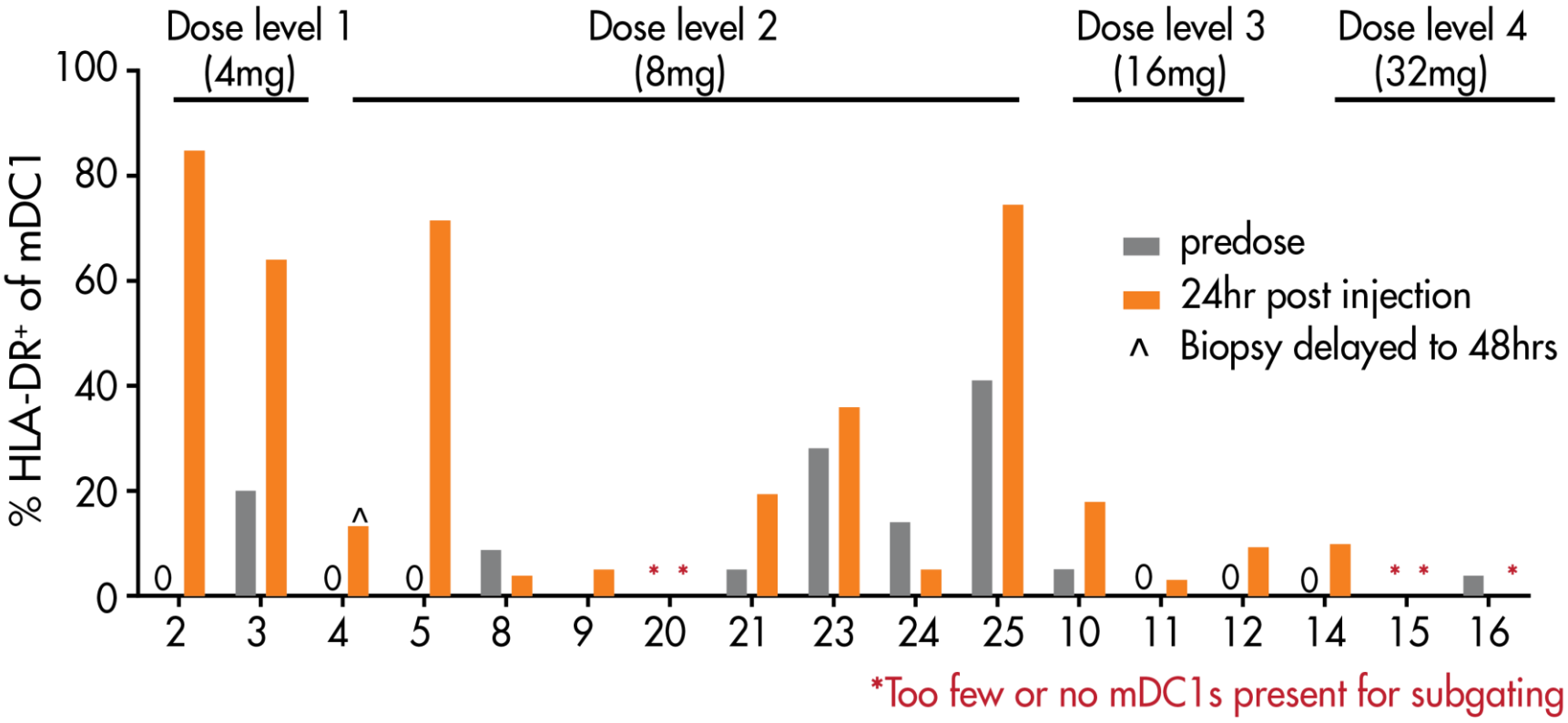
Intratumoral IMO-2125 Mechanism of Action



Immune Response Monitoring



mDC maturation in the injected tumor



Time = 24 hr

Study 204 – IMO-2125/Ipilimumab Combination Arm

IMO-2125 Phase 2 Trial Protocol

RP2D of IMO-2125 is 8mg

Dose-finding: IMO-2125 + ipilimumab SAFETY ASSESSMENT COMPLETED	→ Phase 2 IMO-2125 + ipilimumab OPEN
Dose-finding: IMO-2125 + pembrolizumab ONGOING	→ Phase 2 IMO-2125 + pembrolizumab PLANNED

Dosing:

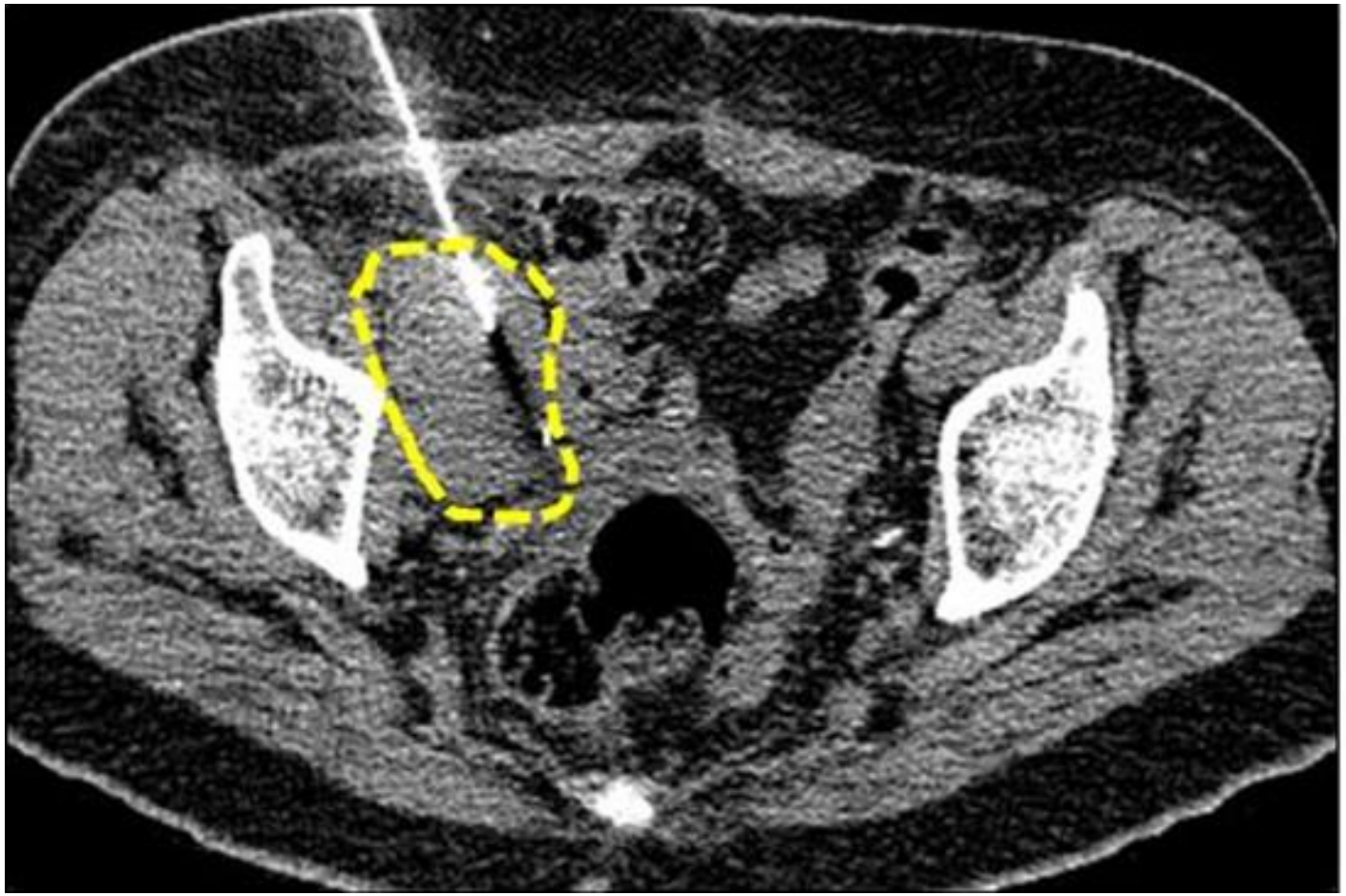
IMO-2125 is given as a single intratumoral injection week 1,2,3,5,8,11

Ipilimumab and pembrolizumab are administered per label beginning week 2

Deep injections are permitted with interventional radiology guidance

No need for infectious precautions

Deep injections of IMO-2125 can be administered safely via an image guided approach



Patient and Disease Characteristics

IMO-2125 + ipilimumab safety population (N=18)

	N (%)
Age, median (range)	60.5 (39,78)
Male	11 (61)
Race Caucasian Asian	 17 (94) 1 (6)
Stage IIIC IV	 2 (11) 15 (83)
Histology Cutaneous Mucosal	 15 (83) 2 (11)
Brain metastases	3 (17)
Visceral metastases	**13 (72)**
Elevated LDH	4 (22)
BRAF mutation	10 (56)

Data cut-off 31 May 2017

Prior Treatment

IMO-2125 + ipilimumab safety population (N=18)

	N (%)
PD-(L)1 inhibitor	17 (94)*
CTLA-inhibitor	8 (44)
BRAF inhibitor	5 (28)
MEK inhibitor	5 (28)
Interferon	6 (33)
IL-2	1 (6)
Other systemic therapy	6 (33)
Radiation	7 (39)

*PD-1 refractory requirement added through Amendment

Data cut-off 31 May 2017

Exposure

IMO-2125 + ipilimumab safety population (N=18)

IMO-2125 dose mg (N)	# IMO-2125 injections Median (range)	# ipilimumab infusions Median (range)	# discontinuations (reasons)
4 (3)	6 (3,6)	3 (1,4)	2 (death, other)
8 (9)	6 (4,6)	4 (2,4)	1 (w/drawal)
16 (3)	5 (3,6)	2 (1,4)	3 (2 death, w/dr)
32 (3)	6 (6,6)	4 (2,4)	

Ipilimumab dose = 3 mg/kg Q3wks x 4

Data cut-off 31 May 2017

Safety Summary

IMO-2125 + ipilimumab safety population (N=18)

IMO-2125 dose	4 mg (N=3)	8 mg (N=9)	16 mg (N=3)	32 mg (N=3)	Total (N=18)
≥ 1 TEAE	3 (100)	9 (100)	3 (100)	3 (100)	18 (100)
Related TEAE	2 (67)	9 (100)	3 (100)	3 (100)	17 (94)
≥ 1 SAE	2 (67)	4 (44)	2 (67)	1 (33)	9 (50)
Discontinued for AE	0	0	0	0	0
Death from AE	0	0	0	0	0
DLT	0	0	0	0	0
irAE[1]	1 (33)	3 (33)	2 (67)	0	6 (33)

[1]immune-related adverse event: hypophysitis (2), autoimmune hepatitis (2), adrenal insufficiency, colitis, hemorrhagic gastritis, Guillain-Barre

Data cut-off 31 May 2017

Most Frequent Treatment-Emergent Adverse Events

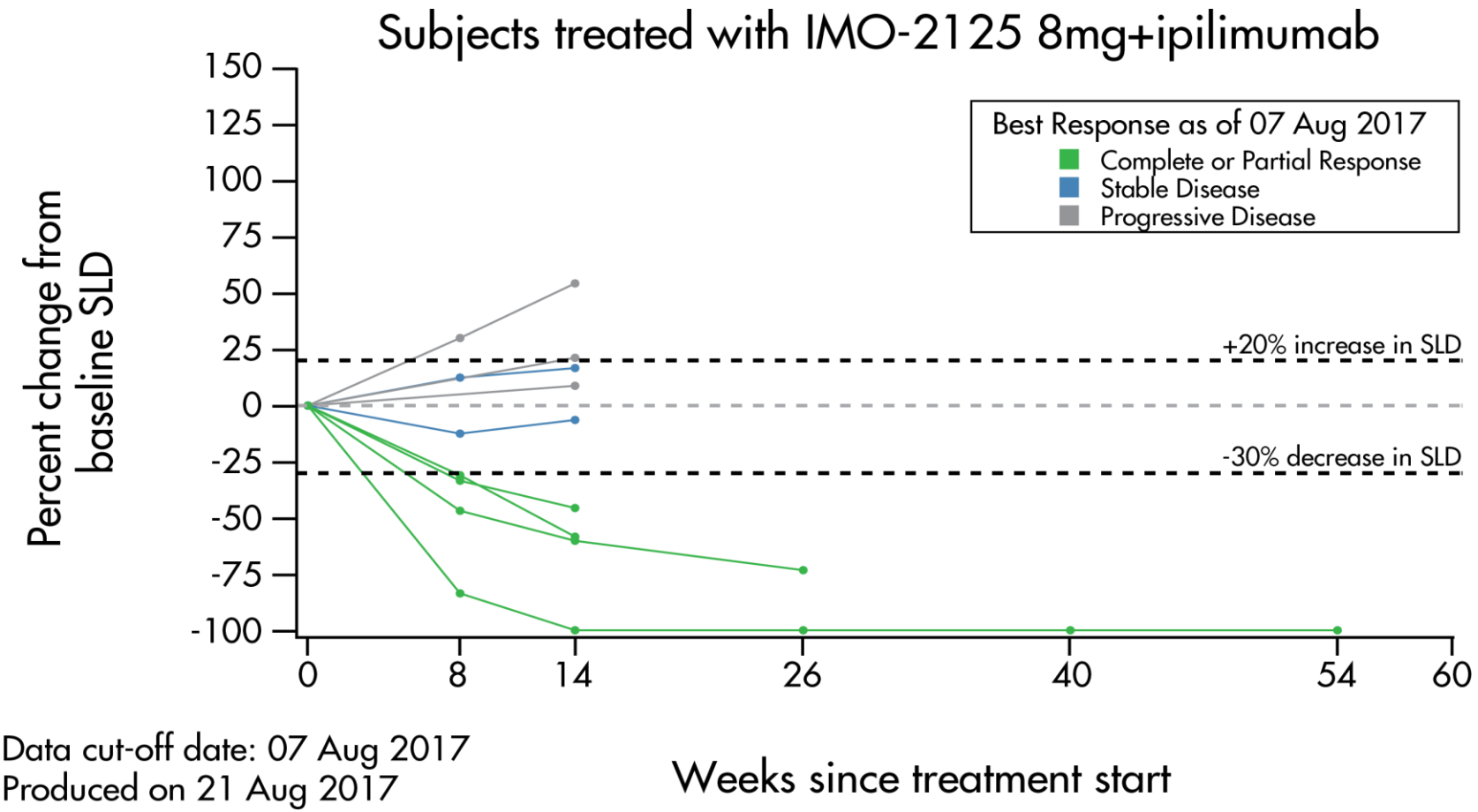
IMO-2125 + ipilimumab RP2D (N=9)

AE preferred term	All grade, N (%)	Grade 3, N (%)	Grade 4, N (%)
Any	9 (100)	4 (44)	0
Fatigue	6 (67)	-	-
Decreased WBC	5 (56)	-	-
Pyrexia	5 (56)	1 (11)	-
Nausea	4 (44)	1 (11)	-
Vomiting	4 (44)	1 (11)	-
Diarrhea	4 (44)	-	-
Anemia	4 (44)	1 (11)	-
Decreased appetite	3 (33)	-	-

No safety events associated with deep injections (liver, adrenal)

*Data cut-off 31 May 2017

Percent Change from Baseline Sum of Longest Diameters by RECIST v1.1



Data cut-off date: 07 Aug 2017
Produced on 21 Aug 2017

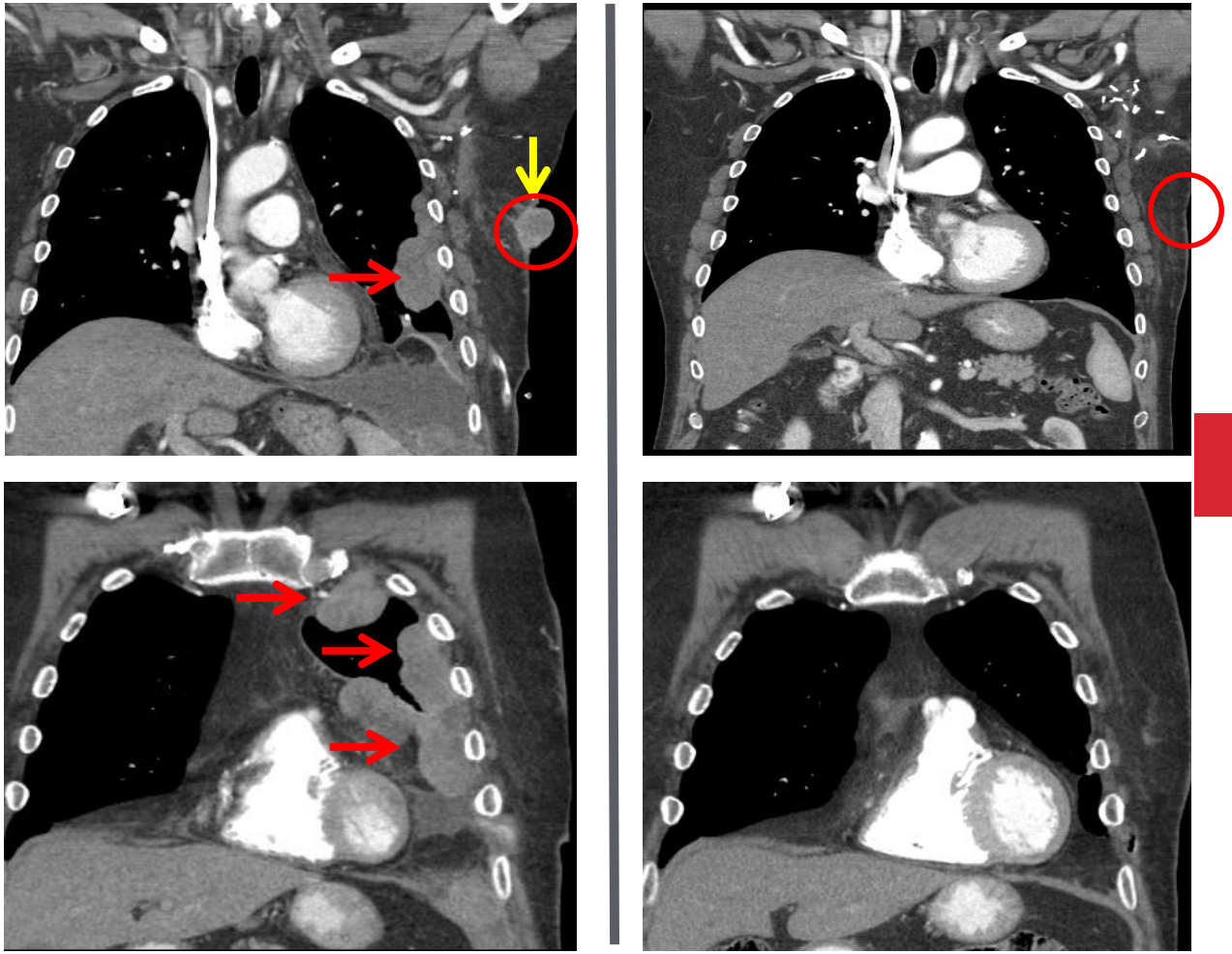
Subject 001-004 (durable CR)

Cohort 2 – IMO-2125 8 mg + ipilimumab 3 mg/kg x 4

- 68 y/o male with Stage IV cutaneous melanoma
  - $BRAF^{+}$
  - Metastatic to lung (bulky), LN, soft tissue
- Prior therapy w/ 4 doses Nivo + Urelumab (anti-4-1BB)
  - Marked progression as best response
- Received IMO x 6; ipi x 4
  - Treatment continued thru AE of hypophysitis
- Unmaintained CR (> 12 mos), beginning W6

Tumor Imaging: Patient 004 Remains a CR over 1 Year

Ipilimumab 3mg plus i.t. IMO-2125 8 mg



Pre-Therapy 03/2016

Post-Therapy 08/2016

Injected Lesion

Distant Lesions

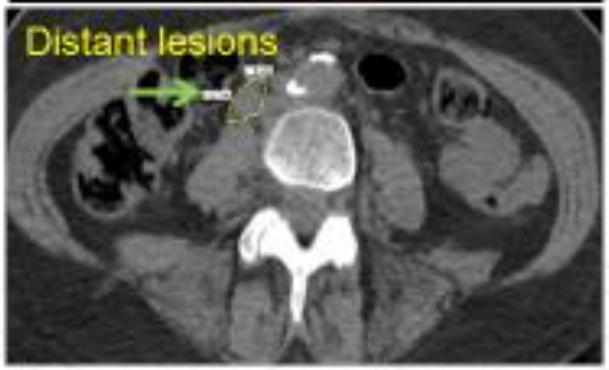
Subject 001-023 (near-CR)

Cohort 6 – IMO-2125 8 mg + ipilimumab 3 mg/kg x 4

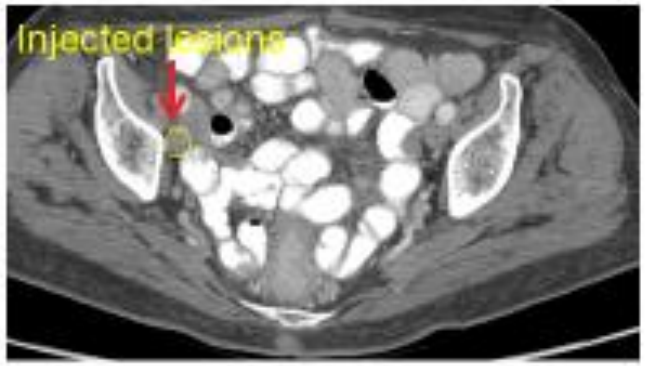
- 70 y/o WF with Stage IV cutaneous melanoma
  - Elevated LDH
  - Unknown BRAF status
  - Metastatic to pelvis and LN
- Prior therapy with interferon + tamoxifen (18 months); pembrolizumab (~9 months) with relapse during tx
- Received IMO x 5; ipi x 3.
  - Discontinued due to SAE of autoimmune hepatitis
- Confirmed PR at Week 13 (unscheduled visit)

Tumor Imaging of Patient 001-023 (near-CR)

Pretreatment

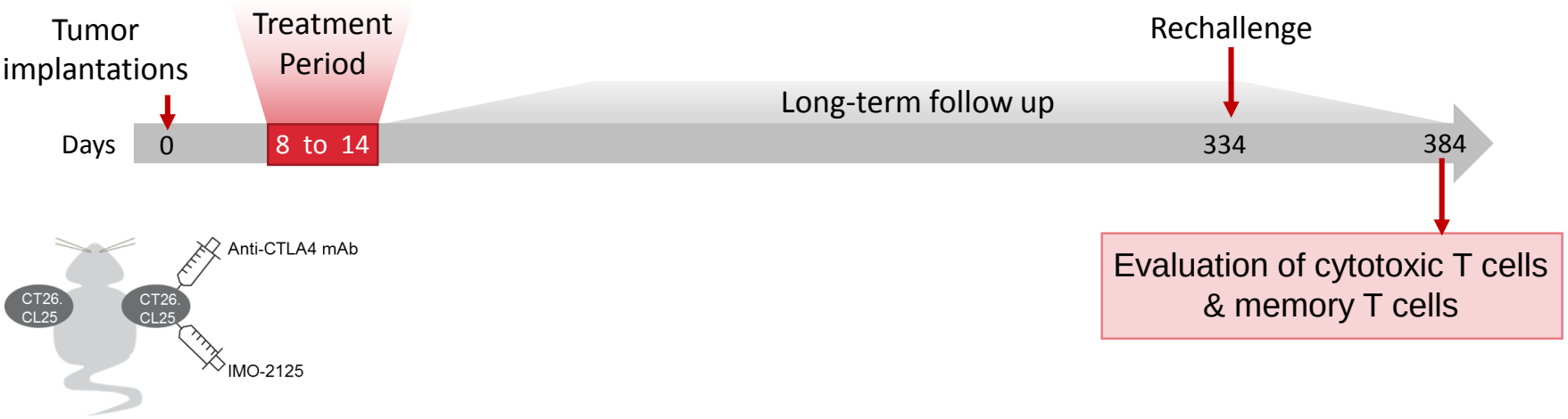


Post-treatment
End of study



IMO-2125 Pre-Clinical Clinical Data
Joint International Immunotherapy Conference

Outline of the Pre-clinical Study to Evaluate Durable Anti-tumor Activity with Combination Therapy of i.t. IMO-2125 and anti-CTLA4 mAb



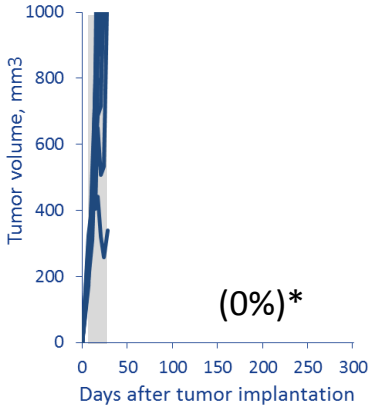
BALB/c mice (n=10 per group) were implanted s.c with 2 x 10^6 CT26.CL25 cells in right and left flanks. Mice implanted with tumors were randomized into four groups to be treated with PBS, IMO-2125 monotherapy, Anti-CTLA4 mAb monotherapy, and combination therapy of both agents. Treatment was initiated when tumor volume reached 100-250 mm3. Treatment with IMO-2125 at the dose of 2.5 mg/kg (50 µg in 100 µl PBS) or anti-CTLA4 mAb (clone 9H10 from BioXcell) at the dose of 0.5 mg/kg (10 µg in 100 µl) was administered by i.t injections into Tumor 1 on days 8, 11 and 14. PBS regimen of 100 µl PBS per mouse was administered by i.t injections into Tumor 1 on days 8, 11 and 14. Combination treatment groups received the treatment regimen for both treatment agents.

During the treatment and the follow-up period, all mice were followed up for safety and tolerability. Treatment in all groups was well tolerated during both periods.

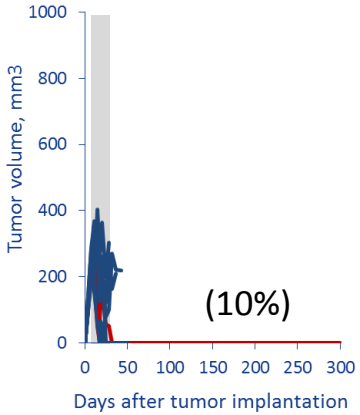
Durability of the antitumor activity during the follow-up period in Pre-Clinical Study

Treated Tumor

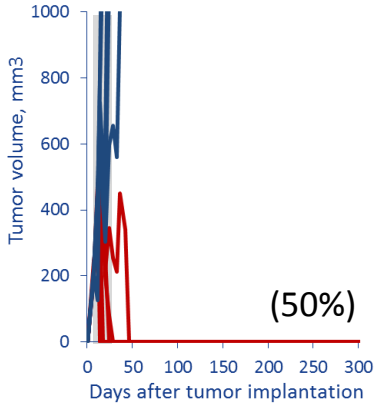
PBS



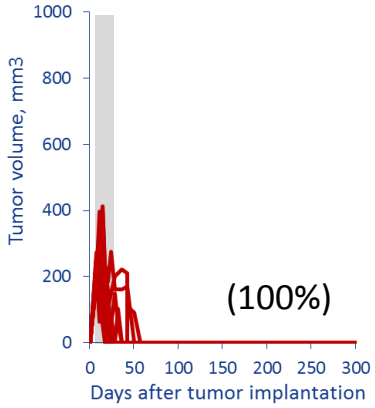
IMO-2125



aCTLA4

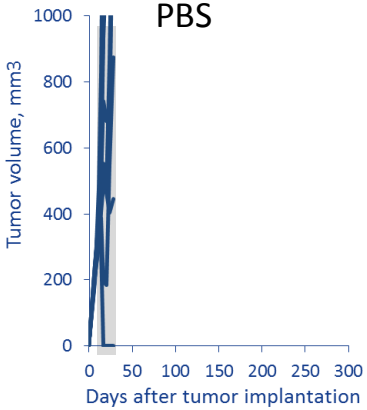


Combination

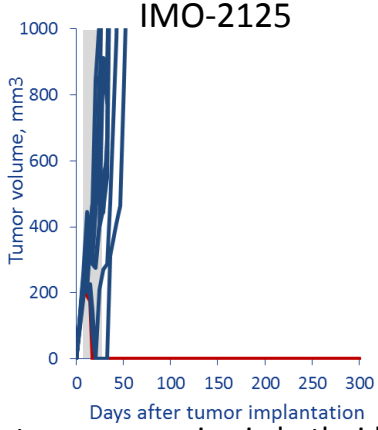


Distant Tumor

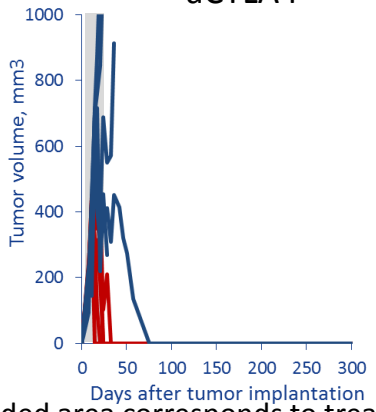
PBS



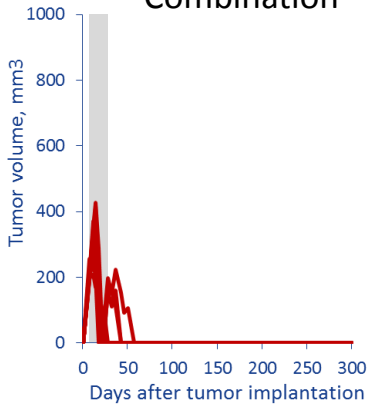
IMO-2125



aCTLA4

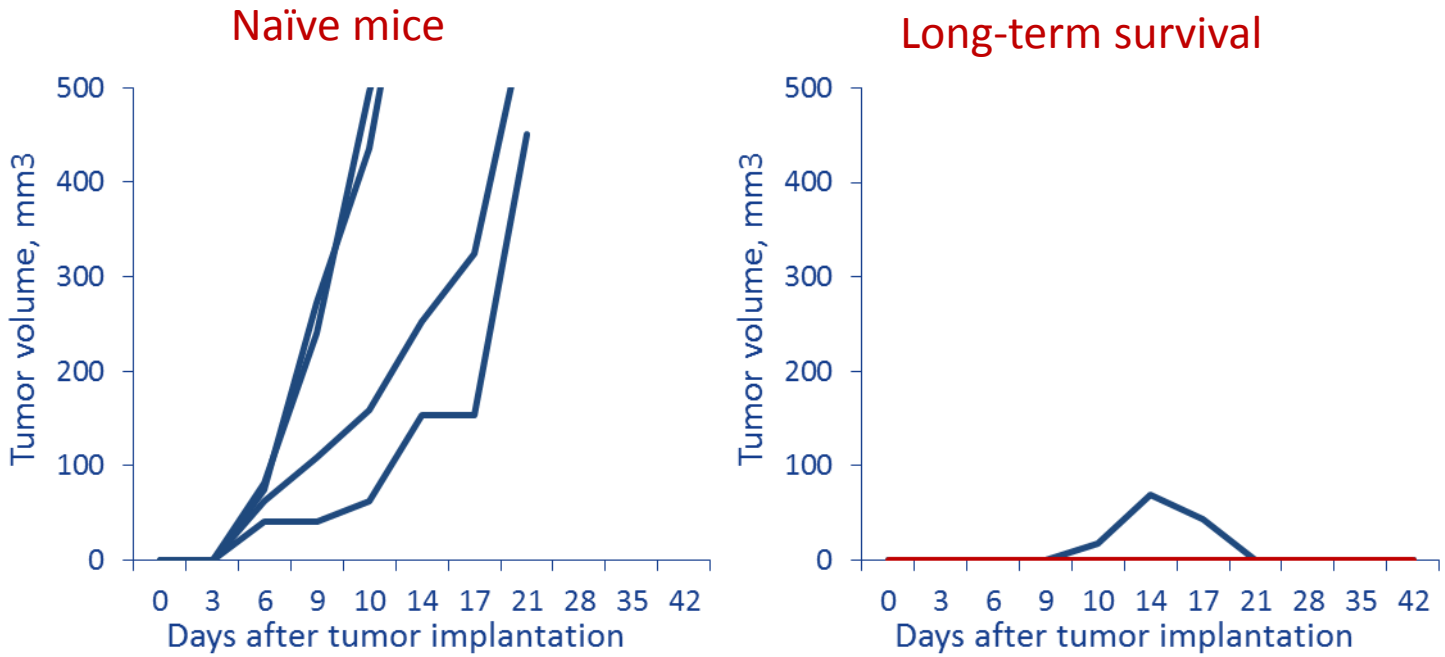


Combination



Red: Complete tumor regression in both sides Shaded area corresponds to treatment period

Tumor-free mice developed tumor specific memory responses following i.t. IMO-2125 and anti-CTLA-4 mAb treatment



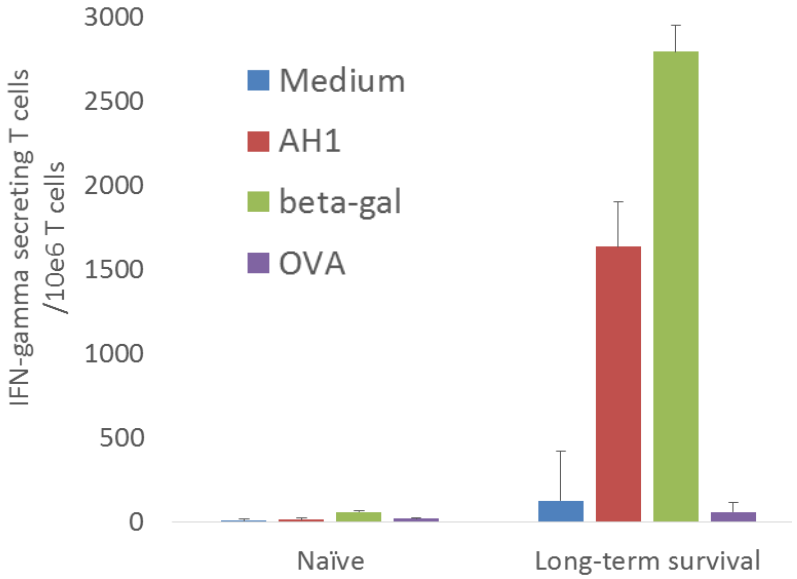
BALB/c mice whose tumors completely regressed (n=6) after IMO-2125 and anti-CTLA4 mAb treatment were rechallenged with 2 x 10^6 CT26.CL25 cells by s.c inoculation on day 334.

As a control, age-matched naïve BALB/c mice (n=4) were inoculated with the same number of cells by s.c injection.

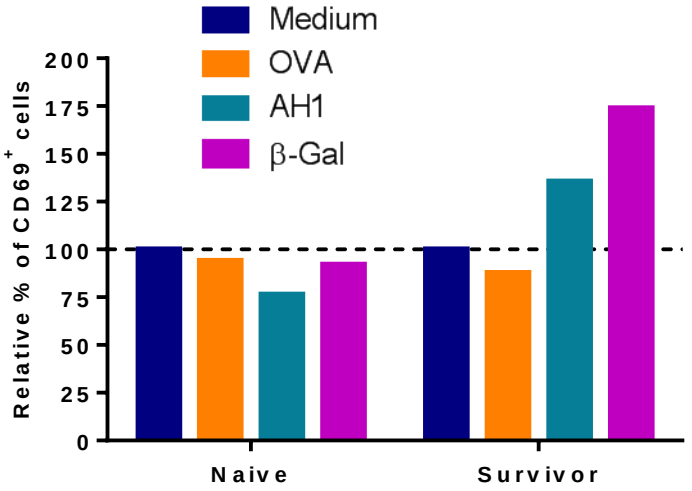
In control mice, tumors were established in all four animals, whereas in the rechallenge group, there were no measurable tumors observed.

Durable anti-tumor activity is associated with tumor-specific immune responses

CTLs against tumor-specific antigens



Specific memory antitumor immune activation



- T-cells from spleens of naïve mice (n=6) and from mice treated with IMO-2125/aCTLA-4 mAb (n=6) were collected on day 384
- ELISPOT was employed to detect IFN-γ secreting T-cells against tumor internal antigen AH1 and marker antigen βgal
- Splenocytes from naïve mice (n=6) and from mice treated with IMO-2125/aCTLA-4 mAb (n=6) incubated with 20 µg/ml of various peptide for 48 hrs were analyzed by flow cytometry

IMO-2125 Development Plan

IMO-2125 Anti-PD-1 Refractory Melanoma Development Plan

- Phase 2 Trial Expansion – 60 Patients
  - Up to 10 Centers
  - Expanded to include Ipilimumab-experienced patients
  - Open label design
    - Allows for continuous data updates
    - Opportunistic engagements with regulatory authorities
- Phase 3 Trial to Initiate in Q1 2018
  - Approximately 300 patients target enrollment
  - Conducted at approximately 70 centers globally

Appendix

RECIST Responders

Study 2125-204

RECIST v1.1

- Established in 2000; updated in 2009
- Provide:
  - Reproducible results
  - Objective efficacy measurement
  - Consistency across sites, countries, and solid tumor cancers
- Assures rigor in the assessment of response to a therapy
  - Improvement and stability is measured relative to the tumor burden at the start of therapy
  - Progression is measured relative to the smallest tumor burden at or after the start of therapy
  - Requires confirmation of tumor responses after at least 4 weeks
  - Patients re-challenged after progression have a new baseline established for subsequent response assessment

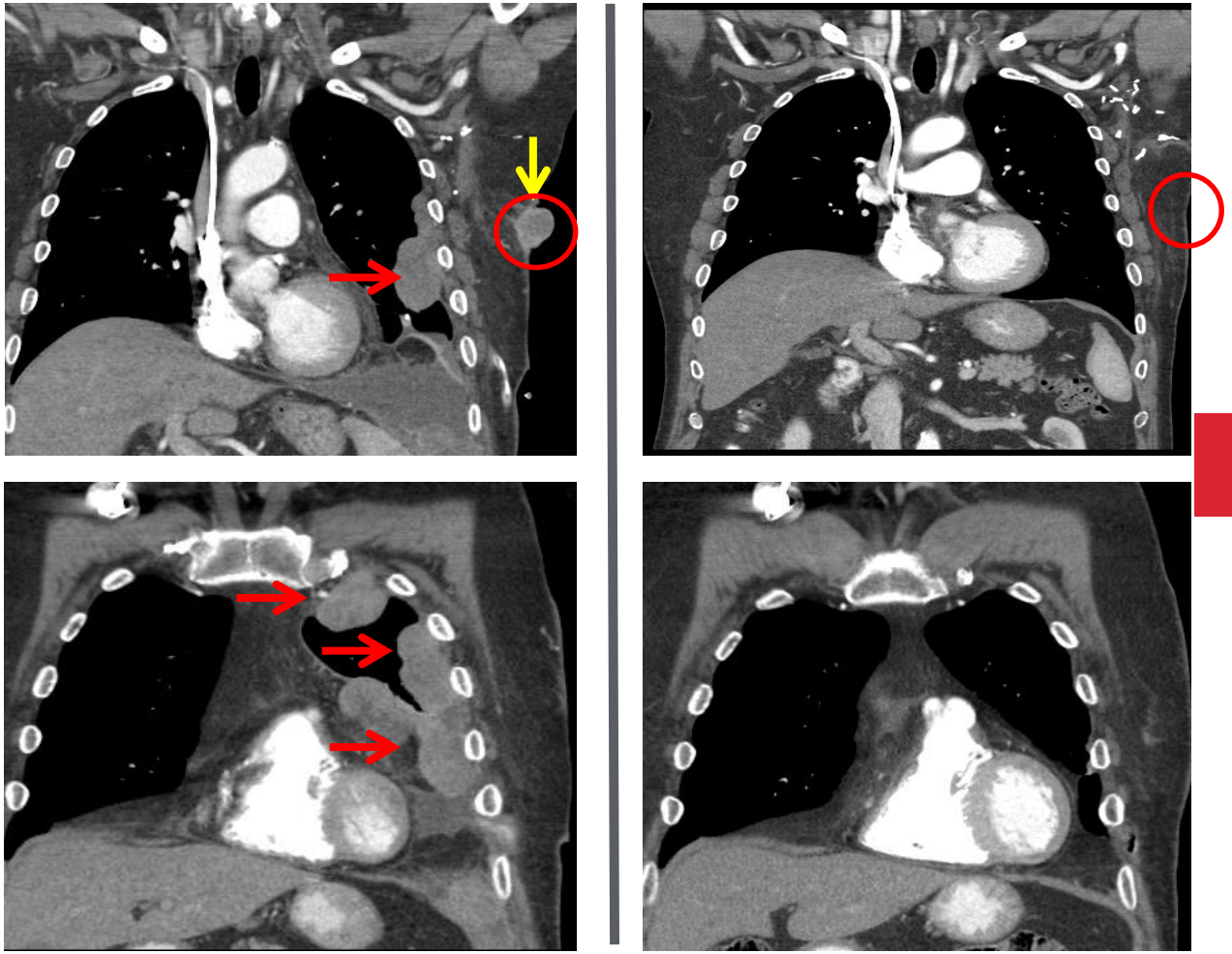
Subject 001-004 (durable CR)

Cohort 2 – IMO-2125 8 mg + ipilimumab 3 mg/kg x 4

- 68 y/o male with Stage IV cutaneous melanoma
  - $BRAF^{+}$
  - Metastatic to lung (bulky), LN, soft tissue
- Prior therapy w/ 4 doses Nivo + Urelumab (anti-4-1BB)
  - Marked progression as best response
- Received IMO x 6; ipi x 4
  - Treatment continued thru AE of hypophysitis
- Unmaintained CR (> 12 mos), beginning W6

Tumor Imaging: Patient 004 Remains a CR over 1 Year

Ipilimumab 3mg plus i.t. IMO-2125 8 mg



Pre-Therapy 03/2016

Post-Therapy 08/2016

Injected Lesion

Distant Lesions

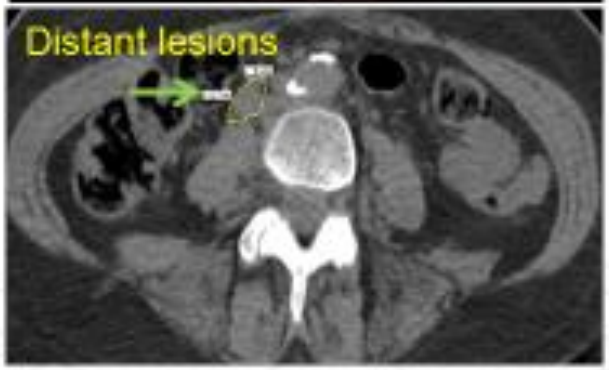
Subject 001-023 (near-CR)

Cohort 6 – IMO-2125 8 mg + ipilimumab 3 mg/kg x 4

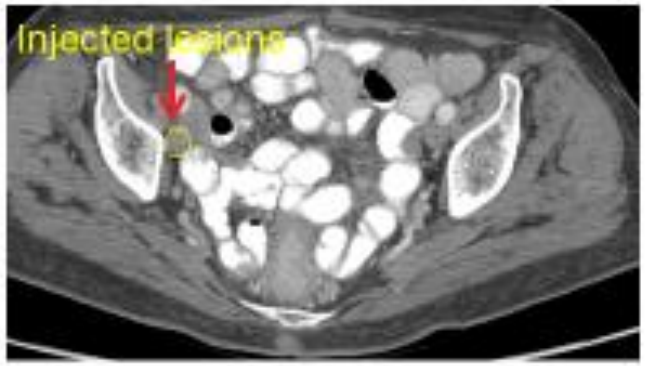
- 70 y/o WF with Stage IV cutaneous melanoma
  - Elevated LDH
  - Unknown BRAF status
  - Metastatic to pelvis and LN
- Prior therapy with interferon + tamoxifen (18 months); pembrolizumab (~9 months) with relapse during tx
- Received IMO x 5; ipi x 3.
  - Discontinued due to SAE of autoimmune hepatitis
- Confirmed PR at Week 13 (unscheduled visit)

Tumor Imaging of Patient 001-023 (near-CR)

Pretreatment



Post-treatment
End of study



Subject 001-003 (durable PR)

Cohort 1 – IMO-2125 4 mg + ipilimumab 3 mg/kg x 4

- 58 WM w/ Stage IV cutaneous melanoma
  - BRAF wt
  - LN and liver mets
- Prior treatment ~2 mos nivolumab (best response unk)
- Received IMO x 6; ipi x 3
  - Treatment held for hypophysitis
- Unmaintained PR (>12 mos), beginning wk 14

Subject 001-025 (PR)

Cohort 6 – IMO-2125 8 mg + ipilimumab 3 mg/kg x 4

- 62 y/o WM with Stage IIIc cutaneous melanoma
  - BRAF wt
  - Head and neck LN and soft tissue mets and lung nodules
- Prior treatment with pembrolizumab (~3 months)
  - Progression
- Received IMO x 6; ipi x 4
- Confirmed PR at Week 14

Subject 001-008 (PR)

Cohort 2 – IMO-2125 8 mg + ipilimumab 3 mg/kg x 4

- 71 y/o WF w/ Stage IV cutaneous melanoma
  - $BRAF^{+}$
  - Extensive LN mets
- Prior treatment with dabrafenib + trametinib (~2 yrs); ipilimumab (4 doses); pembrolizumab (~14 months)
  - Progression
- Received IMO x 6; ipi x 4
- Confirmed PR at W14; PD during follow-up

Subject 001-022 (PR)

Cohort 7 – IMO-2125 16 mg + pembrolizumab 2 mg/kg

- 56 y/o Hispanic female with Stage IV cutaneous melanoma
  - $BRAF^{+}$
  - Metastatic to head (occipital sc nodules) and LN
- Prior therapy with interferon (~10 months), ipilimumab (3 doses), dabrafenib + trametinib (~3 months), pembrolizumab (18 doses) discontinued for progression
- Received IMO x 6; pembro ongoing (x 8)
- Confirmed PR at Week 14

Clinical Conclusions

- The combination of IMO-2125 with ipilimumab is tolerable at all dose levels studied
- IMO-2125 with ipilimumab has substantial clinical activity at the RP2D of 8 mg in anti-PD-1 refractory melanoma. An additional PR of > 1 year has been reported at 4 mg.
- Dendritic cell activation, detectable within 24 hrs of the first IMO-2125 injection, is evidence for target acquisition at the RP2D
- Further investigation of IMO-2125 with ipilimumab in anti-PD-1 refractory melanoma is warranted. The planned Phase 2 expansion is underway and maintenance doses of IMO-2125 have been added
- Dose finding for IMO-2125 with pembrolizumab is ongoing and one partial response has been seen to date

PROGRAM	MECHANISM	INDICATION	COMMERCIAL RIGHTS	DISCOVERY	PHASE 1	PHASE 2	PIVOTAL
IMMUNO-ONCOLOGY	TLR9 Agonist	IMO-2125 Refractory PD-1 Metastatic Melanoma / IPI Comb.	idera				
		IMO-2125 Refractory PD-1 Metastatic Melanoma / PD-1 Comb.					
		IMO-2125 Monotherapy Additional Tumor Types					
		IMO-2125 Combo Additional Tumor Types – CPI Comb.					
RARE DISEASES	TLR 7,8,9 Antagonist	IMO-8400 Dermatomyositis	idera				
	3GA - Undisclosed Target	Undisclosed Rare Liver Condition					
	3GA-NLRP3	3GA Undisclosed Indication					
	3GA-DUX4	3GA Undisclosed Indication					
PARTNERED PROGRAMS	3GA	3GA Renal Diseases	gsk				
	TLR 7,8,9 Antagonist	IMO-9200 Autoimmune Diseases	Vivelix				

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