Presenter Disclosure Information

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Preliminary Results From a Phase 1/2 Study of Epacadostat (INCB024360) in Combination With Pembrolizumab in Patients With Selected Advanced Cancers

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Abstract # O7
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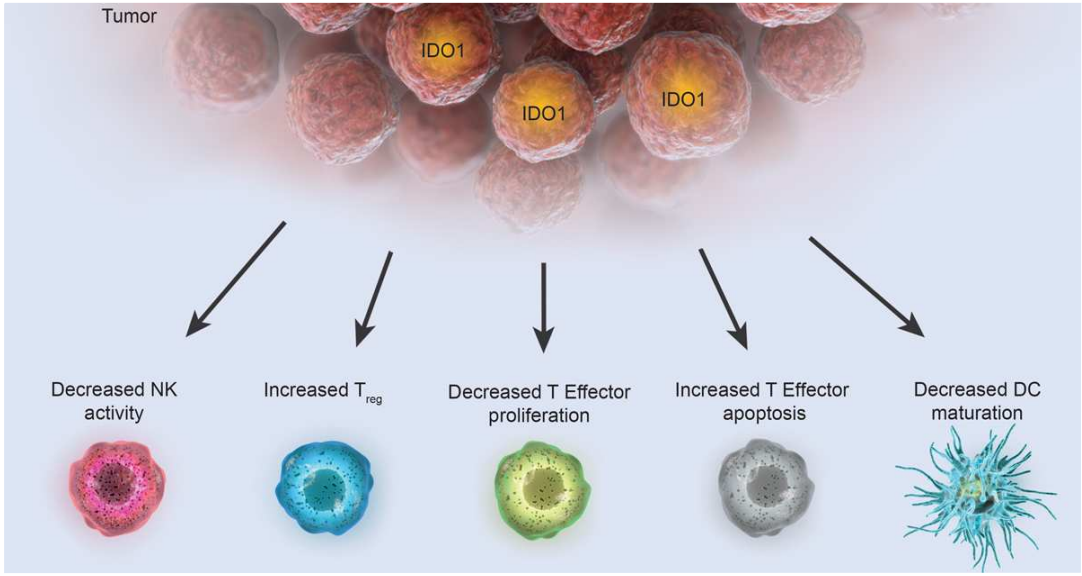
Background (I)

- IDO1 is a tryptophan-catabolizing enzyme that is overexpressed in many cancers[1-3] and induces immune tolerance by suppressing T-cell responses[4]
  - IDO1 is expressed in human tumors and in dendritic cells within tumor draining lymph nodes[5]
  - IDO1 expression is associated with more rapid tumor progression and reduced survival[5]
  - IDO1 inhibition exhibits antitumor activity through the reactivation of effector T cells[3] and is synergistic with PD-1 blockade[6]



IDO1, indoleamine 2,3 dioxygenase 1.

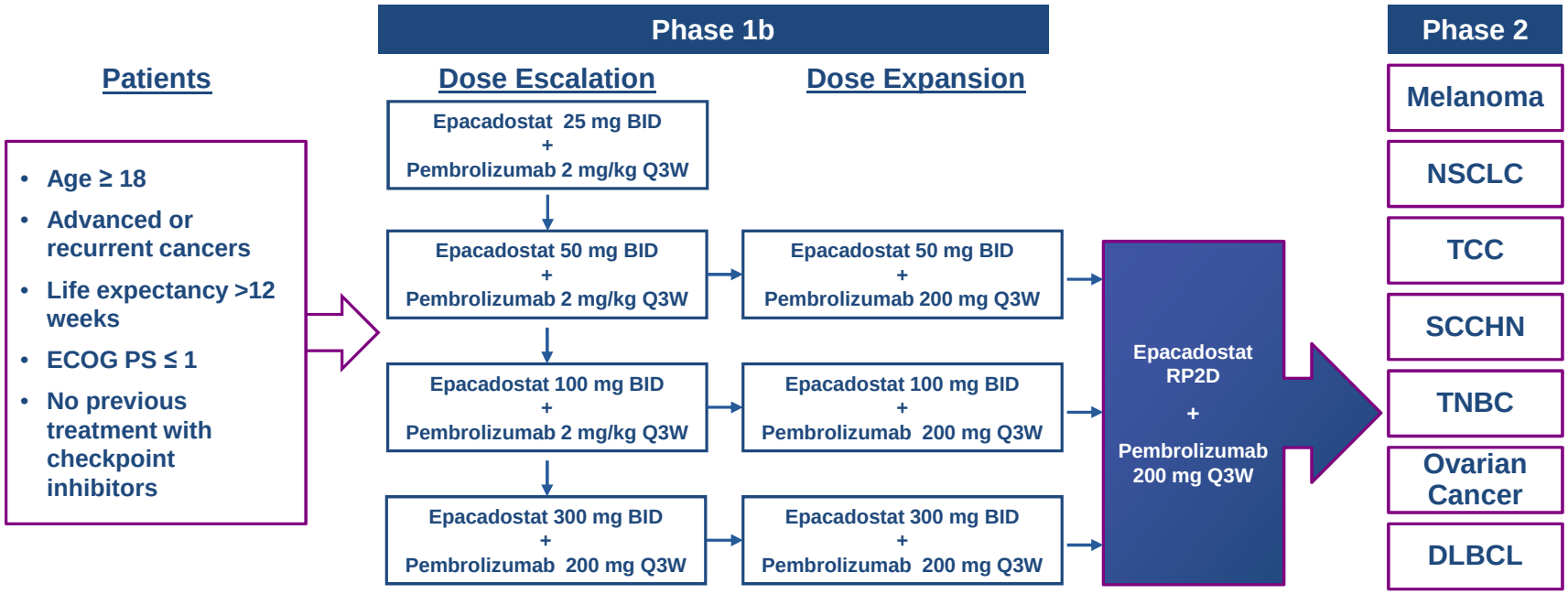
1. Moretti et al. *J Clin Endocrinol Metab*. 2014:jc20133351; **2.** Yu et al. *Clin Dev Immunol*. 2011;2011:469135; **3.** Uyttenhove et al. *Nat Med*. 2003; 9(10):1269-1274;
4. Munn et al. *J Clin Invest*. 2007;117(5):1147-1154; **5.** Godin-Ethier et al. *Clin Cancer Res*. 2011;17(22):6985-6991; **6.** Spranger et al. *J Immunother Cancer*. 2014 Feb 18;2:3.

Background (II)

- Epacadostat (INCB024360) is a potent, selective, oral IDO1 inhibitor[1]
- In a dose-escalation study in patients with metastatic melanoma, combination of epacadostat (≤ 50 mg BID) with ipilimumab was generally well tolerated[2]
  - In immunotherapy-naive patients, favorable response rates and PFS were observed
  - Pharmacodynamic analysis showed dose-dependent inhibition of IDO1 at all doses
- Pembrolizumab (MK-3475) is an anti−PD-1 monoclonal antibody that is approved in several countries for patients with advanced melanoma
  - Approved in the US for patients with metastatic NSCLC whose tumors express PD-L1[3]
  - Demonstrated clinical activity in other solid tumors including SCCHN, urothelial carcinoma, and TNBC[4]
- **Objective (Phase 1)**
  - To evaluate the safety of epacadostat in combination with pembrolizumab in patients with advanced or metastatic cancers

1. Liu et al. *Blood*. 2010;115(17):3520-3530; **2.** Gibney et al. Abstract 511. Presented at: 2015 European Cancer Congress; September 25-29, 2015; Vienna, Austria; **3.** KEYTRUDA (pembrolizumab) [prescribing information] (2015). Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Whitehouse Station, NJ; **4.** Khoja et al. *J Immunother Cancer*. 2015 Aug 18;3:36.

Study Design



- Response assessment every 9 weeks per RECIST 1.1

Clinicaltrials.gov: NCT02178722

Patient Demographics and Disease Characteristics

Variable	TOTAL (N=56)	25 mg BID (n=4)	50 mg BID (n=19)	100 mg BID (n=18)	300 mg BID (n=15)*
Tumor type, n (%)					
Melanoma	20 (36)	2 (50)	13 (68)	4 (22)	1 (7)
RCC	11 (20)	0	4 (21)	1 (6)	6 (40)
NSCLC	10 (18)	1 (25)	0	7 (39)	2 (13)
TCC	5 (9)	1 (25)	0	3 (17)	1 (7)
EA	5 (9)	0	1 (5)	2 (11)	2 (13)
TNBC	3 (5)	0	0	0	3 (20)
SCCHN	2 (4)	0	1 (5)	1 (6)	0
Median age, y (range)	59 (30, 88)	47 (30, 63)	60 (37, 81)	61.5 (39, 88)	59 (30, 84)
Women, n (%)	25 (45)	3 (75)	9 (47)	6 (33)	7 (47)
Race, n (%)					
White	50 (89)	1 (25)	19 (100)	18 (100)	12 (80)
Black/A-A	3 (5)	1 (25)	0	0	2 (13)
Asian	2 (4)	1 (25)	0	0	1 (7)
NH/PI	1 (2)	1 (25)	0	0	0
ECOG score, n (%)					
0	32 (57)	4 (100)	14 (74)	10 (56)	4 (27)
1	24 (43)	0	5 (26)	8 (44)	11 (73)

A-A, African-American; ECOG, Eastern Cooperative Oncology Group; NH, Native Hawaiian; PI, Pacific Islander.

*Enrollment is ongoing in the 300-mg BID group.

Patient Demographics and Disease Characteristics

Variable	Melanoma (n=20)	RCC (n=11)	NSCLC (n=10)	TCC (n=5)	EA (n=5)	TNBC (n=3)	SCCHN (n=2)
ECOG PS, n (%) 0 1	 16 (80) 4 (20)	 7 (64) 4 (36)	 5 (50) 5 (50)	 1 (20) 4 (80)	 2 (40) 3 (60)	 0 3 (100)	 1 (50) 1 (50)
Prior systemic therapies for advanced/metastatic disease, n (%) 0 1-2 >2	 17 (85) 3 (15) 0	 1 (9) 6 (55) 4 (36)	 1 (10) 9 (90) 0	 2 (40) 2 (40) 1 (20)	 0 4 (80) 1 (20)	 0 1 (33) 2 (67)	 0 2 (100) 0
Prior radiation, n (%)	5 (25)	3 (27)	5 (50)	1 (20)	2 (40)	3 (100)	2 (100)

Dose-Limiting Toxicities

Dose Group	No. of Patients With DLT/ No. Evaluable*	Description of DLT
25 mg BID	0/4	
50 mg BID	1/17	Grade 3 rash (n=1)
100 mg BID	2/15	Grade 3 AST increased (n=1) Grade 3 nervous system disorder, other (n=1)†
300 mg BID	2/10*	Grade 1 skin erythema (n=1)‡ Grade 3 rash (n=1)

*Evaluable patients include those who completed the DLT observation period (6 weeks) or experienced a DLT during that time per protocol. Enrollment is ongoing in the 300-mg BID group.
†Nervous system disorder (unsteady gait due to cerebral edema) occurred in a patient with prior CNS metastases treated with radiation.
‡Grade 2 rash requiring 1 dose reduction.
Data cutoff: October 1, 2015.

Treatment-Related AEs

AE, n (%)	Total (N=56)	25 mg BID (n=4)	50 mg BID (n=19)	100 mg BID (n=18)	300 mg BID (n=15)*
All Grade	**38 (68)**	**3 (75)**	**11 (58)**	**12 (67)**	**12 (80)**
Rash[†]	14 (25)	2 (50)	5 (26)	0	7 (47)
Fatigue	13 (23)	2 (50)	5 (26)	2 (11)	4 (27)
Arthralgia	7 (13)	1 (25)	3 (16)	1 (6)	2 (13)
Pruritus[‡]	7 (13)	2 (50)	2 (11)	0	3 (20)
Nausea	6 (11)	1 (25)	0	2 (11)	3 (20)
Pyrexia	6 (11)	0	1 (5)	0	5 (33)
Grade 3	**6 (11)**	**1 (25)**	**1 (5)**	**2 (11)**	**2 (13)**
Rash[†]	3 (5)	0	1 (5)	0	2 (13)
AST increased	1 (2)	0	0	1 (6)	0
Nervous system disorder, other[§]	1 (2)	0	0	1 (6)	0
Mucosal inflammation	1 (2)	1 (25)	0	0	0

*Enrollment in the 300-mg BID dose cohort is ongoing.
[†]Rash includes the following MedDRA preferred terms: rash, rash generalized, rash maculo-papular, rash pruritic, and rash follicular.
[‡]Pruritus includes the following MedDRA preferred terms: pruritus and pruritus generalized.
[§]Nervous system disorder (unsteady gait due to cerebral edema) occurred in a patient with prior CNS metastases treated with radiation.

- No grade 4 treatment-related AEs
- One patient discontinued for a treatment-related AE: grade 3 AST increased (2%)
- No treatment-related deaths

Best Overall Response by RECIST 1.1

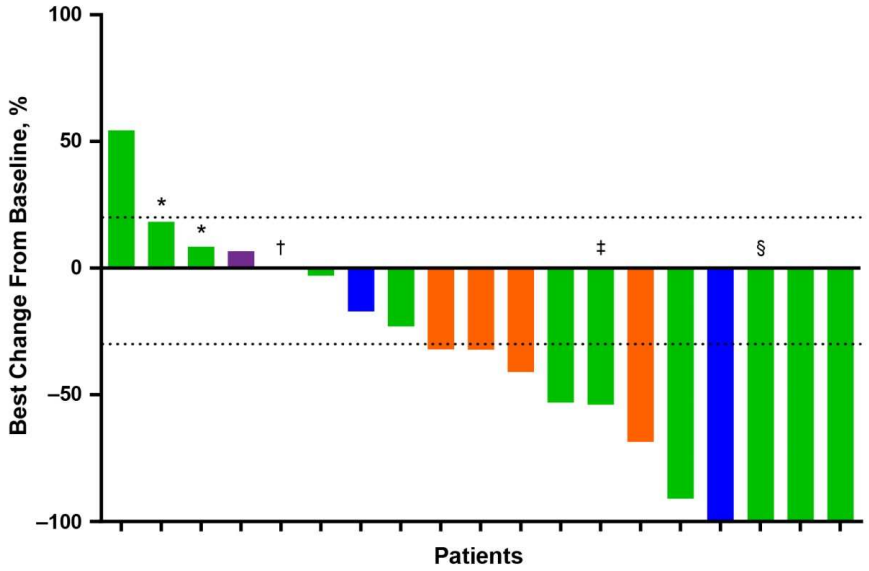
Patients, n (%)	Melanoma (n=20)	RCC (n=11)	NSCLC (n=10)	TCC (n=5)	EA (n=5)	TNBC (n=3)	SCCHN (n=2)
Evaluable*	***19***	***8***	***8***	***4***	***4***	***2***	***2***
ORR (CR+PR)	**10 (53)**	**2 (25)**	**3 (38)**	**1 (25)**	**1 (25)**	**0**	**1 (50)**
CR	3	0	0	0	0	0	0
PR	7	2	3	1	1	0	1
SD	4	5	2	1	0	1[†]	1
DCR (CR+PR+SD)	**14 (74)**	**7 (88)**	**5 (63)**	**2 (50)**	**1 (25)**	**1 (50)**	**2 (100)**
PD	5 (26)	0	1 (13)	1 (25)	3 (75)	1 (50)	0

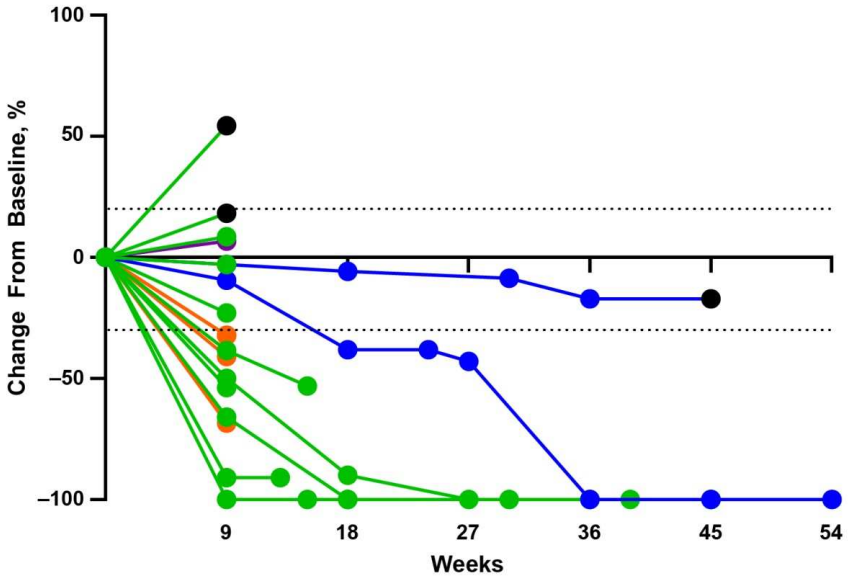
CR, complete response; DCR, disease control rate; ORR, overall response rate; PR, partial response; PD, progressive disease; SD, stable disease.

*By data cutoff, patients had at least 1 postbaseline scan or discontinued or died before the first postbaseline scan.
[†]Patient achieved an SD but discontinued for a DLT (grade 3 rash) prior to the protocol required minimum observation (56 days).
NOTE: All percentages are calculated based on number of evaluable patients.
Data cutoff: October 1, 2015.

Melanoma: Percent Change From Baseline in Target Lesions

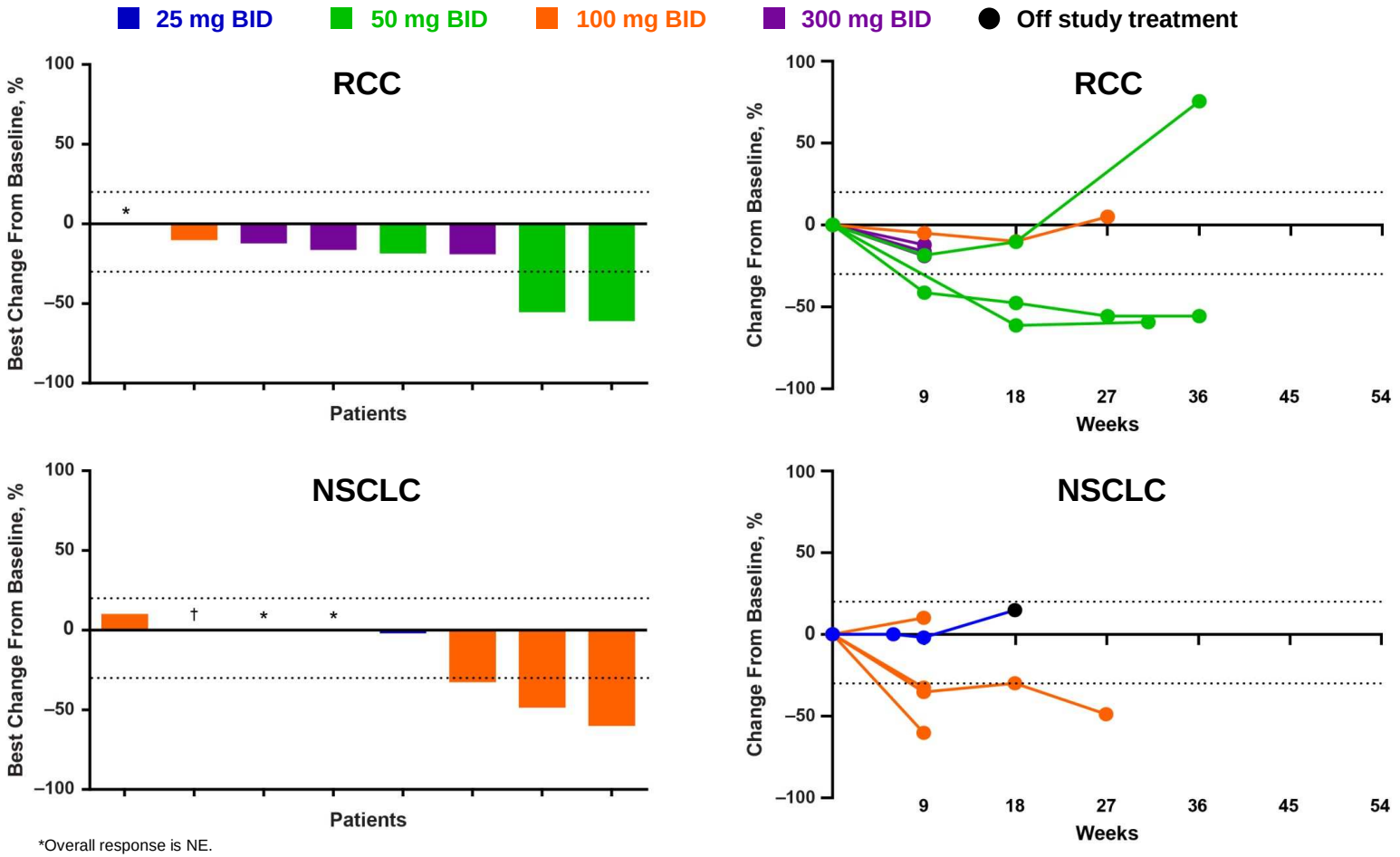
25 mg BID 50 mg BID 100 mg BID 300 mg BID Off study treatment





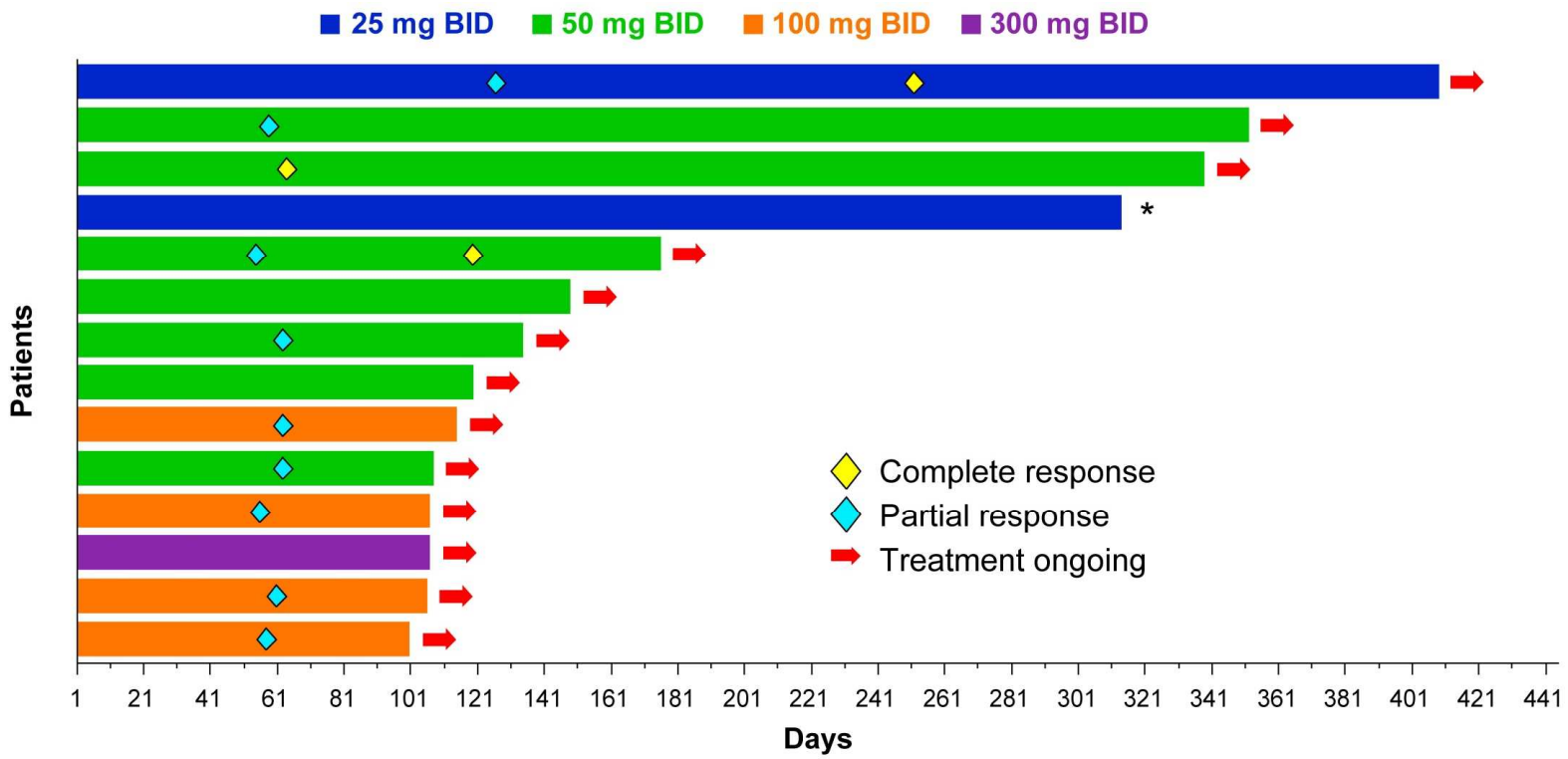
*Overall response is PD (SD for target lesions; PD for non-target lesions).
†Overall response is PD (target lesions not assessed; PD per new lesions).
‡Overall response is PD (PR for target lesions; PD per new lesions).
§Overall response is PR (CR for target lesions; non CR/non PD for non-target lesions).

RCC and NSCLC: Percent Change From Baseline in Target Lesions



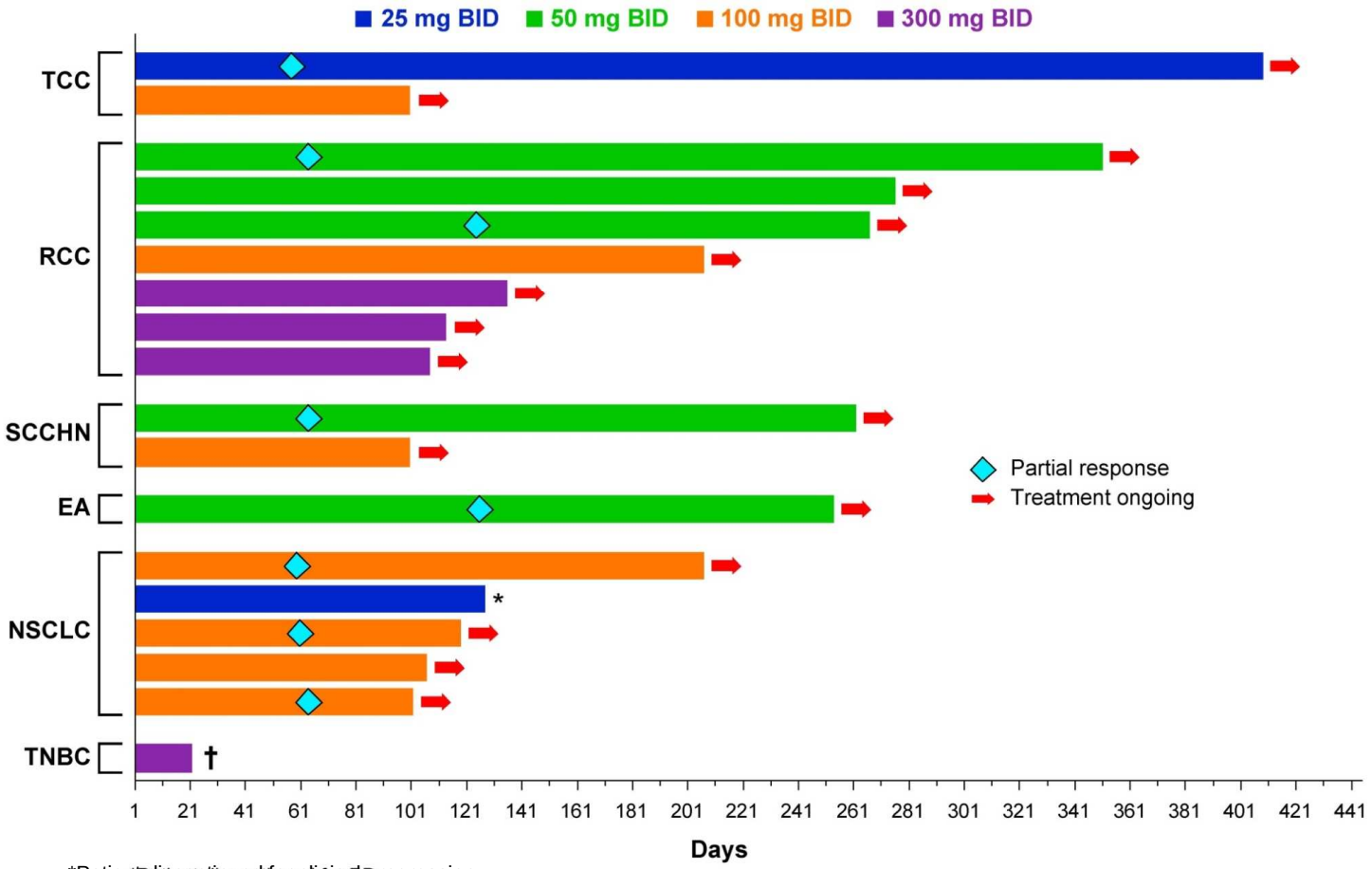
*Overall response is NE.
†Overall response is PD (target lesions not assessed; PD per new lesions).

Melanoma: Duration of Treatment in Patients With SD, PR, or CR



*Patient discontinued for PD.

Non-Melanoma Tumor Types: Duration of Treatment in Patients With SD, PR, or CR



*Patient discontinued for clinical progression.

†Patient achieved an SD but discontinued for a DLT (grade 3 rash) prior to the protocol required minimum observation (56 days).

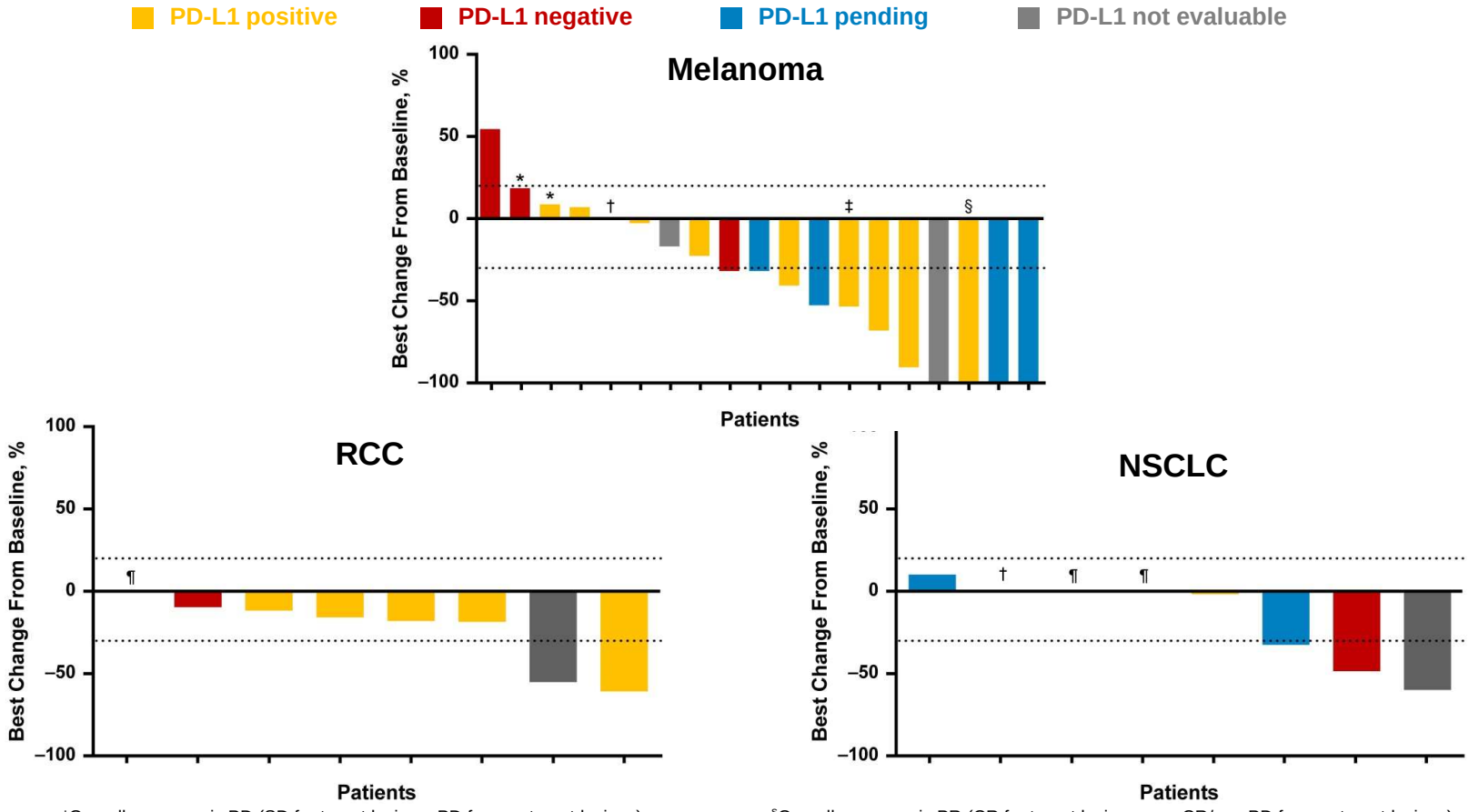
Analysis of PD-L1 Expression

- PD-L1 IHC 22C3 pharmDx Kit
- Cutoff for positivity:
  - NSCLC: ≥50% staining*
  - All other tumor types: ≥1% staining*

PD-L1 expression, No. of patients	Melanoma (n=20)	RCC (n=11)	NSCLC (n=10)	TCC (n=5)	EA (n=5)	TNBC (n=3)	SCCHN (n=2)
Positive	11	5	2	1	4	0	2
Negative	3	1	4	2	0	0	0
Not evaluable	2	1	1	0	0	0	0
Pending	4	4	3	2	1	3	0

*Staining was based on tumor cell PD-L1 only in NSCLC and PD-L1 on both tumor cells and immune infiltrating cells in all other tumor types.

Best Percent Change in Target Lesions by PD-L1 Status



*Overall response is PD (SD for target lesions; PD for non-target lesions).
†Overall response is PD (target lesions not assessed; PD per new lesions).
‡Overall response is PD (PR for target lesions; PD per new lesions).
§Overall response is PR (CR for target lesions; non CR/non PD for non-target lesions).
¶Overall response is NE.

Summary

- Epacadostat with pembrolizumab is a novel combination immune therapy regimen that was generally well tolerated
  - Very few patients experienced DLTs or grade 3 treatment-related AEs
  - No grade 4 treatment-related AEs or deaths and low discontinuation rate for treatment-related AEs (2%)
  - Evaluation of tolerability in the 300 mg BID cohort is ongoing
- Efficacy results suggest promising clinical activity with the combination
  - ORR of 53% and DCR of 74% in patients with melanoma
- Enrollment is ongoing to further evaluate efficacy
- A phase 3 study in patients with advanced melanoma is planned, with initiation expected in 2016