THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Uveal melanoma and Mucosal melanoma

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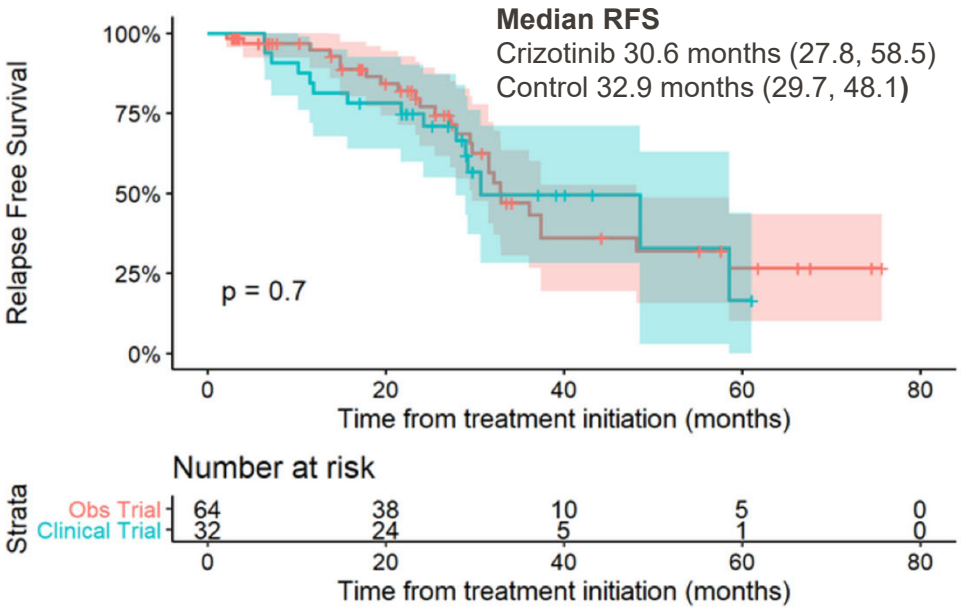
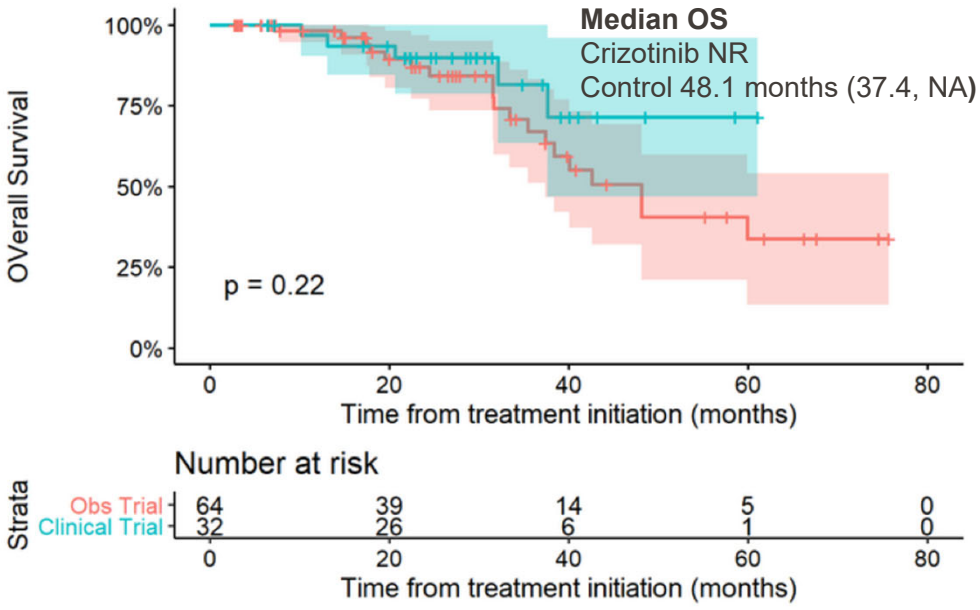
Objectives

1. **Describe current and completed experimental trials in uveal melanoma and mucosal melanoma**

2. **Explore emerging preclinical data and future directions in rare melanomas**

Adjuvant Crizotinib





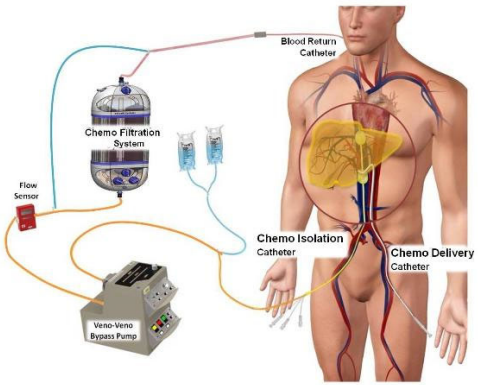
Carvajal RD et al., ASCO 2020

FOCUS

Clinical Trial For Patients with Hepatic-Dominant Ocular Melanoma

Multinational, Multicenter Non-Randomized trial in Patients with Hepatic Dominant Ocular Melanoma (N = 80)

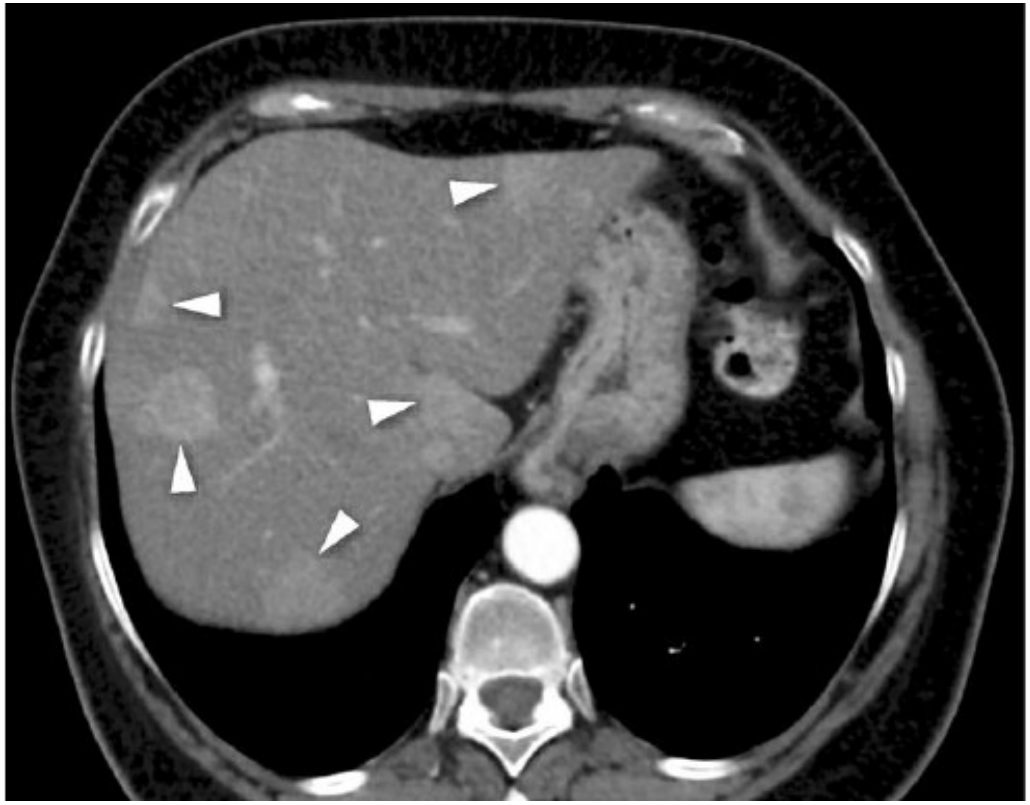
Melphalan/HDS
Q6-8 weeks x ≤ 6 cycles

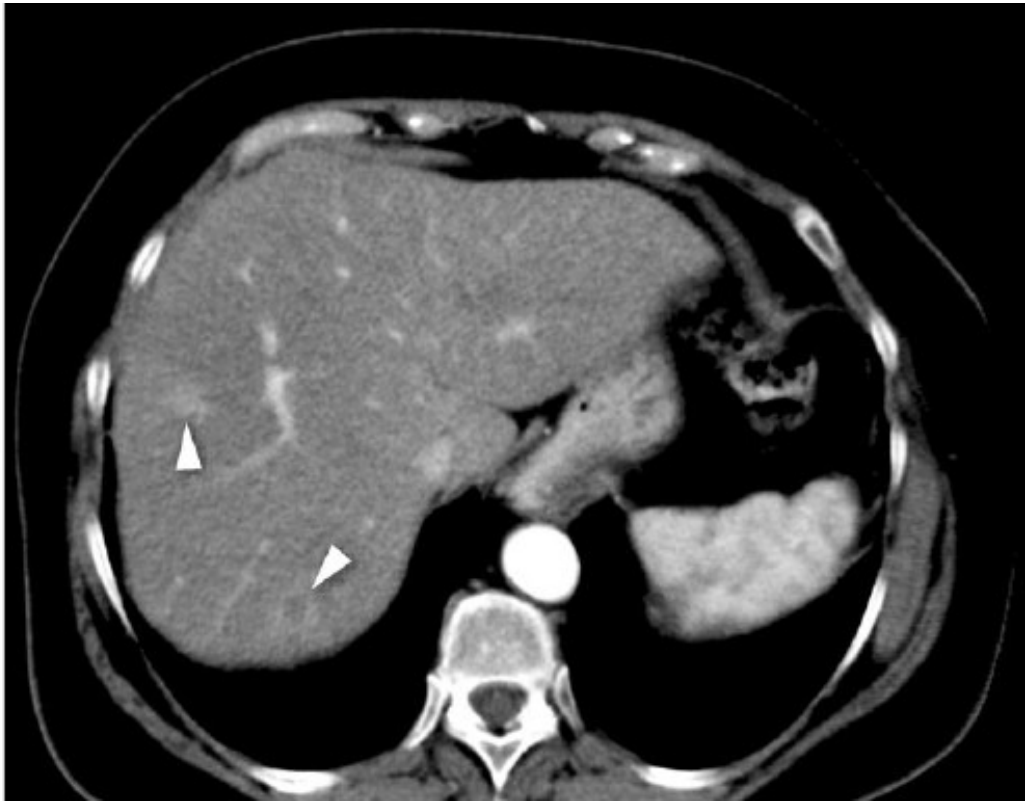


Primary Endpoint
Objective Response Rate

Secondary Endpoints
Duration of Response, Disease Control Rate, Overall Survival, Progression-Free Survival

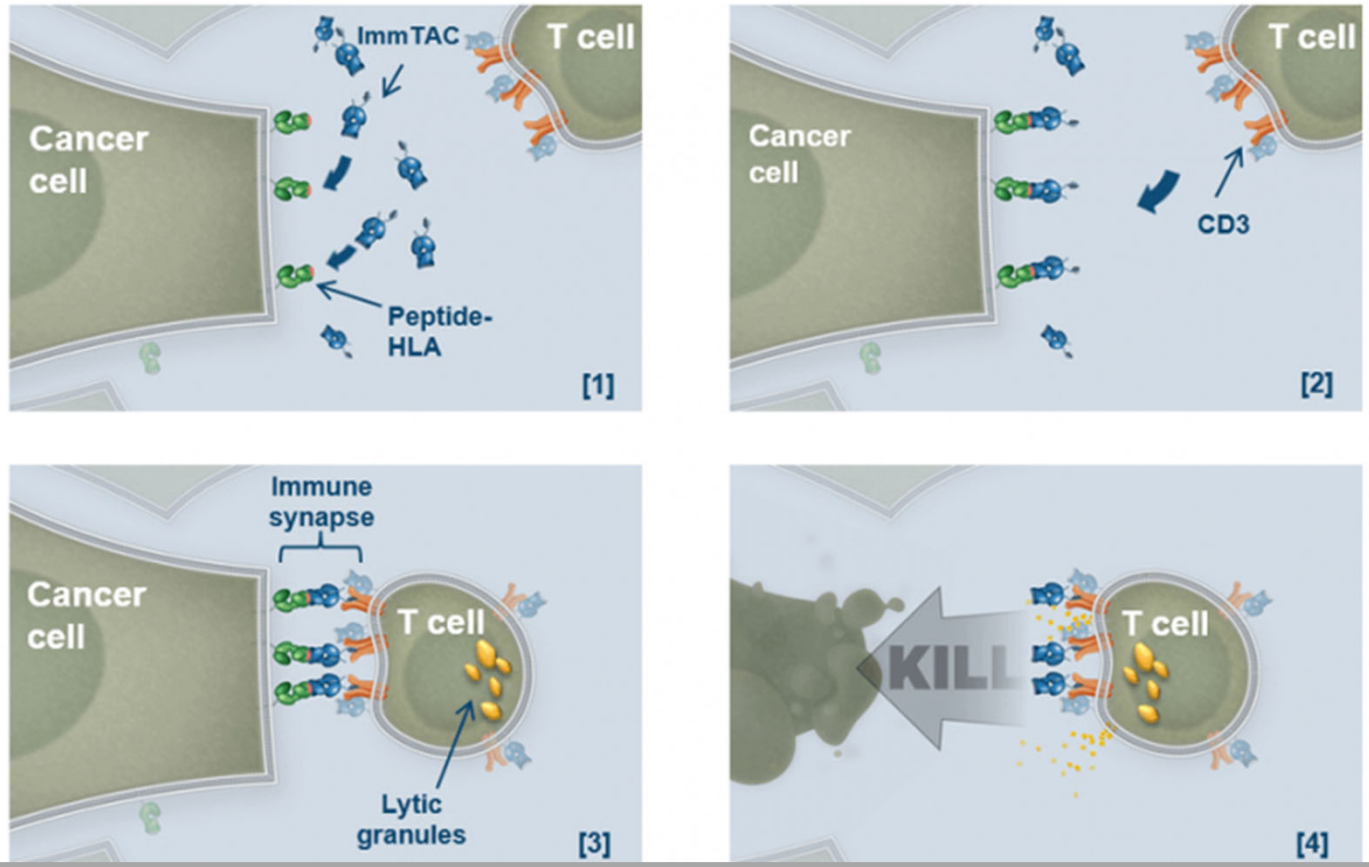
Safety, PK, QoL
Rigorous Analyses to Assess Risk:Benefit Profile



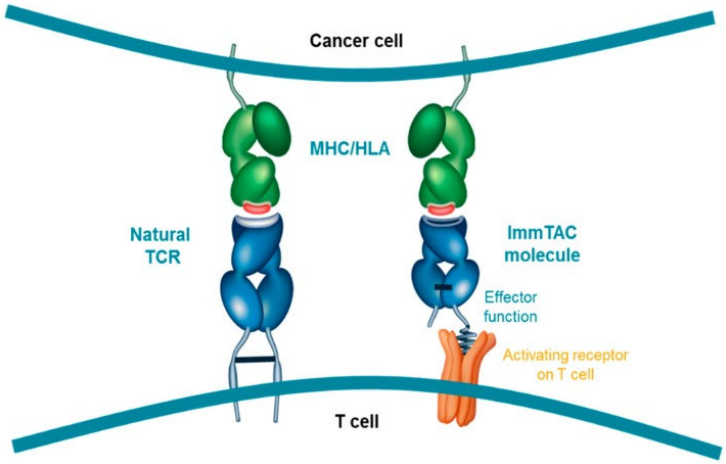


Burgmans ECIO 2019

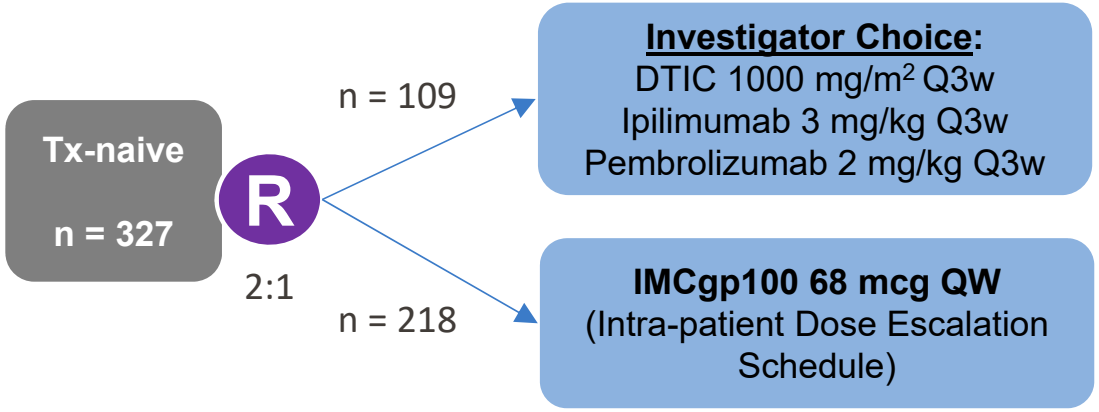
ImmTAC: Immune Mobilizing Monoclonal T-Cell Receptor Against Cancer



IMCgp100-202: Tebentafusp for treatment-naïve metastatic uveal melanoma

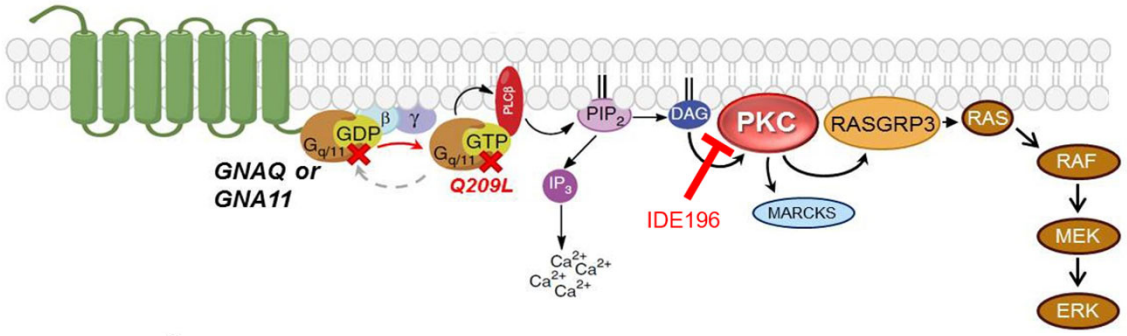


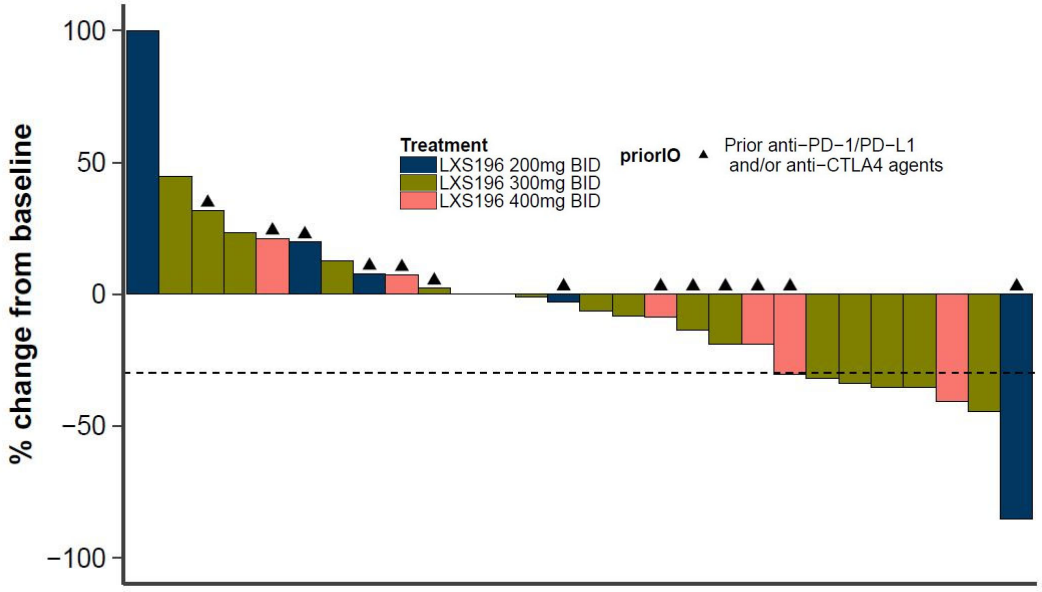
Damato B et al. *Cancers* 2019.



Primary Endpoint:
Overall Survival
Secondary Endpoints:
ORR, PFS, DOR, DCR, HRQoL, PK

Protein Kinase C inhibitor: IDE196

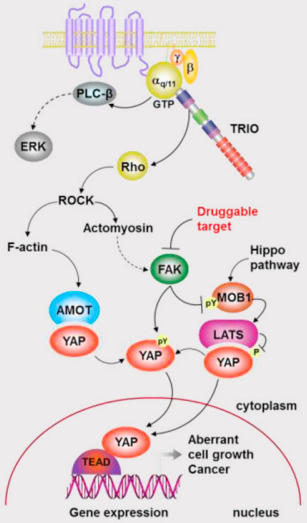




- One patient having a CR remains on therapy as of March 24, 2020
- Duration of response for the four patients with confirmed responses was 91, 395, +554, and +668 days as of April 2019
- SD = stable disease; PR = partial response, CR = complete response, ORR = overall rate of response

IN10018-004-01: FAK inhibitor Study Design

FAK regulates the Hippo pathway



Targeting Gαq-FAK signaling in uveal melanoma

Part 1: IN10018 Monotherapy

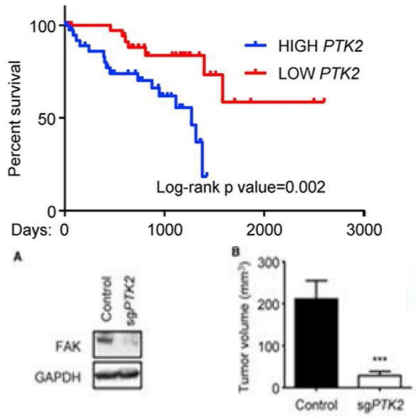
First 6 subjects complete **the 1st 21-day cycle** at 100mg dose level (regardless of subtypes)

→ SMC[1]

→ 100mg as RP2D

→ **Part 2 initiation** in combination with cobimetinib

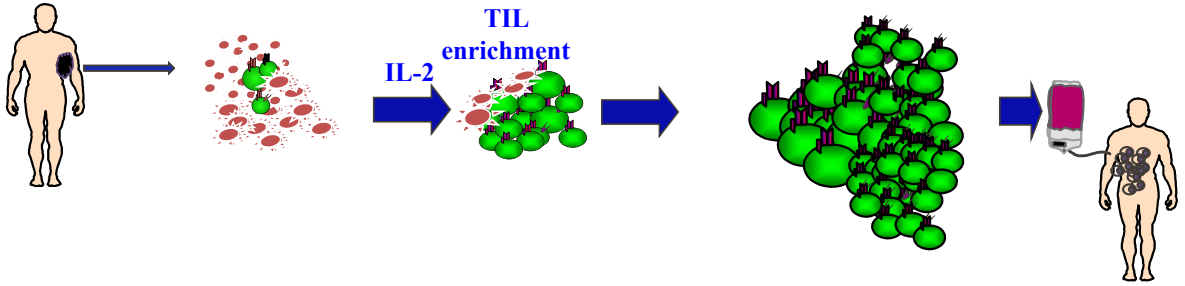
→ Another approximately 14 subjects (1:1)



1 **SMC will review the safety database after first 6 subjects complete the 1st 21-day cycle and determine RP2D.**

How to make T cells

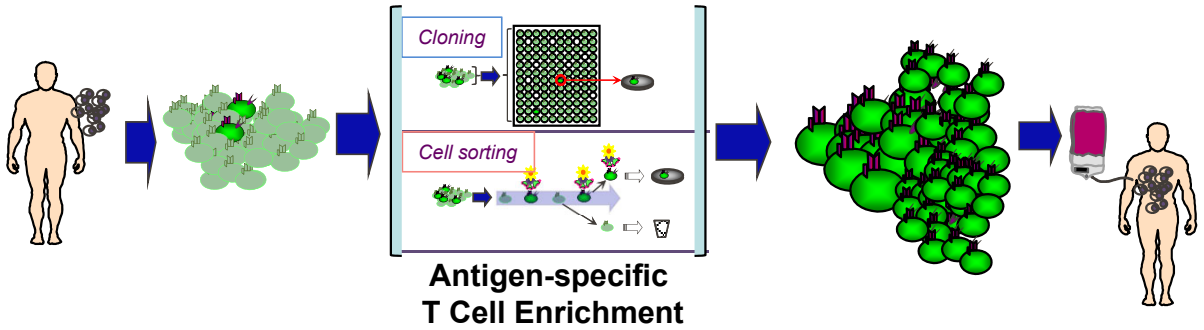
TIL
Tumor-infiltrating Lymphocytes



Ongoing TIL study at UPMC

(PI: Udai Kammula)

ETC
Endogenous T cell Therapy



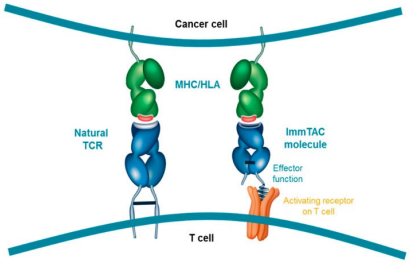
Antigen-specific T Cell Enrichment

SLC45A2 ETC study at MDACC

(PI: Sapna Patel)

Slide courtesy of C Yee

IMC-F106C: ImmTAC for PRAME-Positive Cancers



Damato B et al. *Cancers* 2019.

Arm A Phase 1 Dose-Escalation
IMC-F106C monotherapy

Cohort 1 → Cohort 2 → ⋯ → Arm A MTD / RP2D

Phase 2
Up to 4 indication-specific cohorts
IMC-F106C monotherapy

Arm A MTD/RP2D

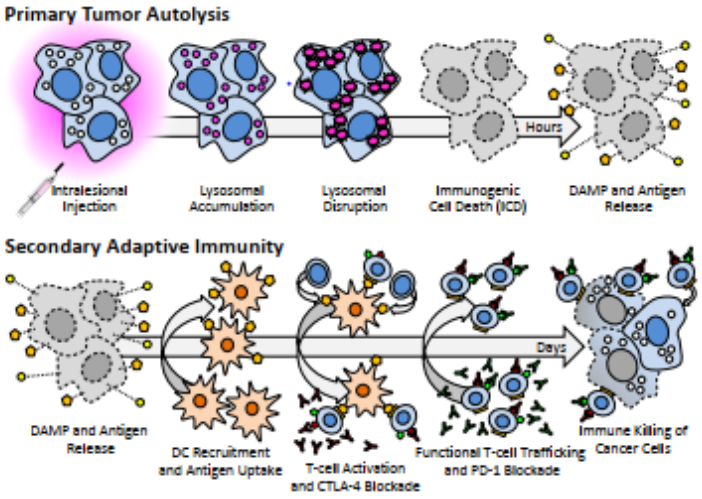
Arm B Phase 1 Dose-Exploration
IMC-F106C + selected checkpoint inhibitor
B1 = atezolizumab; B2 = pembrolizumab

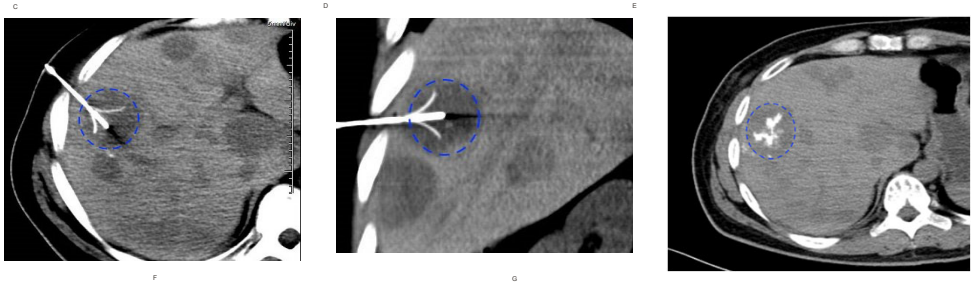
B1: Cohort 1 → ⋯ → Arm B1 MTD / RP2D

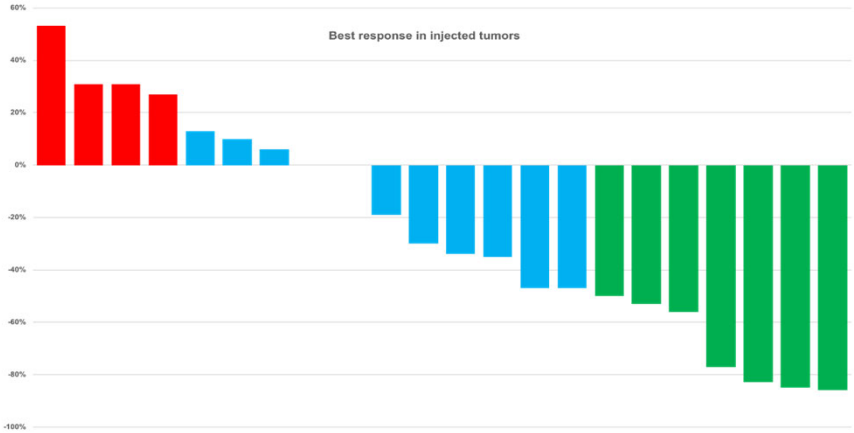
B2: Cohort 1 → ⋯ → Arm B2 MTD / RP2D

- **Population:** HLA-A*02:01 positive and have a PRAME-positive advanced solid tumor
- **Study intervention:**
  - IMC-F106C administered Q1W at escalating doses, starting at 0.3 mcg
  - Checkpoint inhibitors administered per label (eg, atezolizumab 1200 mg Q3W, pembrolizumab 200 mg Q3W)
- **Sample size:**
  - Phase 1 cohorts initially enroll 3-6; may expand to maximum of n=10 to inform dose-escalation decisions
  - Option for biomarker cohorts (maximum 12 / cohort) at dose levels with potential clinical activity
  - Option to enroll up to 12 additional participants in Arm B at the MTD/RP2D
  - Phase 2: Simon 2-stage; enroll 9 initially and expand to total n=24 if at least 1 response

Percutaneous hepatic PV-10







- Enrolling checkpoint inhibitor refractory patients
- Can continue checkpoint inhibitor while receiving PV-10

Preclinical signals

1. **HCQ + MEK inhibition**

   - McMahon et al., *CCR* 2020

2. **HDACi / Hypomethylating agents + MEK inhibition**

   - Smalley et al., *CCR* 2019 *PCMR* 2020

3. **LAG3**

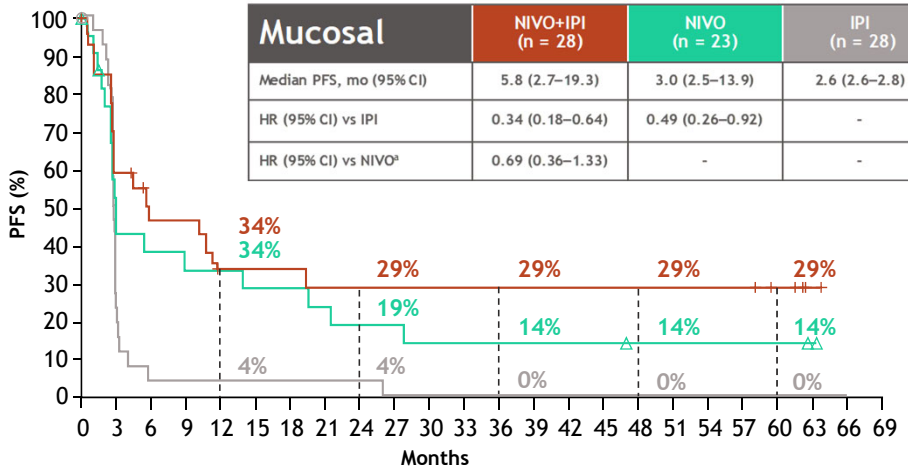
   - Harbour et al., *Nat Commun* 2020

Mucosal Melanoma

…in a flash

Mucosal Melanoma from CheckMate-067

Progression-Free Survival

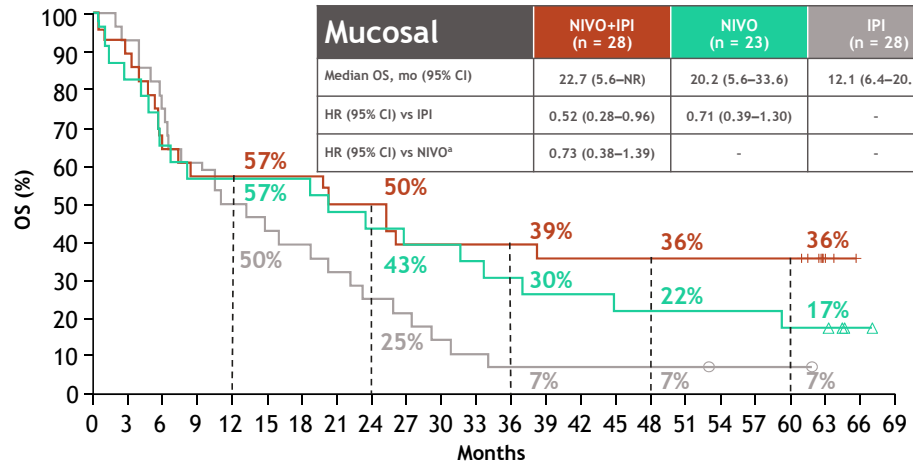


Mucosal	NIVO+IPI (n = 28)	NIVO (n = 23)	IPI (n = 28)
Median PFS, mo (95% CI)	5.8 (2.7–19.3)	3.0 (2.5–13.9)	2.6 (2.6–2.8)
HR (95% CI) vs IPI	0.34 (0.18–0.64)	0.49 (0.26–0.92)	-
HR (95% CI) vs NIVO[a]	0.69 (0.36–1.33)	-	-

Patients at risk:

NIVO+IPI	28	16	11	11	7	7	7	6	6	6	6	6	6	6	6	6	6	6	6	4	1	0	0
NIVO	23	9	8	7	7	6	6	5	4	4	3	3	3	3	3	3	2	2	2	2	2	1	0	0
IPI	28	5	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Overall Survival



Mucosal	NIVO+IPI (n = 28)	NIVO (n = 23)	IPI (n = 28)
Median OS, mo (95% CI)	22.7 (5.6–NR)	20.2 (5.6–33.6)	12.1 (6.4–20.2)
HR (95% CI) vs IPI	0.52 (0.28–0.96)	0.71 (0.39–1.30)	-
HR (95% CI) vs NIVO[a]	0.73 (0.38–1.39)	-	-

Patients at risk:

NIVO+IPI	28	25	18	17	16	16	16	14	14	11	11	11	11	10	10	10	10	10	10	10	2	0	0
NIVO	23	19	15	13	13	13	13	11	10	9	9	8	7	6	6	5	5	5	5	5	4	4	1	0
IPI	28	26	21	16	14	12	11	9	7	6	4	3	2	2	2	2	2	2	1	1	1	0	0	0

PFS, median	Nivo + Ipi	Nivo	Ipi
Mucosal	5.8 (2.7-19.3)	3.0 (2.5–13.9)	2.6 (2.6-2.8)
Cutaneous	11.5 (8.7-19.3)	6.9 (5.1-10.2)	2.9 (2.8-3.2)

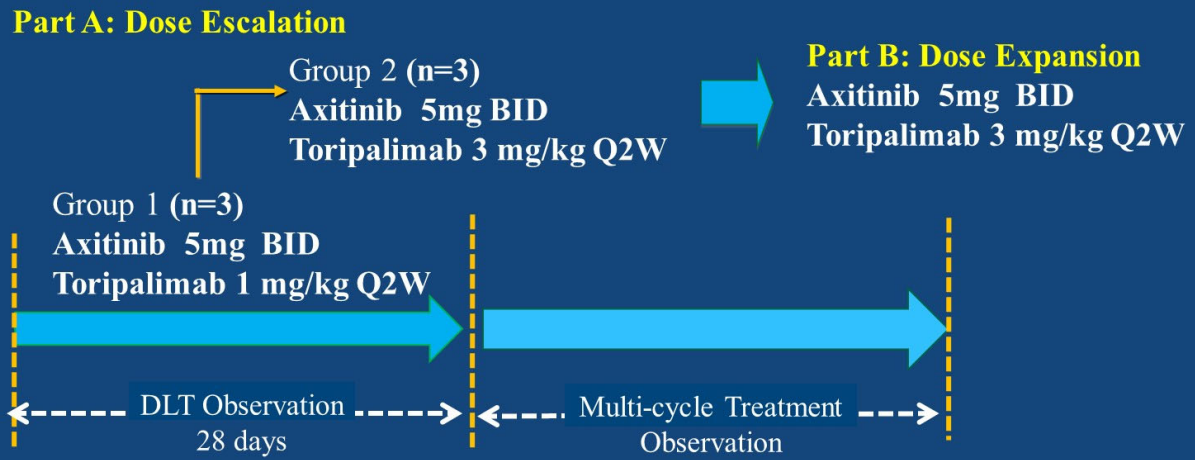
OS, median	Nivo + Ipi	Nivo	Ipi
Mucosal	22.7 (5.6-NR)	20.2 (5.6-33.6)	12.1 (6.4-20.2)
Cutaneous	NR (38.2-NR)	36.9 (28.2-58.7)	19.9 (16.8-24.6)

Derived from Shoushtari AN et al., ASCO 2019

Phase 1b: Toripalimab (IgG4 mAb against PD-1) with axitinib in metastatic mucosal melanoma

Study Design

- Two part (part A involved dose escalation, and part B involved cohort expansion)
- ClinicalTrials.gov identifier:NCT03086174

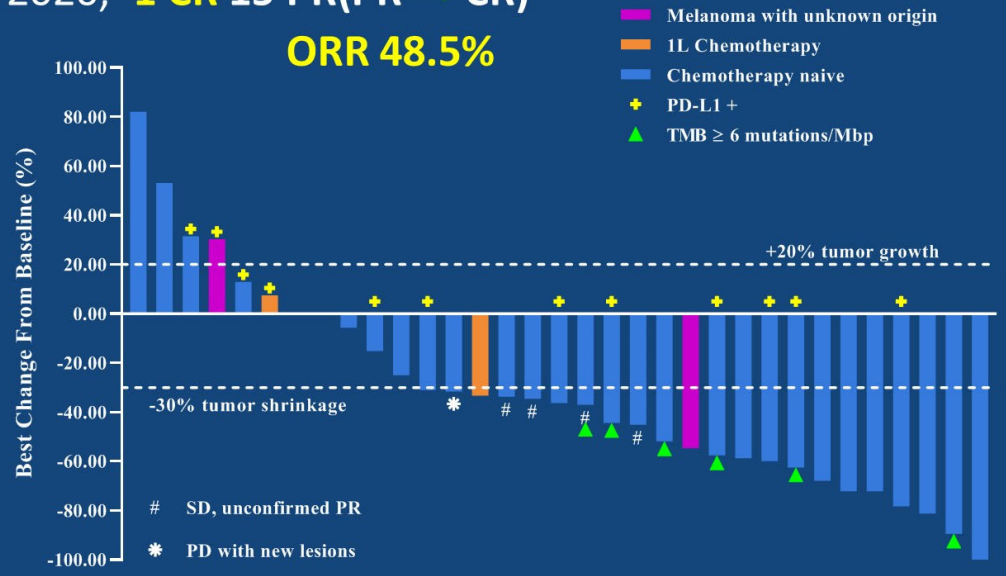


Promising activity

Updated ORR

- By May 02, 2020, **1 CR 15 PR(PR⟶ CR)**

ORR 48.5%



Abbreviations: ORR, Objective Response Rate; CR, Complete Response; PR Partial Response; SD, Stable Disease.

Mucosal melanoma future investigations

1. Neoadjuvant therapy
2. Combination IO with VEGF, multikinase inhibitors
3. VEGF + Chemotherapy

Objectives

1. **Describe current and completed experimental trials in uveal melanoma and mucosal melanoma**

2. **Explore emerging preclinical data and future directions in rare melanomas**

Thank you

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MD Anderson Cancer Center

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