The Role of Immunotherapy in Gastrointestinal Cancer

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Conflicts

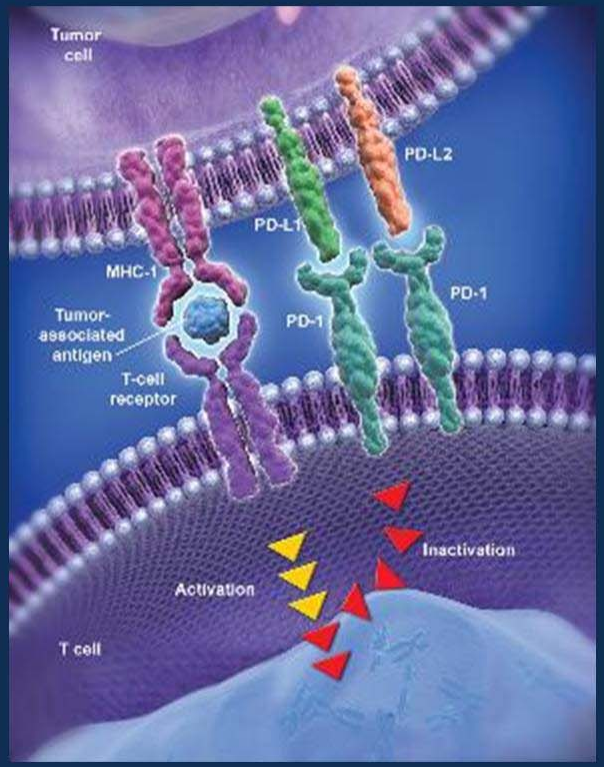
Genentech/Roche

Research Funding

Esophageal and Gastric Cancer

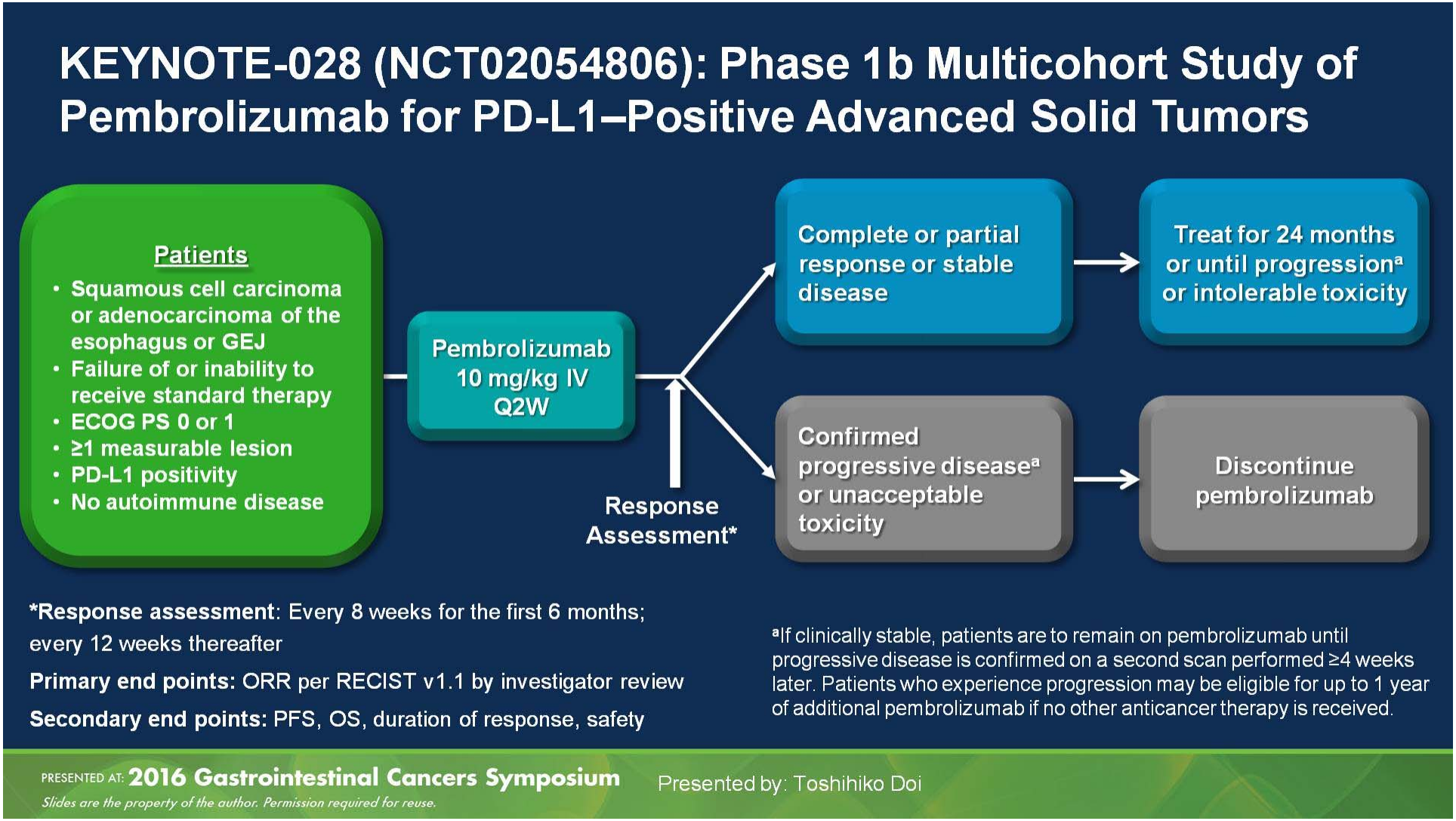
PD-1 and Pembrolizumab

- Pembrolizumab is an anti–PD-1 antibody that helps to restore antitumor immune surveillance
- Approved in several countries for the treatment of advanced melanoma, and, in the US, for metastatic, PD-L1–positive NSCLC[1]
- Rationale for immunotherapy in esophageal cancer
  - PD-L1 frequently overexpressed in esophageal cancer[2,3] and may be associated with poor prognosis[3,4]



1. KEYTRUDA® (pembrolizumab) for injection, for intravenous use. Whitehouse Station,NJ: Merck & Co., Inc, 2014-2015; 2. The Cancer Genome Atlas Research Network. *Nature*. 2014;513:202-09. 3. Chen L et al. *Int J Clin Exp Pathol*. 2014;7:6015-23. 4. Ohigashi Y et al. *Clin Cancer Res*. 2005;11:2947-53.

Cohort Expansion SCC or AdenoCa of Esophagus/GEJ: PD-L1 +



Positive PD-L1 Expression= > 1% T/I cells or positive bands in stroma

Presented By Toshihiko Doi at ASCO GI 2016

Expected AEs

Adverse Events

Treatment-Related AEs	N = 23 n (%)
Any-grade	9 (39)
Grade 3	4 (17)
Decreased appetite	
Grade 1-2	2 (9)
Grade 3	1 (4)
Decreased lymphocytes[a]	
Grade 3	2 (9)
Rash	
Grade 1-2	2 (9)
Liver disorder, grade 3[a]	1 (4)
Pruritic rash, grade 3	1 (4)

[a]Occurred in the same patient.

AEs of Special Interest	N = 23 n (%)
Any	4 (17)
Hypothyroidism (both grade 2)	2 (9)
Adrenal insufficiency (grade 2)	1 (4)
Pruritic rash (grade 3)	1 (4)

- Median follow-up duration: 7.1 months (range, 1.3-19.4)
- No treatment-related deaths or discontinuations

Data cutoff date: November 4, 2015

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ORR: 29% SCC and 40% for AdenoCA

Antitumor Activity (RECIST v1.1, Investigator Review)

Best Overall Response	n (N = 23)	%	95% CI
ORR	7	30	13-53
Complete response	0	0	0-15
Partial response	7	30	13-53
Stable disease	2	9	1-28
Progressive disease	13	56	34-77

- ORR by histology
  - 29% for squamous cell carcinoma (5 of 17)
  - 40% for adenocarcinoma (2 of 5)

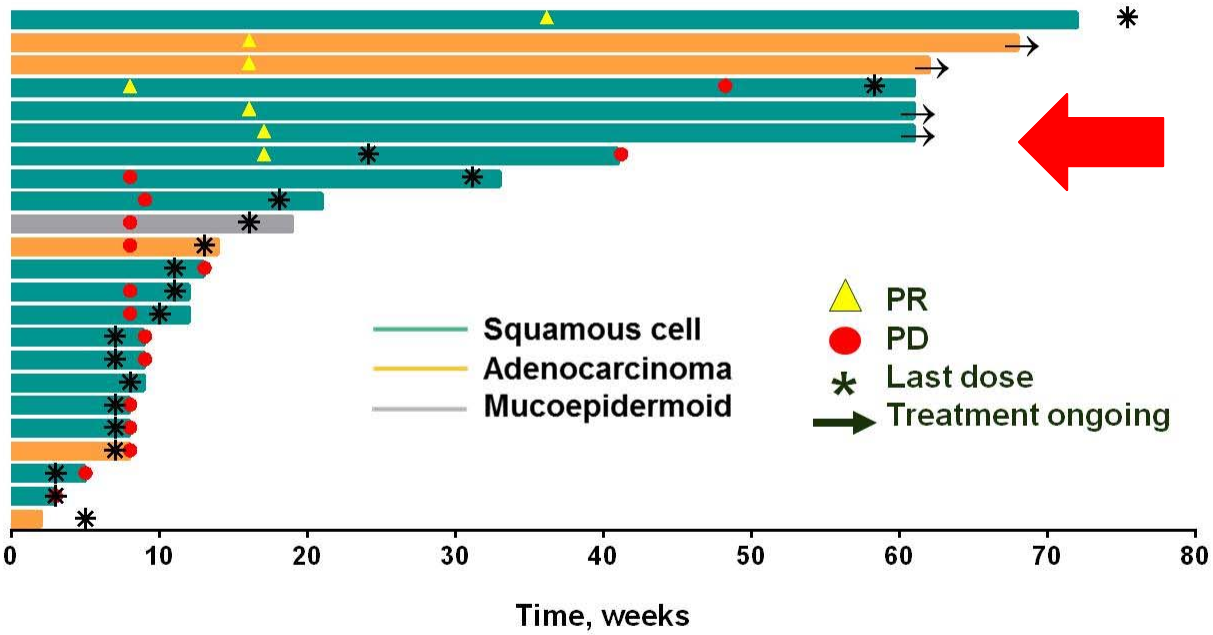
Only confirmed responses are included.
Data cutoff date: November 4, 2015.

PRESENTED AT: 2016 Gastrointestinal Cancers Symposium

Presented by: Toshihiko Doi

Note that longer duration on treatment largely corresponds to OR

Treatment Exposure and Response Duration
(RECIST v1.1, Investigator Review)

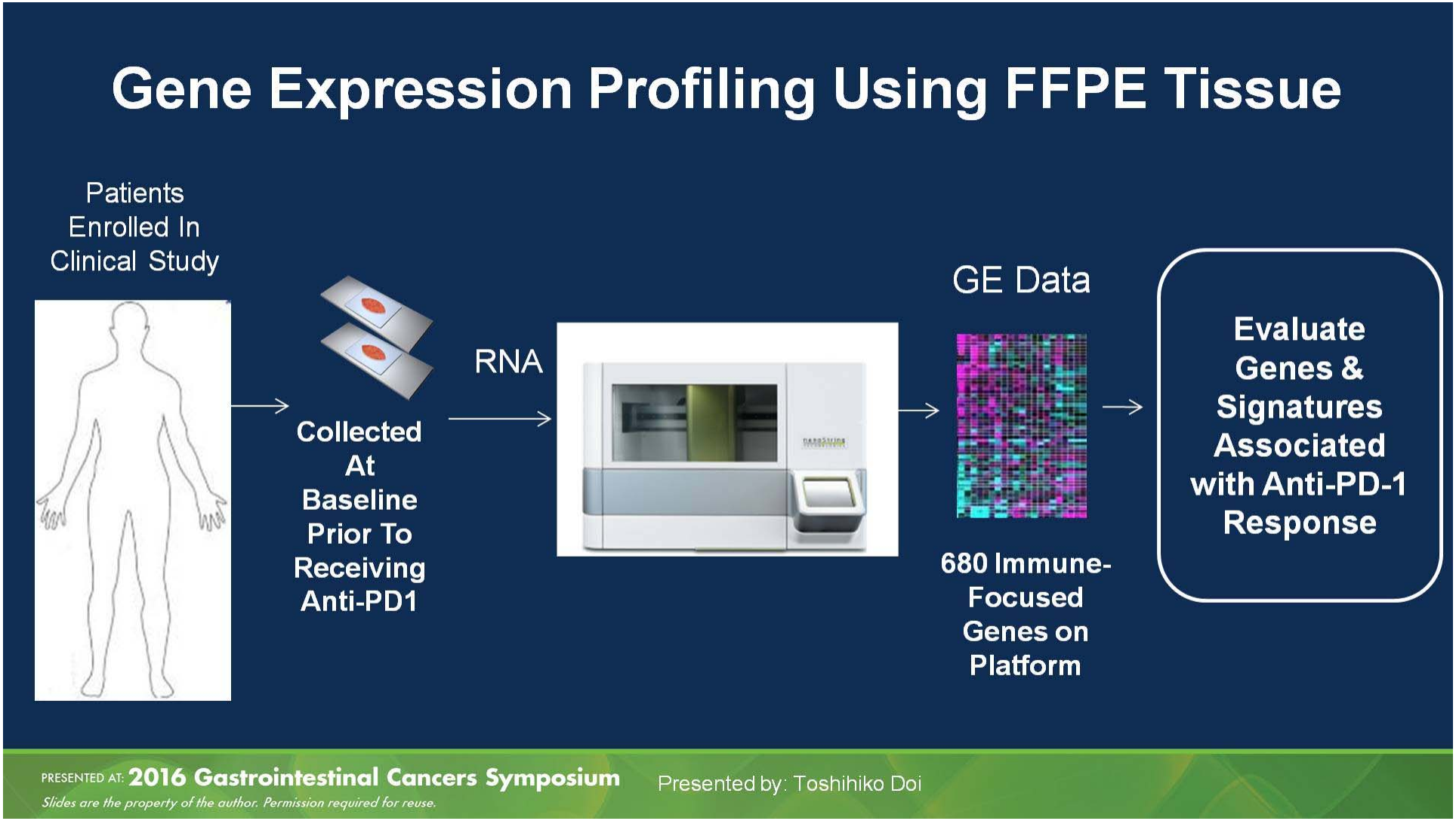


Time to response
- Median: 3.7 months
- Range: 1.8-8.3 months

Duration of response
- Median: not reached
- Range: 5.5-11.8+ months

Data cutoff date: November 4, 2015

Interesting but question of whether primary *versus* metastatic tissue best for this?



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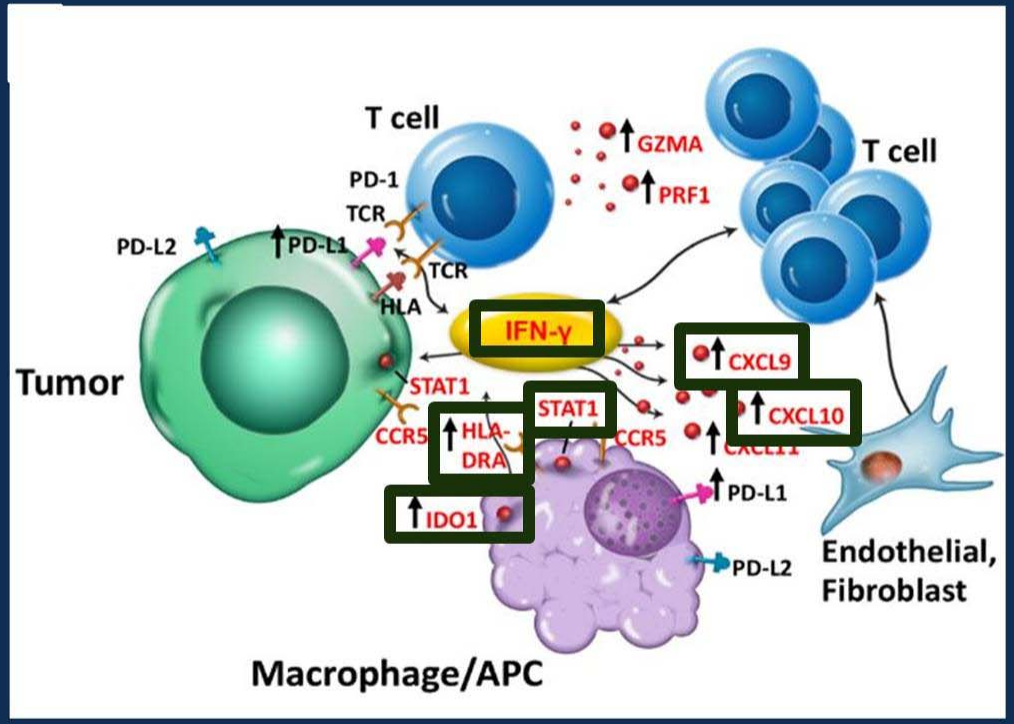
ASCO GI 2016

Correlation between signature and PFS hypothesis generating (N=23)

Interferon-Inflammatory Gene Expression Signature



The 6-gene signature captures part of a complex signaling pathway related to pre-existing IFN-γ adaptive immune response within the tumor microenvironment

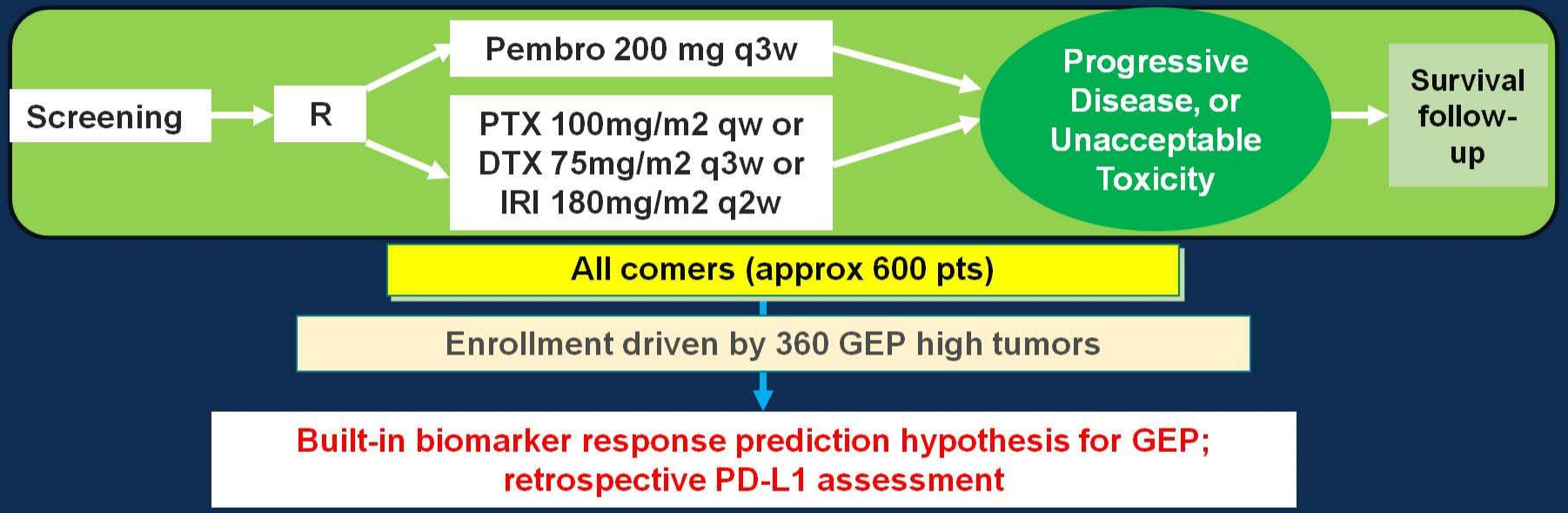
- *IDO1*
- *CXCL10*
- *CXCL9*
- *HLA-DRA*
- *STAT1*
- *IFN-γ*

Adapted from *J Clin Oncol* 33, 2015 (suppl; abstr 3001)

- **The gene signature was derived from melanoma test set**
- **Despite some potential weaknesses in approach we need more of these studies to justify toxicities and expense of IT**

Further Validation of GEP 2nd line: Primary versus Metastatic?

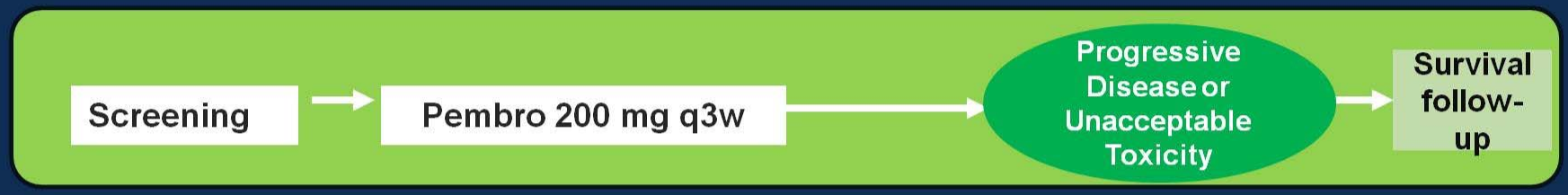
KN181: Pembrolizumab Monotherapy vs Physicians' Choice of Docetaxel, Paclitaxel or Irinotecan in 2L Esophageal Cancer



- Co-primary endpoint: OS and PFS / Secondary endpoints: ORR and DOR
- Scans will be performed every 9 weeks
- Sites: Approx. 600 patients total, 150 sites in 32 countries
  - In the US, 16 sites are selected with 74 patients allocated

Target= 100 patients, 3rd line

KN180: Pembrolizumab Monotherapy in 3L Esophageal Cancer



- Confirmed RECIST 1.1 measurable disease by central imaging vendor prior to treatment allocation
- Imaging every 9 weeks
- Retrospective biomarker response prediction assessment for GEP and PD-L1
- Sites:
  - Approx 100 patients, 9 countries, 60 sites total
  - In the US, currently 24 sites are selected with 85 patients allocated

Questions: 1) Site or timing of tissue acquisition important?
2) Will PD-L1 or GEP "trump" the other or will they be additive in refining patient selection?

Keynote-012 Gastric Cancer/GEJ PD-L1+ ORR 22-33%

Best Overall Response, RECIST v1.1

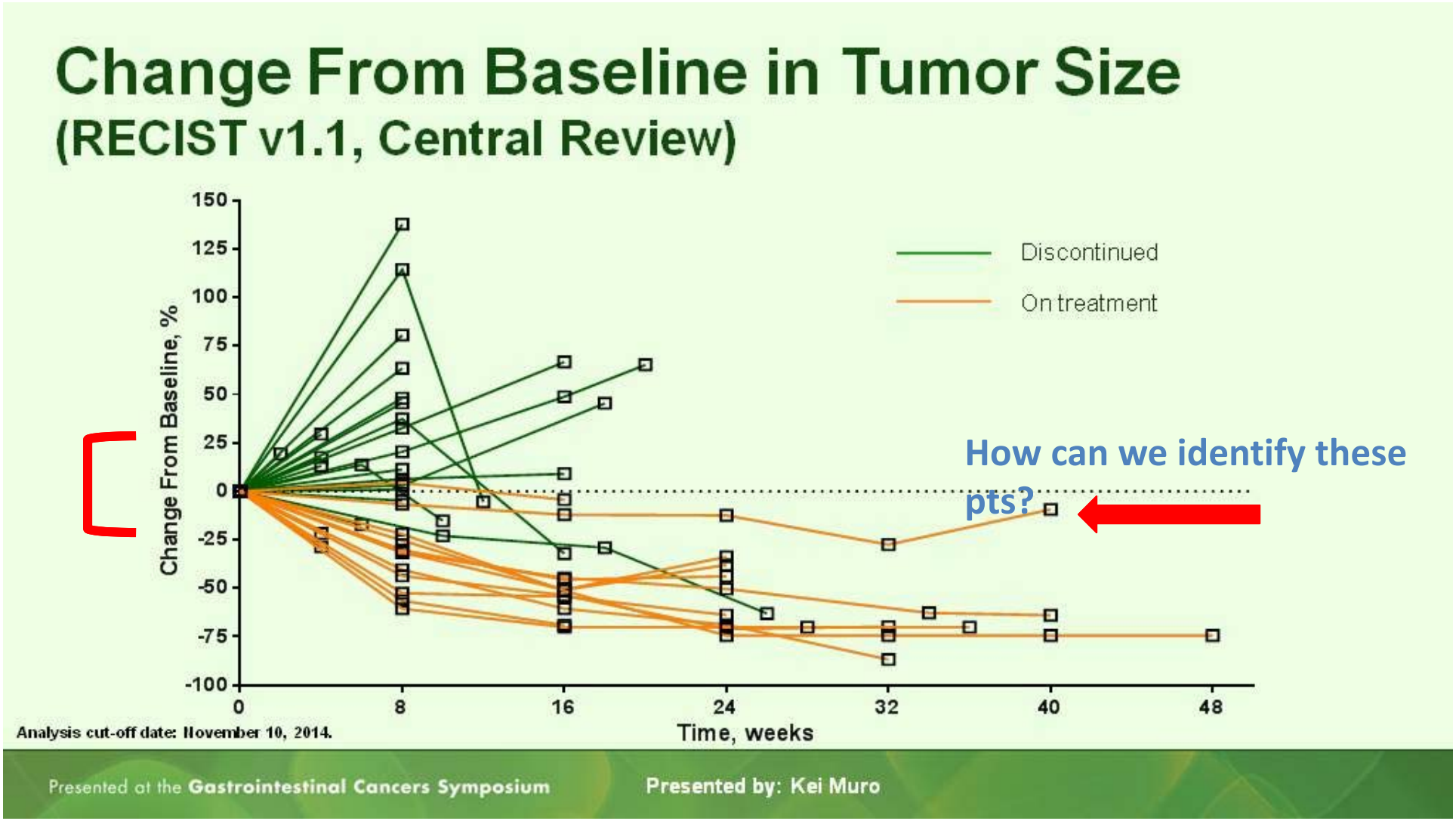
	Central Review N = 36[a]	Investigator Review N = 39
ORR,[b] % (95% CI)	22.2 (10.1, 39.2)	33.3 (19.1, 50.2)
Best overall response, n (%)		
Complete response[b]	0	0
Partial response[b]	8 (22.2)	13 (33.3)
Stable disease	5 (13.9)	5 (12.8)
Progressive disease	19 (52.8)	21 (53.8)
No assessment[c]	1 (2.8)	—
Not determined[d]	3 (8.3)	—

[a]Patients with measurable disease per RECIST v1.1 by central review at baseline. [b]All responses were confirmed. [c]Patient with centrally evaluable disease at baseline who discontinued therapy due to clinical progression before the first scan. [d]Patients with centrally evaluable disease at baseline for whom best overall response could not be determined.
Analysis cut-off date: November 10, 2014.

Presented at the Gastrointestinal Cancers Symposium Presented by: Kei Muro

Presented By Kei Muro at 2015 Gastrointestinal Cancers Symposium

Most patients with prolonged treatment duration exhibited OR, but…



Gastric Cancer/GEJ Nivolumab

Study Design

Gastric Cancer[a] (N = 163)

- Nivolumab 3 mg/kg IV Q2W (n = 59)
- Nivolumab 1 mg/kg + Ipilimumab 1 mg/kg IV Q3W for 4 cycles[b] (n = 3)
- Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg IV Q3W for 4 cycles[b] (n = 49)
- Nivolumab 3 mg/kg + Ipilimumab 1 mg/kg IV Q3W for 4 cycles[b] (n = 52)

Primary Endpoint[c]
- Objective response rate

Secondary Endpoints
- Adverse events (AEs)
- Overall survival (OS), OS rate
- Progression-free survival (PFS), PFS rate
- Duration of response

Exploratory Endpoints
- Pharmacokinetics
- Pharmacodynamics
- Immunogenicity
- Biomarkers

Inclusion Criteria[d]
- ≥18 years of age
- Histologically confirmed tumor of the lower esophagus, gastroesophageal junction, or stomach
- Radiologically confirmed measurable disease
- Progressive or chemo-refractory disease
- Received ≥1 prior therapy
- ECOG performance status of 0 or 1
- No autoimmune disease
- No prior vaccine or immune checkpoint inhibitor therapy

[a] Cohorts were enrolled sequentially in the order shown.
[b] Followed by single agent nivolumab 3 mg/kg IV Q2W.
[c] Follow-up continued until disease progression and/or resolution of AEs, after which they were followed every 3 months for survival. Follow up time ranged from 5-24 months.
[d] PD-L1 positivity was not mandated for inclusion.
ECOG, Eastern Cooperative Oncology Group; IV, intravenous; Q2W, every 2 weeks; Q3W, every 3 weeks.

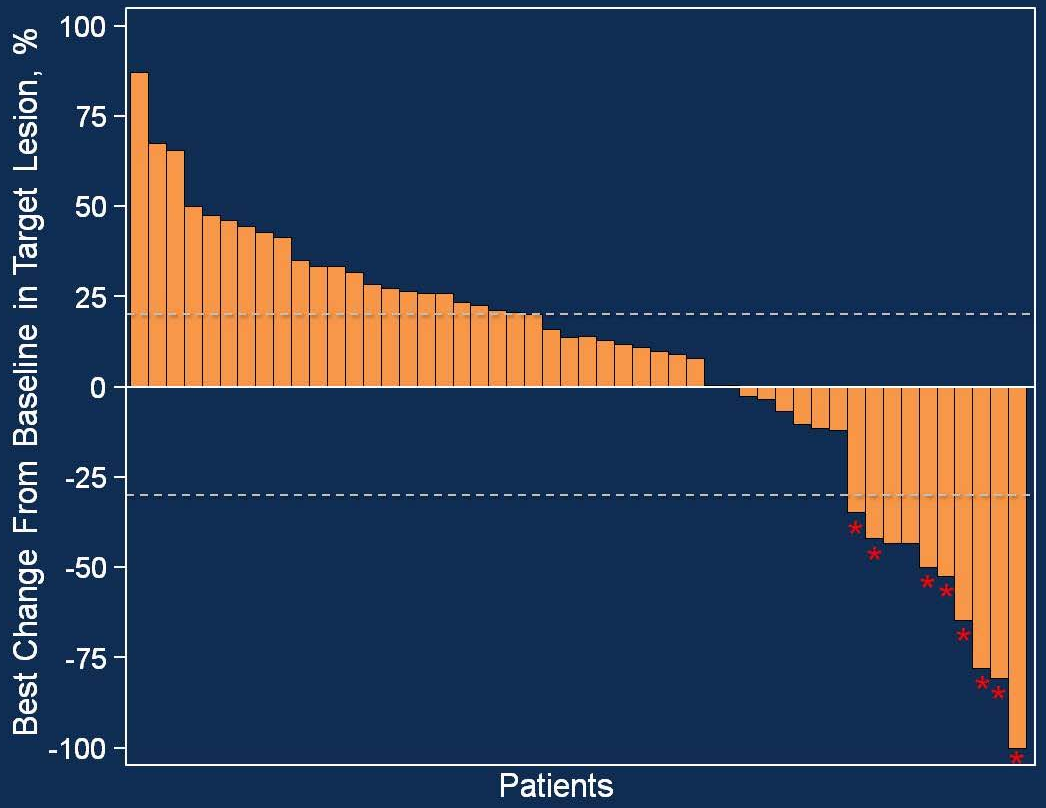
PRESENTED AT: 2016 Gastrointestinal Cancers Symposium

Patients were required to have received ≥ 1 prior regimen; most patients received ≥2 regimens

Presented By Dung Le at ASCO GI 2016

ORR=14%

Best Reduction in Target Lesion Size



* patients with a confirmed response.

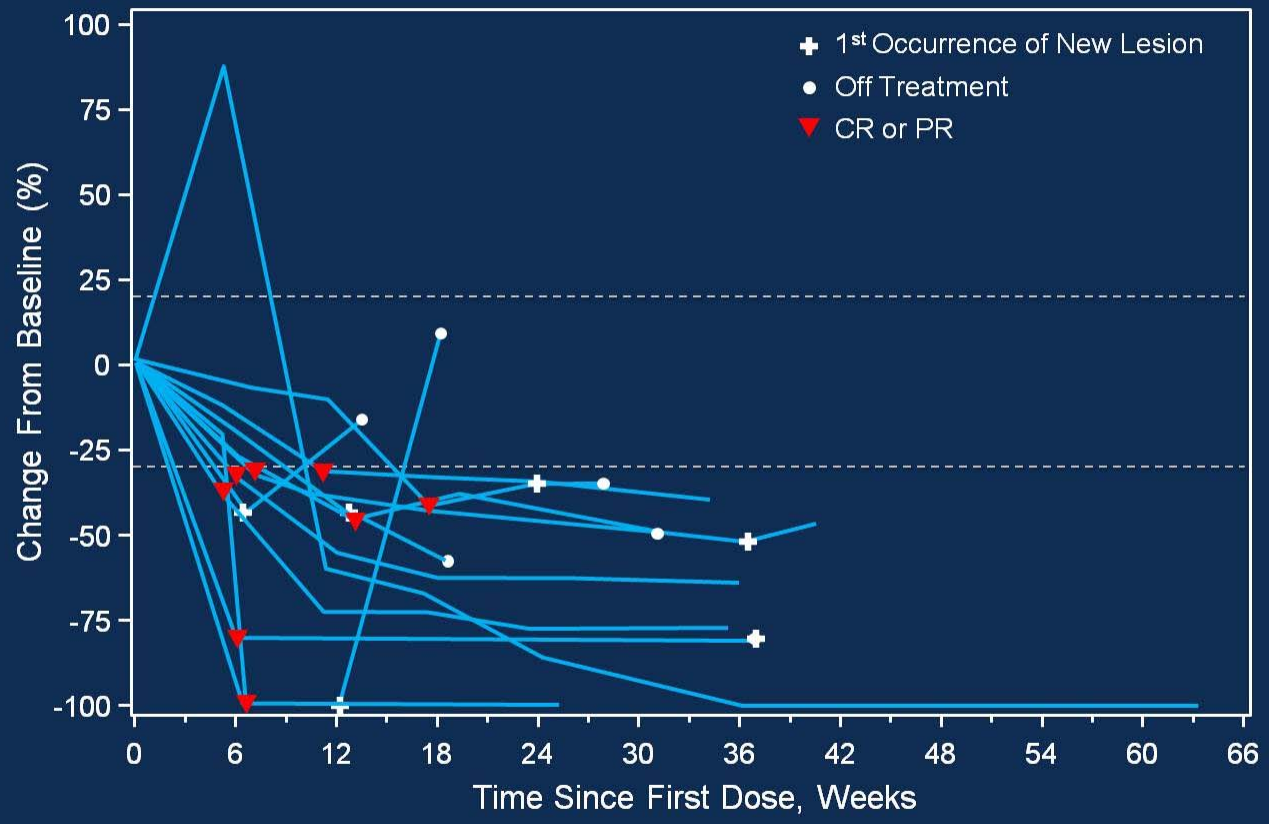
- 8/59 patients had objective responses
- Median time to response was 1.6 months (range: 1.2–4.0)
- Median duration of response was 7.1 months (95% CI, 0.0+ to 13.2)

+ indicates censored observations included.

Presented By Dung Le at ASCO GI 2016

Most responses occurred in 1st 12 weeks after initiation of therapy

Change From Baseline in Target Lesions Over Time



PRESENTED AT: 2016 Gastrointestinal Cancers Symposium

CR, complete response; PR, partial response.

Presented By Dung Le at ASCO GI 2016

Other Gastric/GEJ Studies

- **Checkmate-032**: Phase I/II Nivo + Ipi (unselected): Nivo 1 mg/kg and Ipi 3mg/kg (45 pts) **ORR=12%**; OS=6.9 months; 12 month OS=34%. Expected AEs, *Phase III planned*
- **Nivolumab 2nd line** N=64 (Kojima et al/ASCO 2016): Second-line phase II study: **ORR 17.2%**; mOS=10.78 mos; mPFS= 1.51 months.

Other Enrolling Gastric/GEJ Studies

- **Keynote-180**: Phase II **3rd** line pembro monotherapy (unselected): target=100 pts
- **Keynote-062:** Phase III **1st** line pembro alone versus 5FU/Cis versus pembro + 5FU/Cis (**PD-L1+**): target=750 1:1:1 (Keynote-059 demonstrated safety of combo)
- **Keynote-061**: Phase III **2nd** line pembro versus paclitaxel (unselected): target=720 pts
- **Keynote-181**: Phase III **2nd** line pembro versus clinician's choice (unselected): target=600 pts
- **Javelin Gastric 300 trial**: Phase III **3rd** line avelumab + BSC versus BSC + chemo (unselected): target=330 pts

Upper GI Cancers and IT Comments

- Clearly IT is active in upper GI cancers, but more evidence is needed to establish benefit beyond OR
- Ongoing trials will establish activity in various lines of therapy
  - One could question whether in patients with initial benefit, IT should be incorporated into all lines of therapy?
- In my view, most important question will be the role of PD-L1 positivity in patient selection in conjunction with other biomarkers such as GEP
- Perhaps more *mechanism-based* combinations are needed to achieve better long-term disease control

Pancreatic Cancer

Pancreatic Studies

- **Randomized phase 2 of BTK inhibitor acalabrutinib alone or with pembro**: Reasonably well tolerated; ORR 7% in combo arm and some hint of efficacy in patients with familial panc or breast cancer.
- **Ongoing:** Combination trial of nivo with gem/abraxane

Bottom line: Immunotherapy results in this disease continue to be disappointing and indicate we need better methods of patient selection and/or better mechanism-based combination strategies

HCC

Nivolumab in HCC

Draft

4012

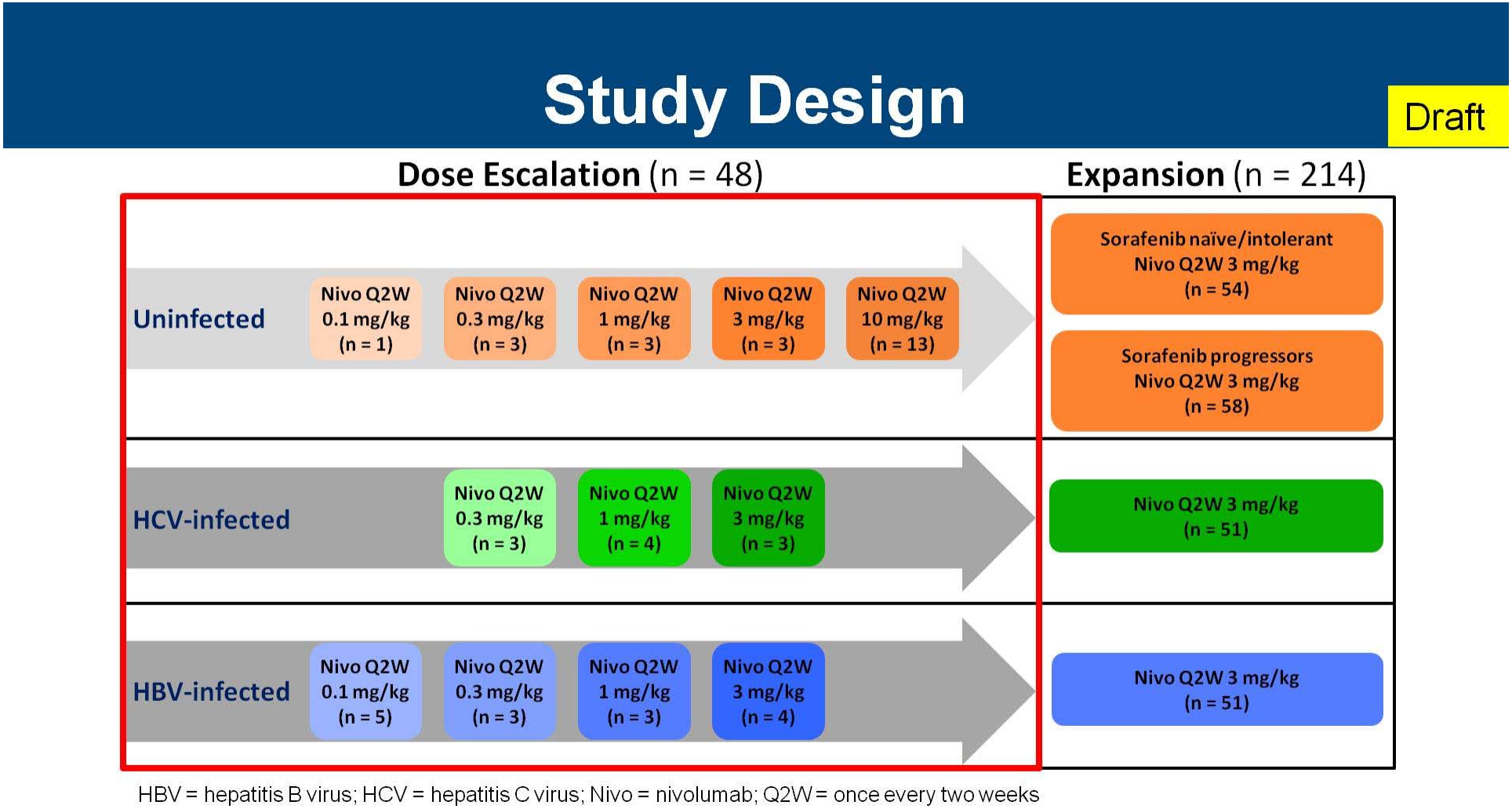
Phase 1/2 Safety and Antitumor Activity of Nivolumab in Patients with Advanced Hepatocellular Carcinoma: Interim Analysis of the CheckMate-040 Dose Escalation Study

Anthony B. El-Khoueiry,[1] Bruno Sangro,[2] Thomas Yau,[3] Todd S. Crocenzi,[4] Theodore Hobart Welling III,[5] Winnie Yeo,[6] Akhil Kapopra,[7] Jeffrey Anderson,[8] Christine dela Cruz,[8] Lixin Lang,[8] Jaclyn Neely,[8] Ignacio Melero[2]

[1]University of Southern California Norris Comprehensive Cancer Center, Los Angeles, CA, USA; [2]Clinica Universidad de Navarra and CIBERehd, Pamplona, Spain; [3]University of Hong Kong, Hong Kong, China; [4]Providence Cancer Center; Portland, OR, USA; [5]University of Michigan, Ann Arbor, MI, USA; [6]Chinese University of Hong Kong, Hong Kong; [7]Johns Hopkins Singapore International Medical Centre, Singapore; [8]Bristol-Myers Squibb, Princeton, NJ, USA

PRESENTED AT: ASCO ANNUAL MEETING '16

Interesting design to address several patient subsets



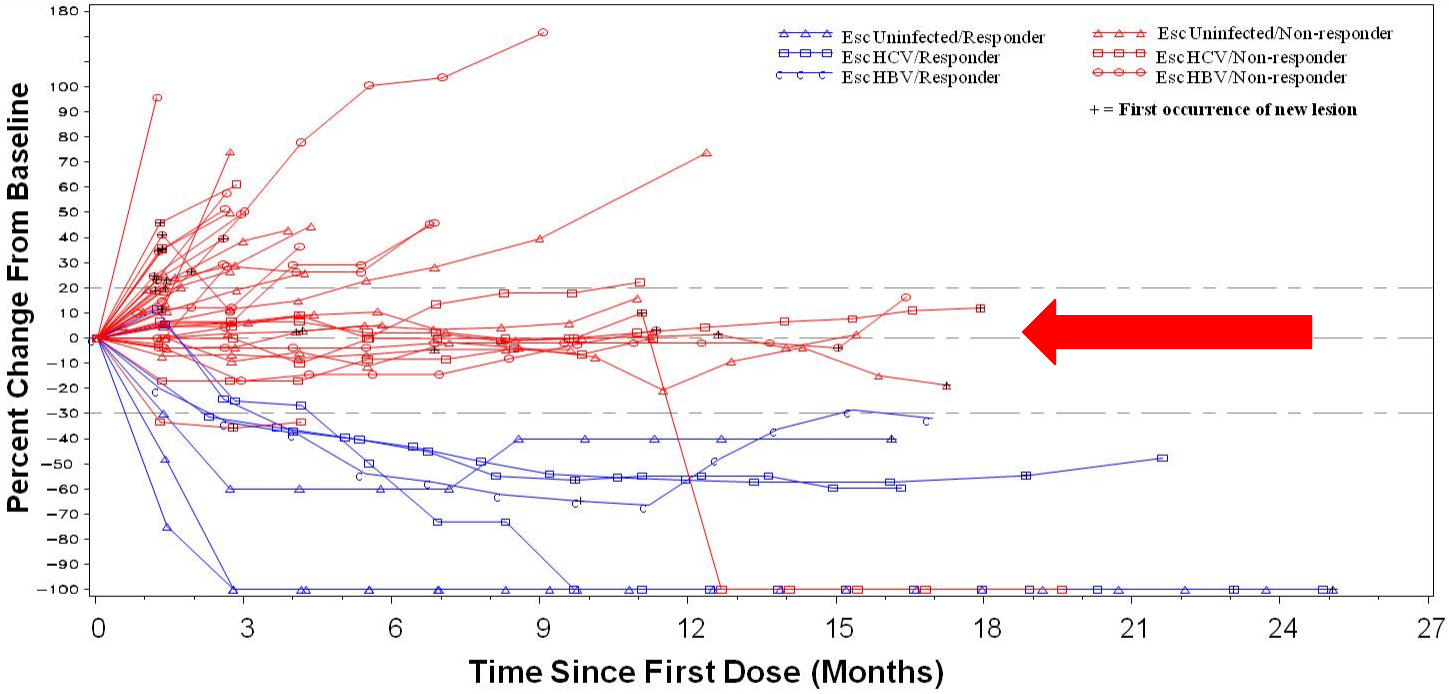
HBV = hepatitis B virus; HCV = hepatitis C virus; Nivo = nivolumab; Q2W = once every two weeks

Intriguing results in a disease where current therapy is insufficient and not well tolerated

Figure will be redrawn with color coding consistent with previous slide (uninfected = orange; HBV = blue; HCV = green)

Individual Tumor Burden Percent Change from Baseline

Draft



- Responses occurred early in treatment, stable responses occurred out to 12–18 months, and in 1 patient with CR, response extended out to beyond 24 months
  - **In contrast to UGI, a subset of HCC patients with best response=SD appeared to have prolonged disease control.**
  - **How can we identify these patients prior to IT and induce regression?**

Colorectal Cancer
Anal Cancer

Study Design

Colorectal Cancers

Cohort A
Deficient in Mismatch Repair (n=28)

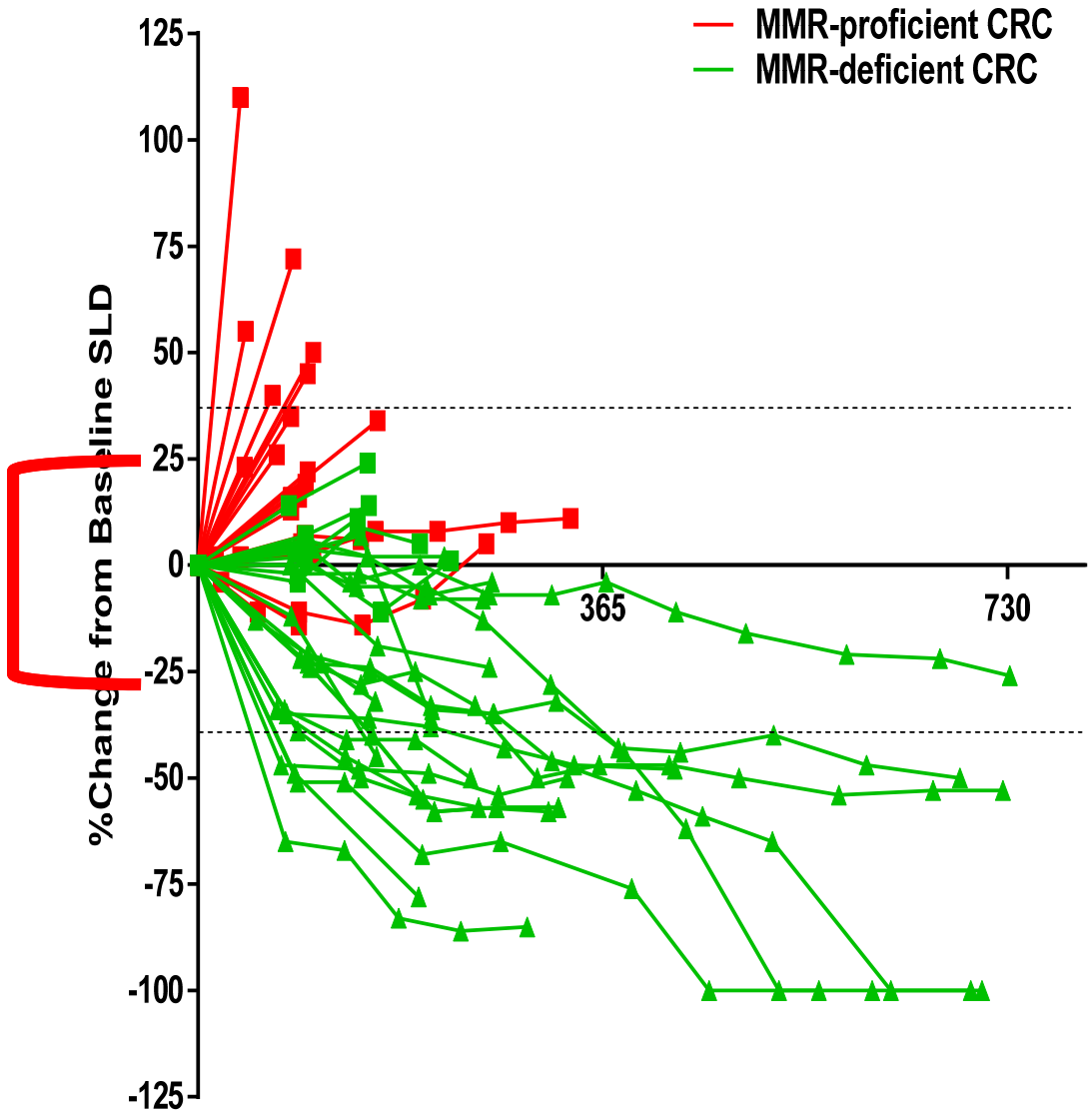
Cohort B
Proficient in Mismatch Repair (n=25)

Non-Colorectal Cancers

Cohort C
Deficient in Mismatch Repair (n=30)

- Anti-PD1 (Pembrolizumab) – 10 mg/kg every 2 weeks
- Here we report and update from the original 13 CRC Cohort A patients reported at ASCO 2015

Radiographic Response



Type of Response-no (%)	MMR-deficient CRC n=28	MMR-proficient CRC n=25
Complete Response	3 (11)	0 (0)
Partial Response	13 (46)	0 (0)
Stable Disease (Week 12)	9 (32)	4 (16)
Progressive Disease	1 (4)	11 (44)
Not Evaluable[1]	2 (7)	10 (40)
Objective Response Rate (%)	16 (57)	0 (0)
95% CI	39 - 73	0 -13
Disease Control Rate (%)	25 (89)	4 (16)
95% CI	73 - 96	6 - 35
Median Follow Up (mos)	9.3	6

[1]Patients were considered not evaluable if they did not undergo a 12 week scan

Clinical activity and safety of cobimetinib and atezolizumab (anti-PD-L1) in colorectal cancer

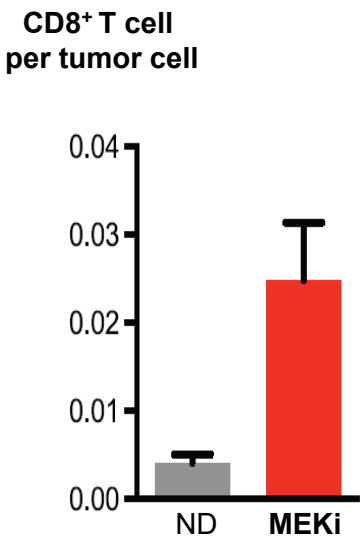
Johanna Bendell,[1] Tae Won Kim,[2] Boon Cher Goh,[3] Jeffrey Wallin,[4] Do-Youn Oh,[5] Sae-Won Han,[5] Carrie Lee,[6] Matthew D. Hellmann,[7] Jayesh Desai,[8] Jeremy Lewin,[9] Benjamin J. Solomon,[10] Laura Q. Chow,[11] Wilson H. Miller Jr,[12] Justin Gainor,[13] Keith Flaherty,[13] Jeffrey Infante,[1] Meghna Das Thakur,[4] Paul Foster,[4] Edward Cha,[4] Yung-Jue Bang[5]

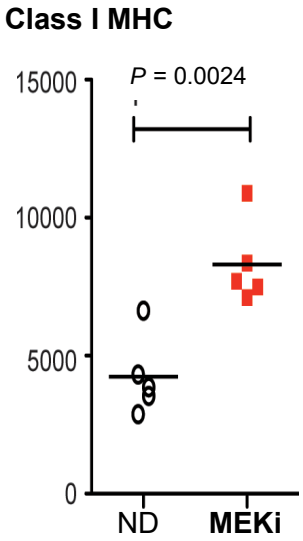
[1]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN; [2]Asan Medical Center, Seoul, South Korea; [3]Cancer Science Institute of Singapore, National University of Singapore, Singapore; [4]Genentech, Inc., South San Francisco, CA; [5]Seoul National University Hospital, Seoul, South Korea; [6]UNC Lineberger Comprehensive Cancer Center, University of North Carolina – Chapel Hill, North Carolina; [7]Memorial Sloan Kettering Cancer Center, New York, NY; [8]Royal Melbourne Hospital, University of Melbourne, Melbourne, VIC, Australia; [9]Princess Margaret Cancer Center, University Health Network, Toronto, ON, Canada; [10]Peter MacCallum Cancer Center, Melbourne, VIC, Australia; [11]University of Washington, Seattle, WA; [12]Segal Cancer Center and Jewish General Hospital, McGill University, Montreal, QC, Canada; [13]Massachusetts General Hospital, Boston, MA

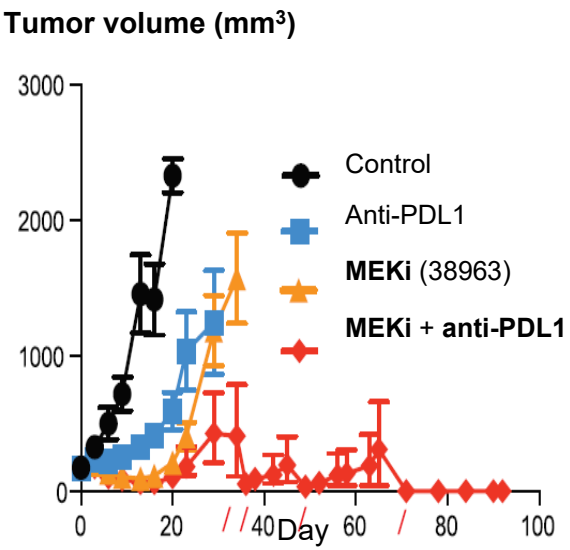
Bendell J, et al. Cobimetinib and atezolizumab in CRC. ASCO 2016

PD-L1 and MEK Inhibition: A Rational Combination

MEK inhibition alone can result in **intratumoral T-cell accumulation** and **MHC I upregulation**, and synergizes with an anti-PDL1 agent to promote **durable tumor regression**[1]



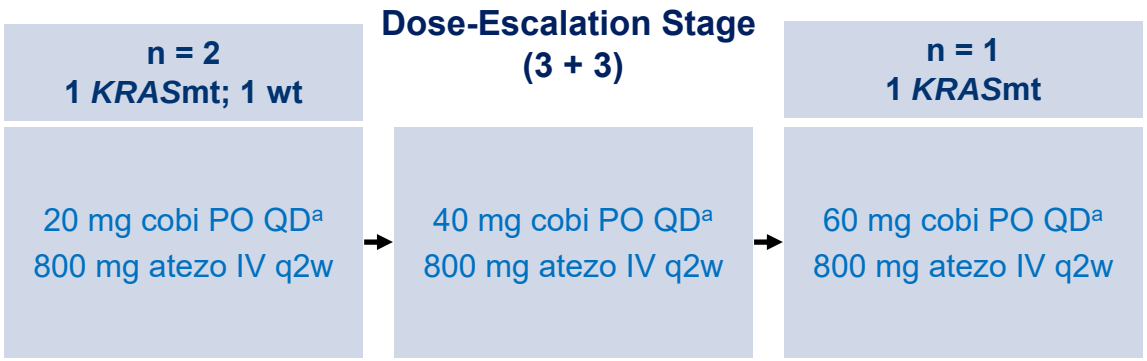




- To examine the possible benefits of MEK inhibition with an anti-PDL1 agent, we evaluated cobimetinib + atezolizumab in patients with advanced solid tumors

MHC, major histocompatibility complex; ND, no drug (vehicle alone).
CT26 (KRASmt) CRC models. 1. Ebert et al. *Immunity* 2016.

Phase Ib Dose Escalation and Cohort Expansion Study (NCT01988896)



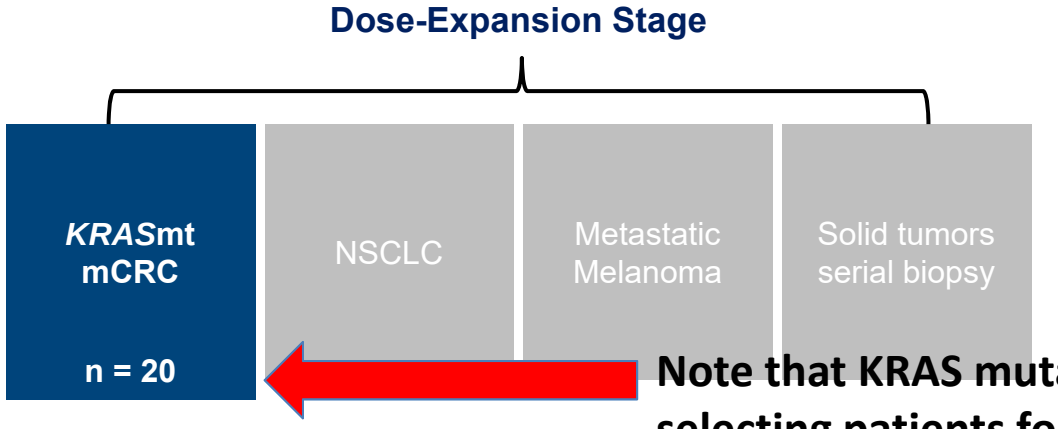
DLT window of 28 days until MTD for combination is defined

Key eligibility Criteria

- ECOG PS of 0 or 1
- Measurable disease per RECIST v1.1

Primary Objectives

Safety and clinical activity of cobimetinib + atezolizumab



Note that KRAS mutation is not very effective in selecting patients for MEK inh

[a]Cobimetinib was administered on 21 days on/7 days off dosing schedule.
atezo, atezolizumab; cobi, cobimetinib; DLT, drug limited toxicity; ECOG PS, Eastern Cooperative Oncology Group performance status; *KRAS*mt, *KRAS* mutant; MTD, maximum tolerated dose; NSCLC, non-small cell lung cancer; RECIST, Response Evaluation Criteria In Solid Tumors.

Baseline Characteristics: Heavily pretreated

Patients with CRC	(N = 23)
Median age, y	57
Range	31–69
Sex	
Male	48%
Female	52%
ECOG PS	
0	61%
1	39%
Ethnicity (Race)	
Asian	39%
White	61%

Patients with CRC	(N = 23)
Region	
Asia	35%
North America, Australia	65%
No. of prior systemic therapies	
Median	3
Range	1-5
Prior oxaliplatin and irinotecan	23 (100%)
Prior adjuvant therapy	12 (52%)
Stage of initial diagnosis	
Stage I-II	13%
Stage III	48%
Stage IV	30%

Baseline Characteristics: Low PD-L1 Expression

Patients with CRC	(N = 23)
Cancer type at diagnosis	
Colon	83%
Rectal	17%
Location of primary tumor	
Left (splenic flexure to rectum)	74%
Right (cecum to hepatic flexure)	26%
Transverse	0%
Metastatic pattern at study entry	
Liver only	0%
Liver metastases and other sites	48%
Extra-hepatic	52%

Patients with CRC	(N = 23)
KRAS	
Wild type[a]	4%
Mutant	96%
PD-L1 expression	
IC2/3	17%
IC0/1	**70%**
Unknown	**13%**
MSI status, investigator-reported	
MSI-high	0%
MSI-low or stable	30%
Unknown	70%

[a]No expanded *RAS*, *BRAF* mutations identified by next generation sequencing.

Efficacy: Confirmed Objective Response

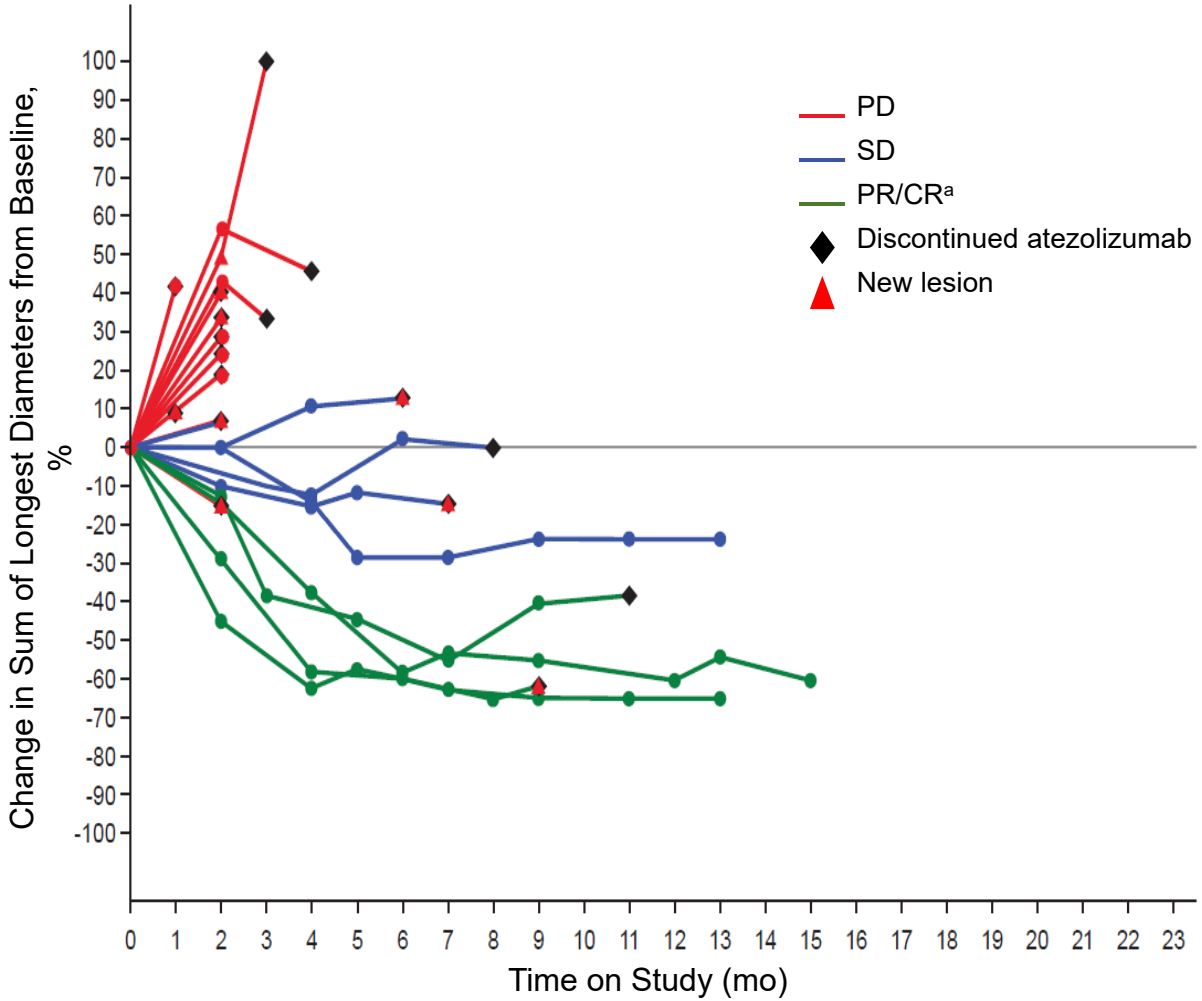
Confirmed Response per RECIST v1.1	*KRAS* mutant CRC Cohort (n = 20)	All CRC Patients (N = 23)
ORR (95% CI)	**20% (5.7, 43.7)**	**17% (5.0, 38.8)**
PR	20%	17%
SD	20%	22%
PD	50%	52%
NE	10%	9%

- Response did not correlate with PD-L1 status: IC0 (n = 2), IC1 (n = 1) and IC3 (n = 1)

This RR is clearly much better than that of current 3rd line therapy

NE, not evaluable; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease.
Efficacy-evaluable patients. Data cutoff, February 12, 2016.

Efficacy: Change in Tumor Burden



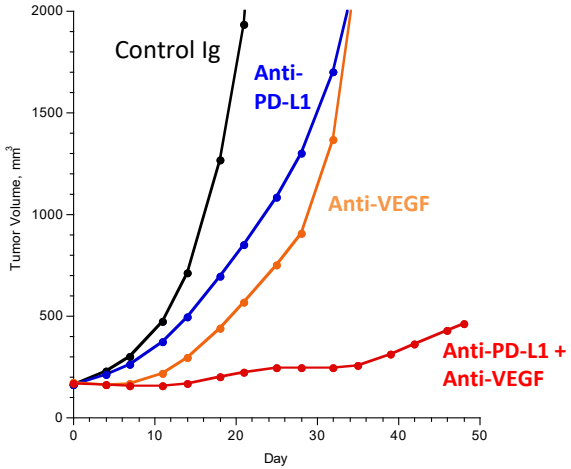
- Median duration of response was not reached (range: 5.4 to 11.1+ mo)
- Responses are ongoing in 2 of 4 responding patients

- Interesting kinetics of patients that had either rapid PD or OR, less evidence of SD
- Has been advanced to Phase III: Atezo + Cobi vs. Atezo vs. Regorafenib

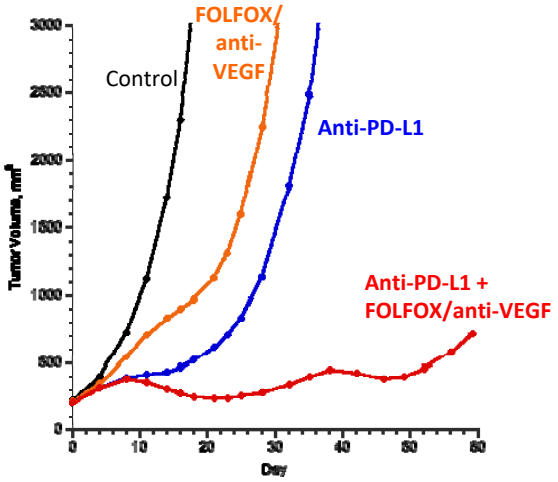
Meanwhile, back in 2012: Rationale to Combine With Bevacizumab and FOLFOX

- **Anti-VEGF has immunomodulatory properties:**
  - Increases trafficking of T cells into tumors[1-2]
  - Reduces frequency of myeloid-derived suppressor cells (MDSCs)[3]
  - Reduces suppressive cytokines and infiltrating Tregs and MDSCs[4]
  - Increases both CD8+ and CD4+ central memory T cells in combination with ipilimumab[5]
- **FOLFOX may have immunogenic effects:**
  - 5-FU reduces tumor-associated MDSCs and increases INFγ-producing CD8 tumor-infiltrating lymphocytes[6]
  - Oxaliplatin induces immunogenic cell death (calreticulin exposure, release of ATP and HMGB1)[7,8]
  - FOLFOX reduces percentage and numbers of Tregs in CRC patients[9,10]

Anti-PD-L1 + anti-VEGF activity in the Cloudman melanoma model

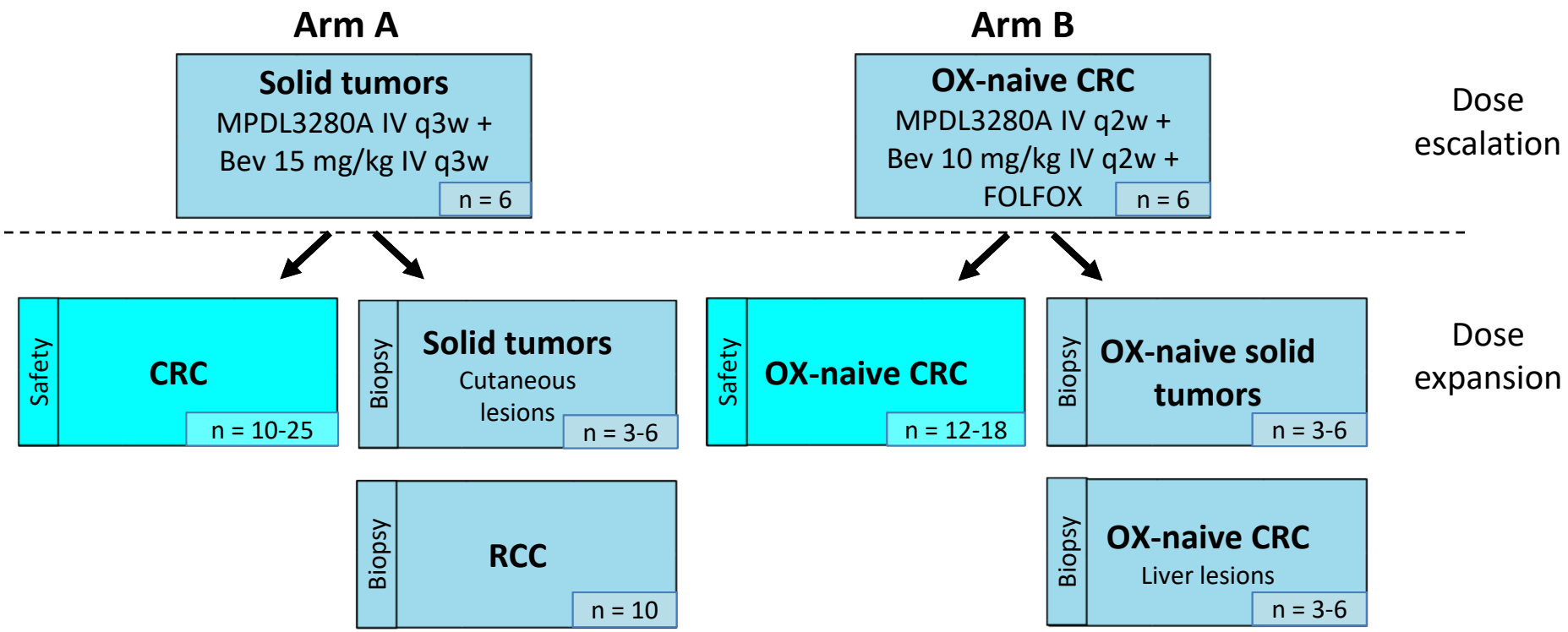


Anti-PD-L1 + FOLFOX/anti-VEGF activity in the MC38 CRC model



1. Manning. *Clin Cancer Res.* 2007. 2. Shrimrali. *Cancer Res.* 2010. 3. Kutsmartsev. *J Immunol.* 2008.
4. Roland. *PLOS One.* 2009. 5. Hodi. *J Clin Oncol. Suppl.* 2011. 6. Vincent. *Cancer Res.* 2010.
7. Michaud. *Science*. 2011. 8. Tesniere. *Oncogene.* 2010. 9. Maeda. *Anticancer Res.* 2011.
10. Correale. *J Clin Oncol.* 2005.

World's Largest Phase Ib Study: 4+ years



- Primary objectives: safety and tolerability, DLT and MTD
- Secondary objectives: ORR, DOR, PFS, PK

N numbers represent target enrollments.
Bev, bevacizumab; OX, oxaliplatin.

Summary of Responses

MPDL3280A + Bevacizumab

Indication	n	ORR
1L RCC	10	40%
CRC	13	**8%**

Minimum follow-up in Arm A: 2.1 months for 1L RCC and 1.9 months for CRC

MPDL3280A + Bevacizumab + FOLFOX

Indication	n	ORR
CRC	25	**36%**
1L CRC	18	**44%**

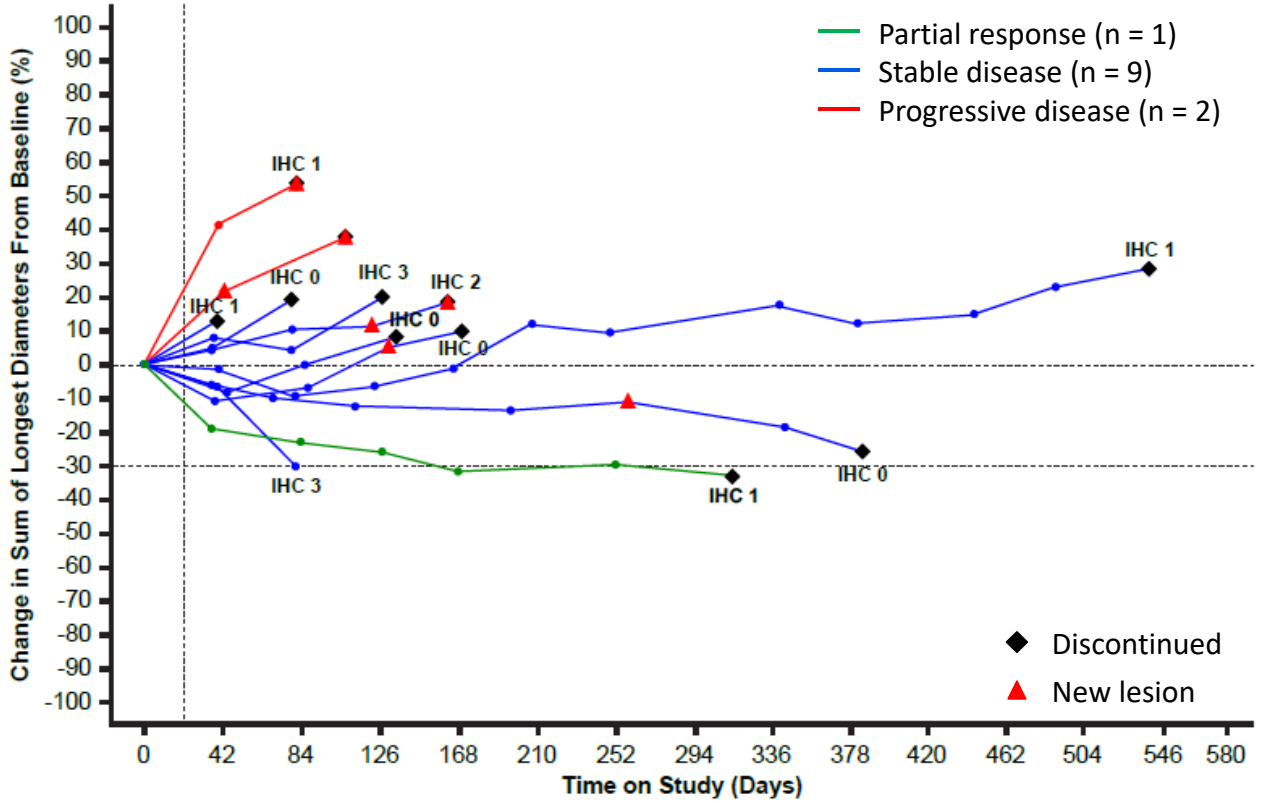
Minimum follow-up in Arm B: 2.2 months for CRC

- Responses in other cohorts
  - Arm A: melanoma (1/4 PR), breast cancer (1/1 PR)
  - Arm B: RCC (1/1 CR), breast cancer (1/2 PR)

Investigator-assessed unconfirmed response per RECIST v1.1.
Efficacy evaluable patients dosed by April 7, 2014, who had at least 1 scan; data cutoff July 7, 2014.

MPDL3280A + Bevacizumab: Tumor Burden Over Time in CRC

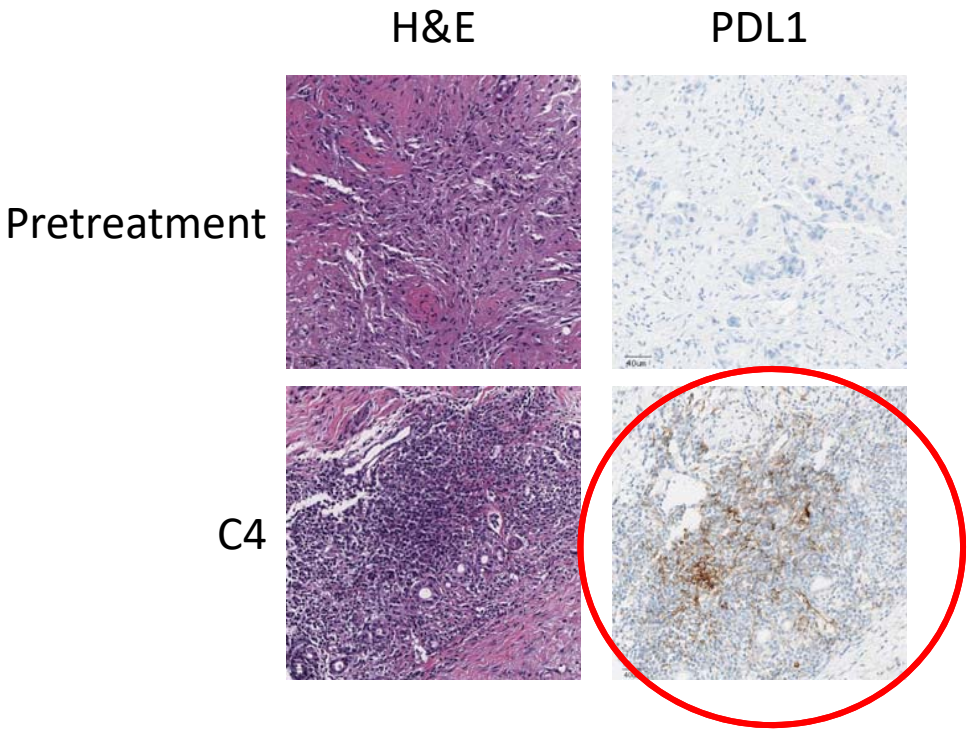
Clearly not the regression observed in other diseases

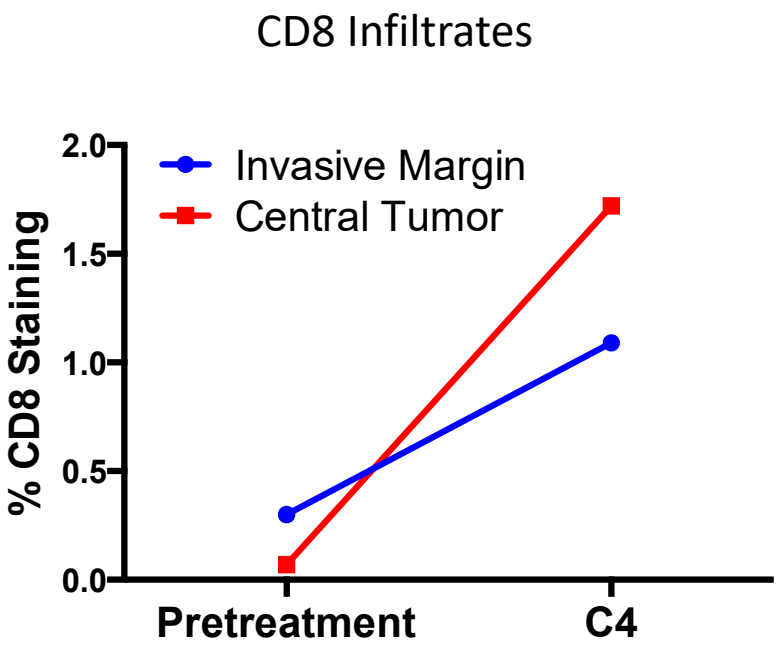


- **SD ≥ 24 weeks in 2 patients**
- **Median duration of follow-up: 5.6 months**

Investigator-assessed unconfirmed response per RECIST v1.1.
Does not include 2 patients: 1 patient did not have a scan post baseline and another patient had 1 target lesion that was not evaluable.
IHC 3, 2, 1, 0: ≥ 10%, ≥ 5% and < 10%, ≥ 1% and < 5%, < 1% tumor-infiltrating immune cells positive for PD-L1, respectively; IHC status not available for 1 patient.
Efficacy evaluable patients dosed by April 7, 2014, who had at least 1 scan; data cutoff July 7, 2014.

Increase in Tumor PD-L1 and CD8+ Infiltrates After MPDL3280A + Bevacizumab + FOLFOX in a CRC Patient



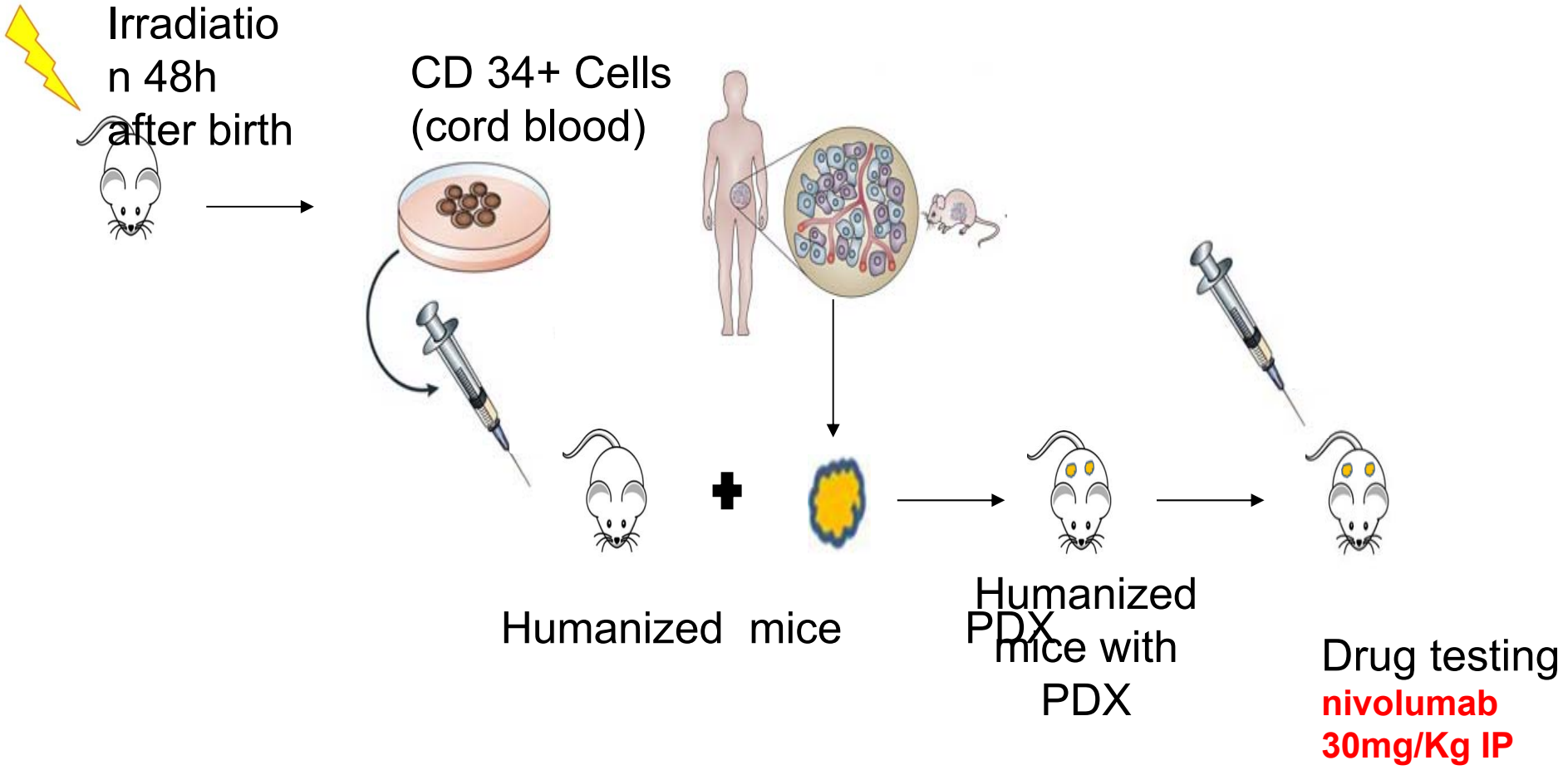


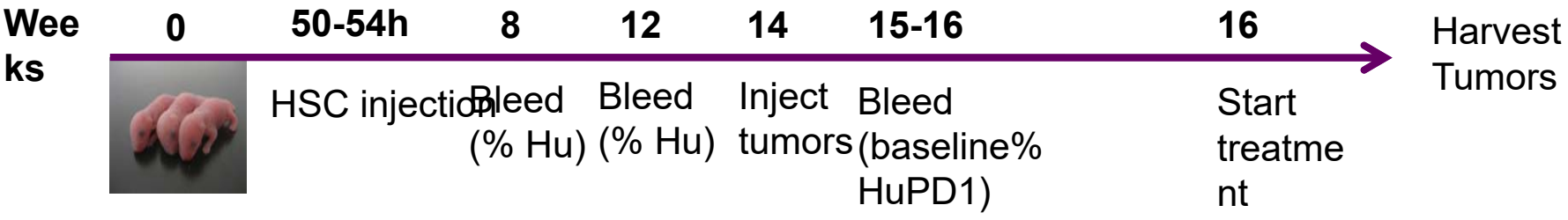
Dr. John Powderly, Carolina BioOncology.

CRC and IT: Comments

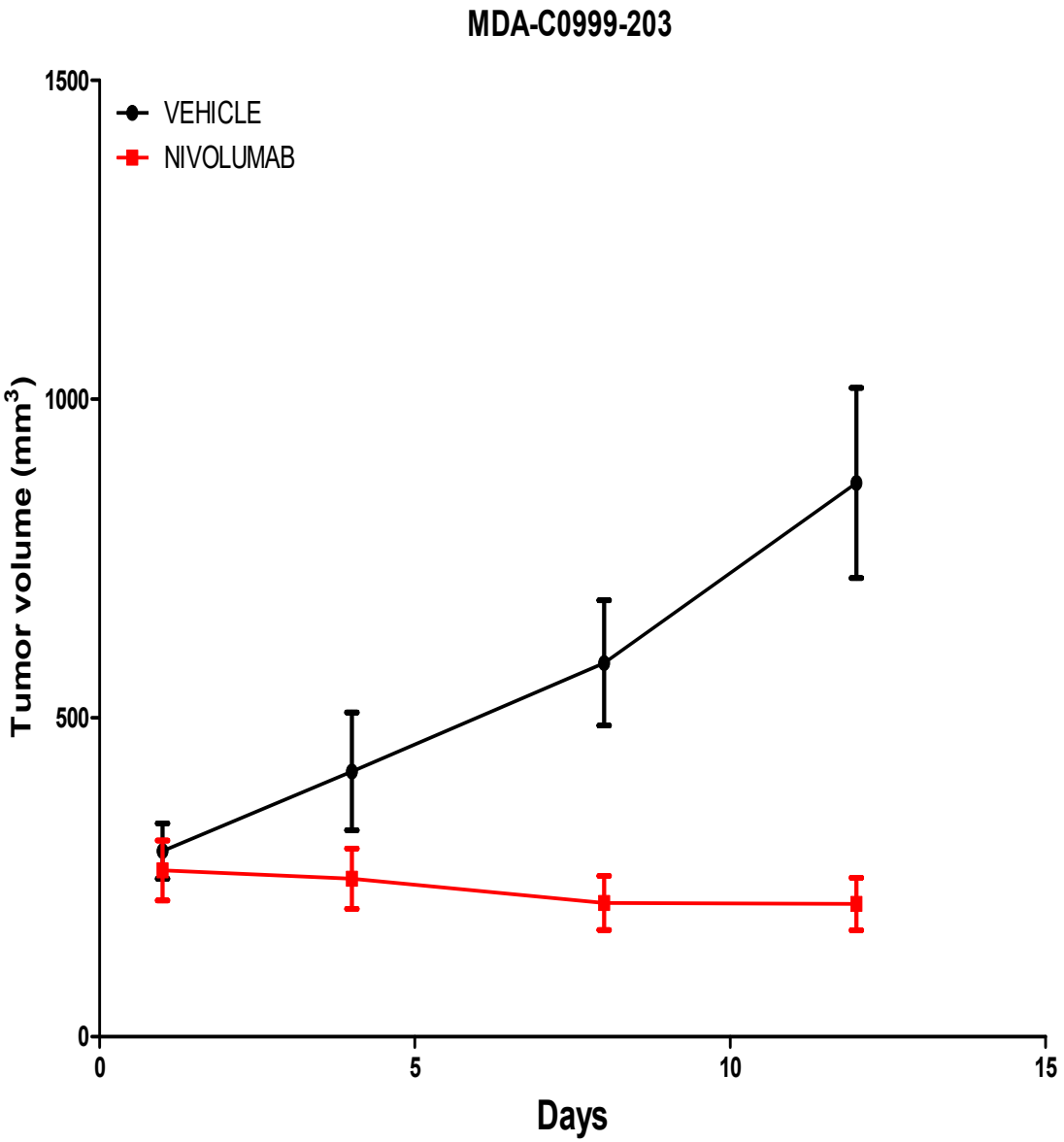
- The data in MSI-h CRC has been most compelling and associated with durable responses, although some patients with SD have experienced prolonged disease control
- Strategies for MSS patients may require more work around mechanism-based combos
- It does not appear that we have adequate patient selection tools for IT in this disease (beyond MSI-h)
- We need to be cautious in relying upon OR as the only read-out for clinical benefit and improve our ability to identify patients that may derive benefit with BR=SD

Methods: Humanized PDX Development





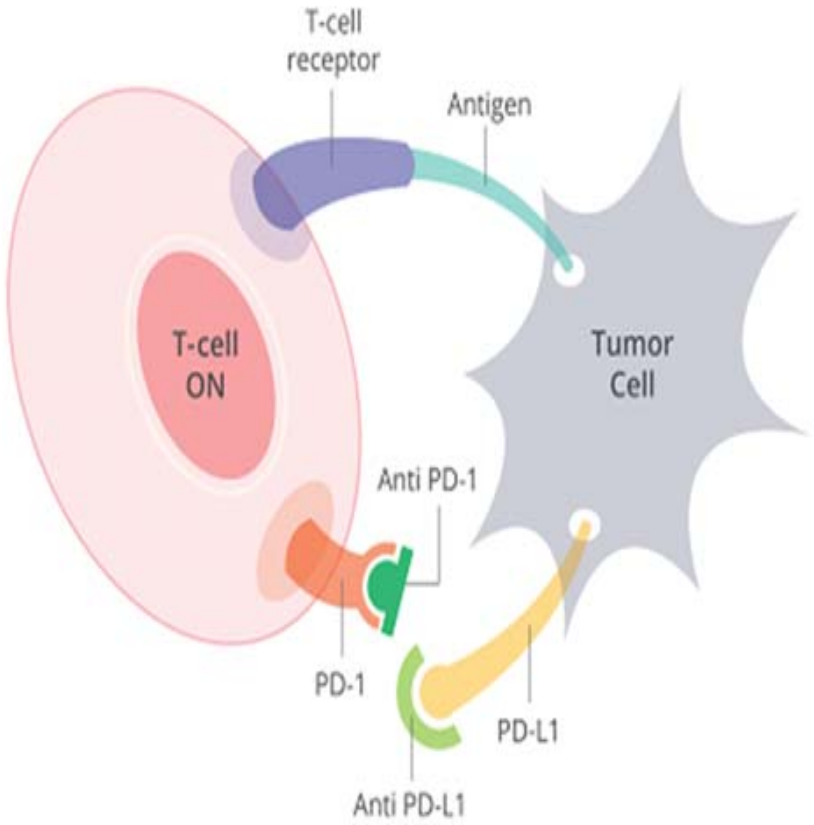
Established POC in MSI-h tumor, now poised to develop rational combos



Rationale for Nivolumab in Metastatic SCCA:

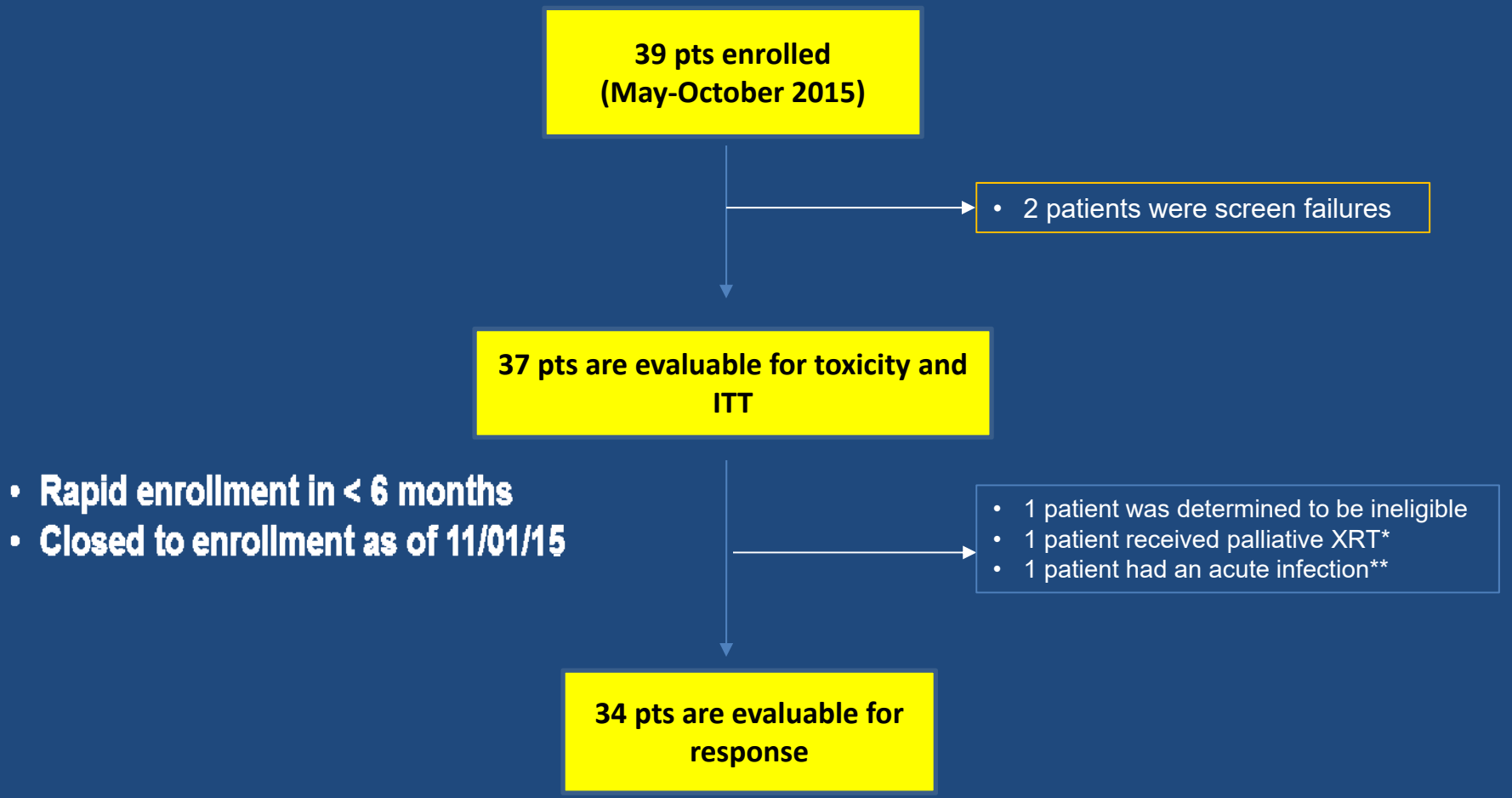
- Approximately 80-95% of cases are linked to human papillomavirus (HPV).

- The role of HPV in the tumorigenesis of SCCA provides rationale for the use of immune checkpoint blockade agents as a novel therapy for treatment of patients with a virally driven disease.



Morris VK et al. The Oncologist, 2015, Sarup-Hansen E et al. J Clin Oncol ,2014

NCI9673: Consort Diagram

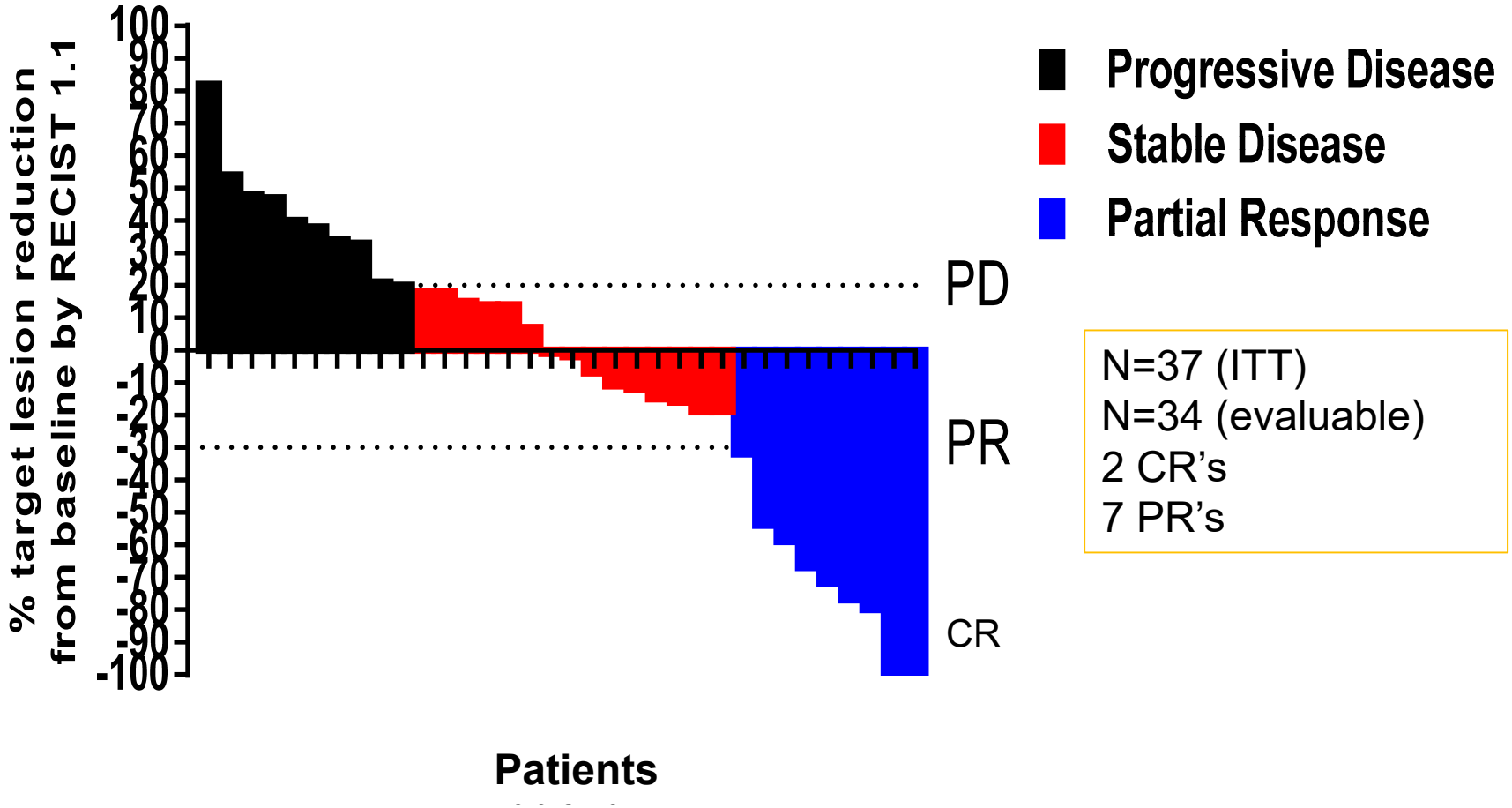


- **Rapid enrollment in < 6 months**
- **Closed to enrollment as of 11/01/15**

*both within < 1 week of enrollment, **not treatment-related

Presented by: Cathy Eng, MD

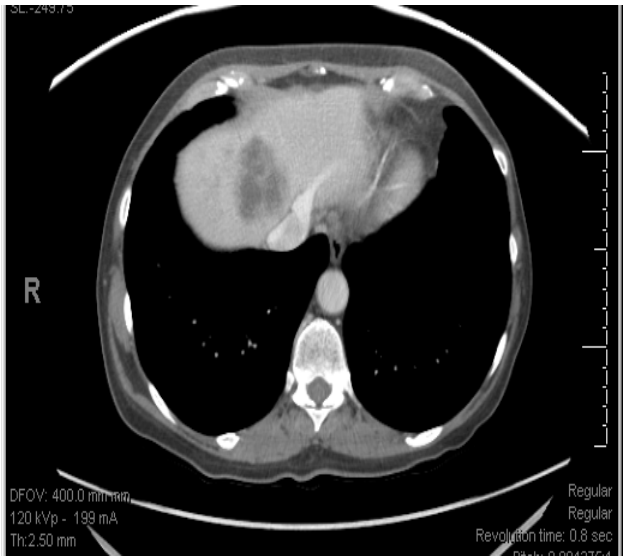
NCI9673: Primary Endpoint of Response Rate

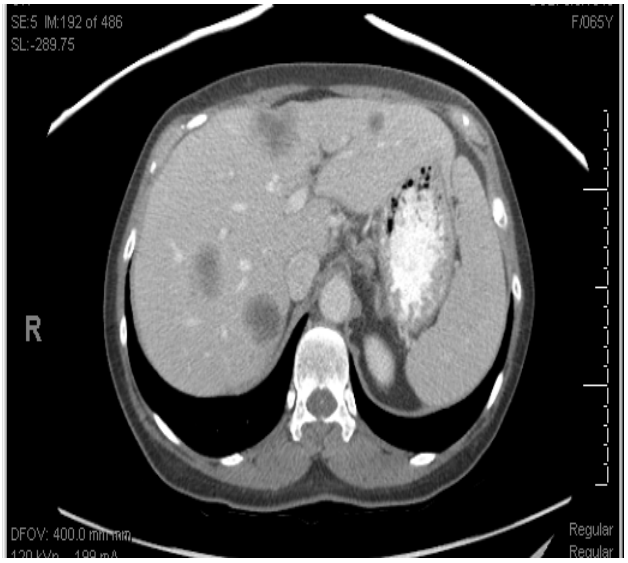


N=37 (ITT)
N=34 (evaluable)
2 CR's
7 PR's

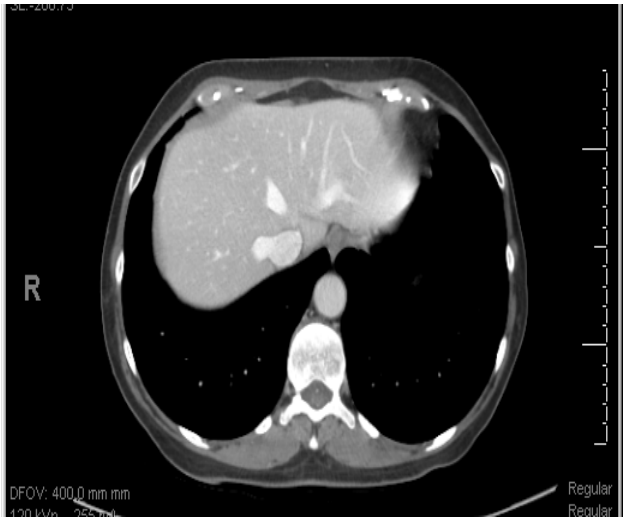
Patient #1:

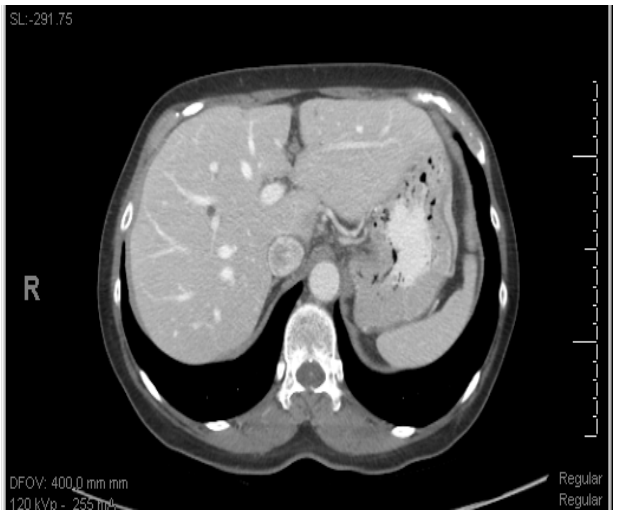
Baseline:
6/7/2015





On Treatment
Cycle #22
5/18/16



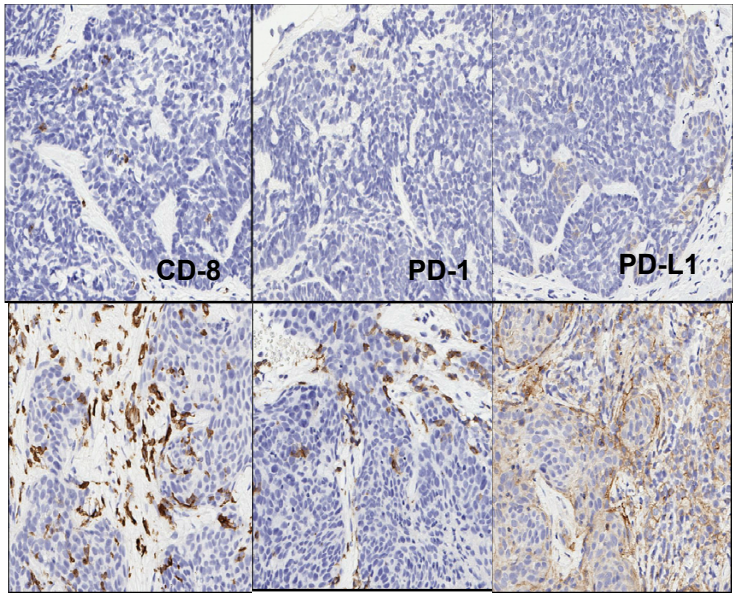


Presented by: Cathy Eng, MD

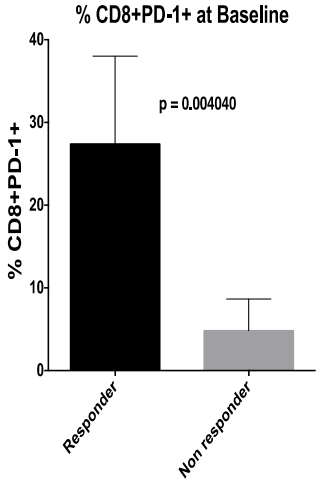
Tumor Correlatives at Baseline by IHC (N=12)

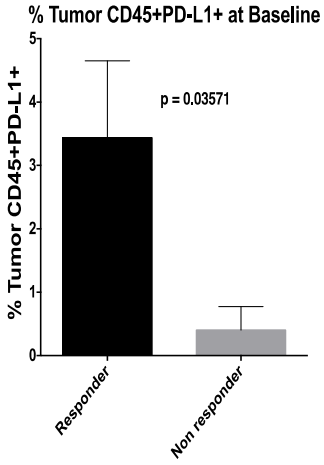
Non-Responder

Responder



Flow Cytometry Confirmation
(Courtesy of MDACC IMT Platform)





Conclusions: IT for GI Cancer

- There is no doubt that IT is changing the landscape of therapeutic options for GI cancer, but there is a lot to learn:
  - Patient selection
  - Rational combinations
  - More robust preclinical models to develop RC
  - Relevant clinical endpoints
  - More work around recalcitrant tumors such as pancreatic cancer
  - Need to avoid overlapping/competing studies that are not designed to provide information whether positive or not (in other words we need to *understand* why trials are + or -)

Thank You!