Phase 1 trial of the adenosine A2A receptor antagonist inupadenant (EOS-850):

Update on tolerability, and antitumor activity potentially associated with the expression of the A2A receptor within the tumor.

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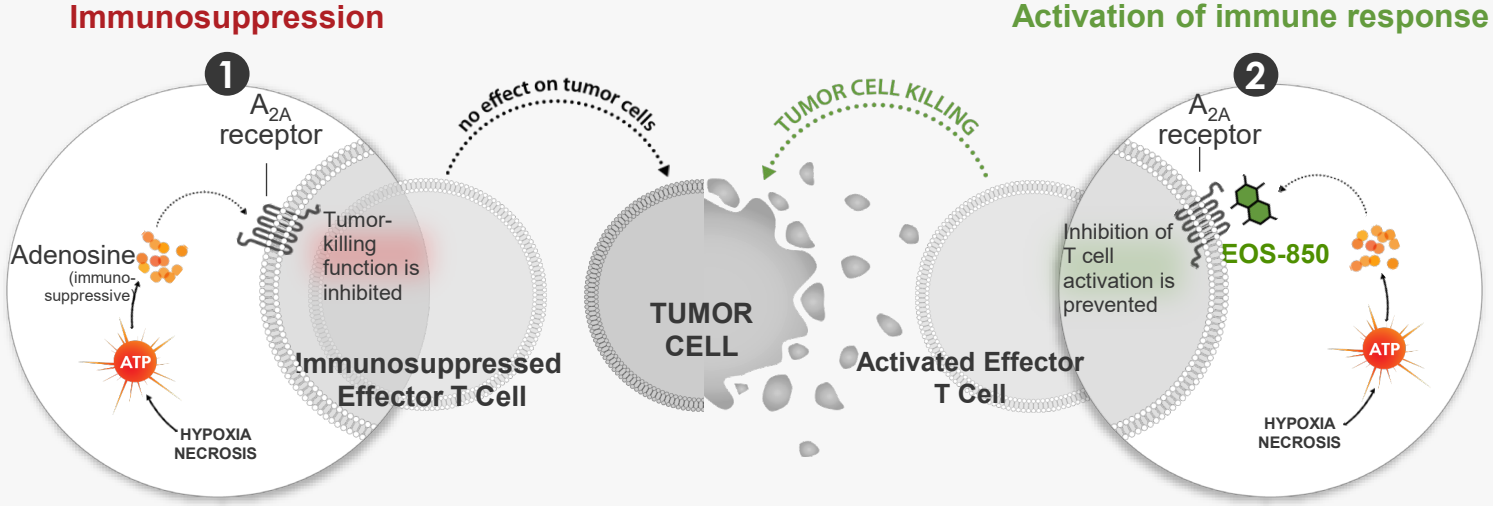
Background and Methods



High levels of adenosine in TME[1] due to hypoxia and necrosis suppress effector T cells

Inupadenant (EOS-850) induces prolonged, targeted inhibition of the adenosine pathway and promotes immune response

Primary Objectives

- Safety and tolerability of inupadenant as a single agent and in combination with pembrolizumab and/or chemotherapy
- Define MTD and RP2D of inupadenant as monotherapy or in combination

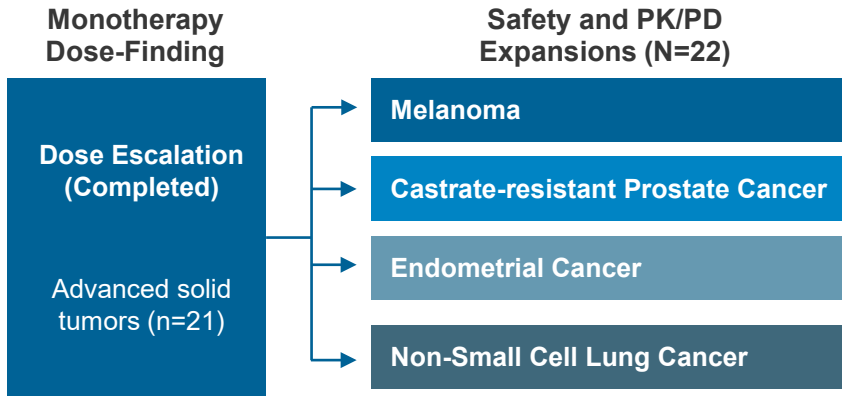
Secondary Objectives

- PK and antitumor activity of inupadenant as monotherapy

Exploratory Objectives

- PD activity and association of plasma PK, safety, efficacy and PD biomarkers of inupadenant as monotherapy

Study Design

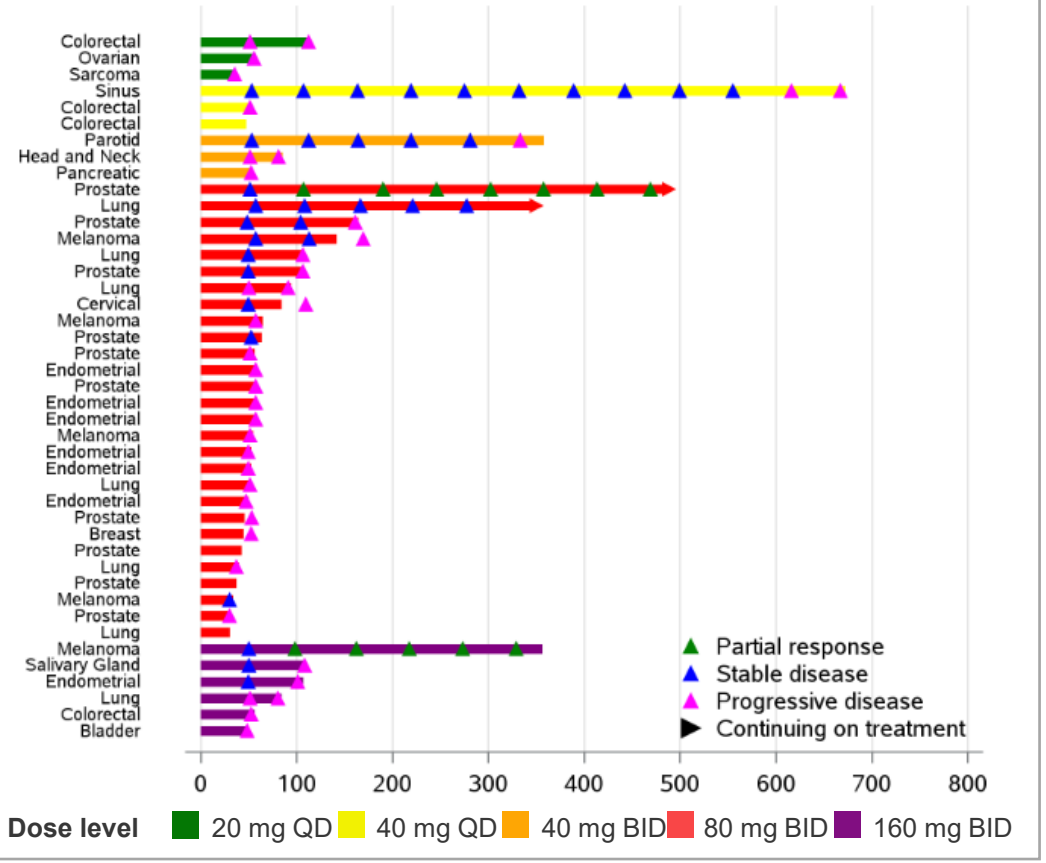


Demographics

	Total (N=43)		Total (N=43)
Age (Yrs, Median, Range)	60 (28-75)	**Lines of prior therapy (Median, Range)**	3 (1-10)
Sex (N, %)		**Prior immunotherapy (N, %)**	
Male	25 (58.1)	No	28 (65.1)
Female	18 (41.9)	Yes	13 (32.6)
Race (N, %)		Missing	1 (2.3)
Asian	1 (2.3)		
Black/African-American	1 (2.3)		
White	40 (93.0)		
Other	1 (2.3)		

Updated safety & efficacy from inupadenant monotherapy – durable responses observed

Activity in patients treated with multiple lines of therapy



Most Frequent (≥15%) TEAEs

Preferred Term	Number of Patients (%)					
	20 mg QD (N=3)	40 mg QD (N=3)	40 mg BID (N=3)	80 mg BID (N=28)	160 mg BID (N=6)	Total (N=43)
Fatigue	1 (33.3)	2 (66.7)	1 (33.3)	9 (32.1)	4 (66.7)	17 (39.5)
Anemia	0 (0.0)	2 (66.7)	0 (0.0)	11 (39.3)	1 (16.7)	14 (32.6)
Decreased appetite	2 (66.7)	1 (33.3)	1 (33.3)	5 (17.9)	3 (50.0)	12 (27.9)
Constipation	2 (66.7)	1 (33.3)	0 (0.0)	7 (25.0)	1 (16.7)	11 (25.6)
Aspartate aminotransferase increased	1 (33.3)	1 (33.3)	0 (0.0)	4 (14.3)	2 (33.3)	8 (18.6)
Alanine aminotransferase increased	2 (66.7)	0 (0.0)	0 (0.0)	3 (10.7)	2 (33.3)	7 (16.3)
Diarrhoea	0 (0.0)	1 (33.3)	1 (33.3)	4 (14.3)	1 (16.7)	7 (16.3)
Dyspepsia	0 (0.0)	1 (33.3)	0 (0.0)	4 (14.3)	2 (33.3)	7 (16.3)
Dyspnoea	0 (0.0)	0 (0.0)	1 (33.3)	3 (10.7)	3 (50.0)	7 (16.3)
Nausea	1 (33.3)	1 (33.3)	1 (33.3)	3 (10.7)	1 (16.7)	7 (16.3)

Drug-related SAEs in 3 patients: Acute myocardial infarction (160 mg BID), atrial fibrillation and pericardial effusion (80 mg BID)

2 durable PRs - Castrate-resistant prostate cancer (ongoing), melanoma

1 SD > 1 yr - Sinus carcinoma

2 SDs > 6 mo - Parotid gland carcinoma and lung cancer (ongoing)

Gene Expression Within Tumors

Inupadenant up-regulates immune-related gene signatures in non-progressors

Biomarker Methods

Biopsy collection
(1 to 3 per patient)

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1–28 days prior to study drug treatment
(SCR), and post-treatment (C1D21)

↓

Formalin fixed, paraffin embedded

RNA analysis
(Nanostring, 780 genes)

↓

Gene signature analysis

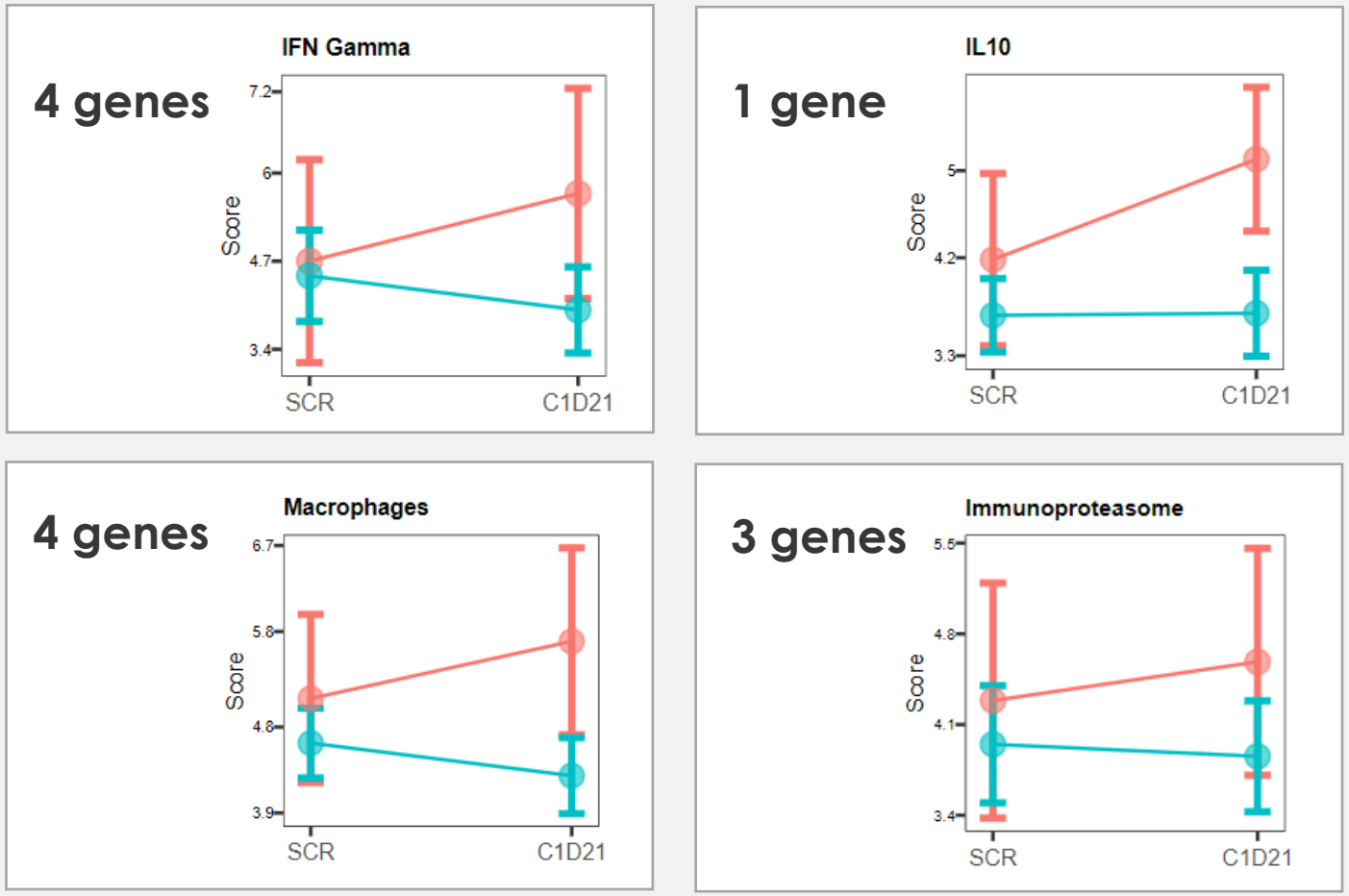
Protein analysis
(Immunohistochemistry)

↓

Receiver operating characteristic (ROC) curve analysis

- Cutoff on baseline density of $A_{2A}R^+$ cells for survival and lesion size analyses

Gene Signature Analysis by Nanostring



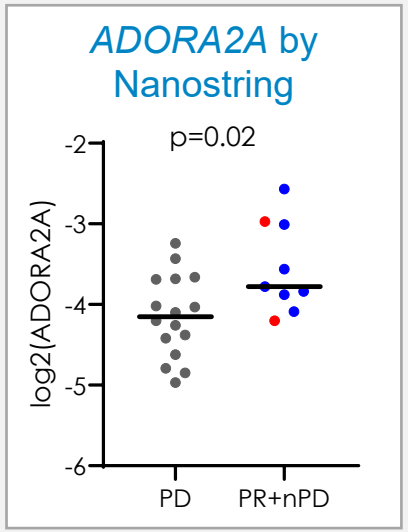
N = 25 patients

Partial Response / non-Progressive Disease (PR/nPD), n=9

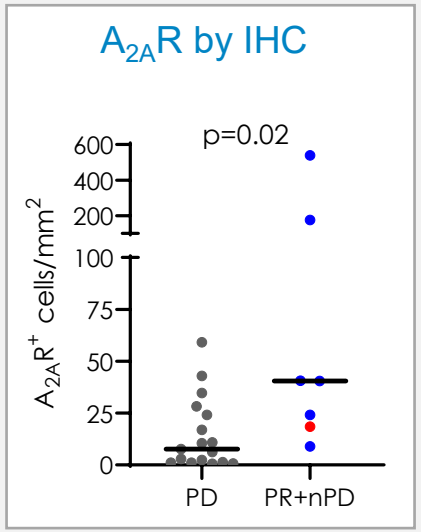
Progressive Disease (PD), n=16

A_{2A} Receptor ($A_{2A}R$) within the tumor

Inupadenant anti-tumor activity is possibly associated with $A_{2A}R$ expression within the tumor area

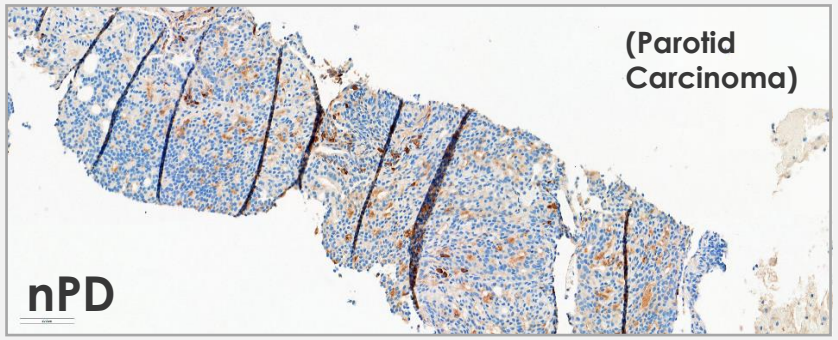


PR: n=2, PD: n=16, nPD: n=7

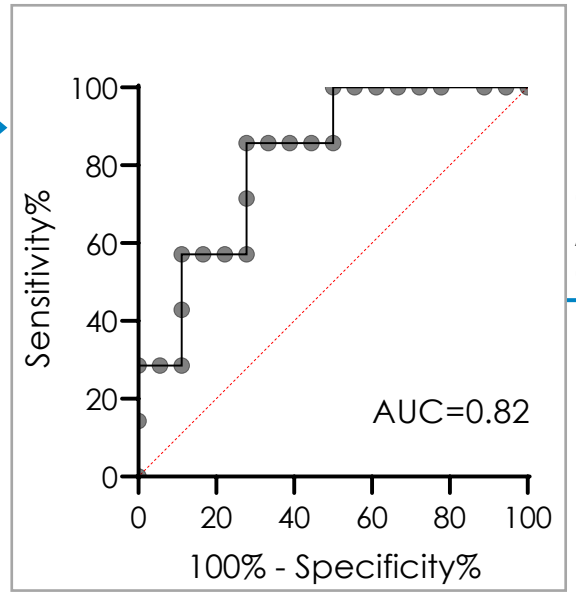


PR: n=1, PD: n=17, nPD: n=6

Progressive Disease (PD)
Partial Response (PR)
non-Progressive Disease (nPD)

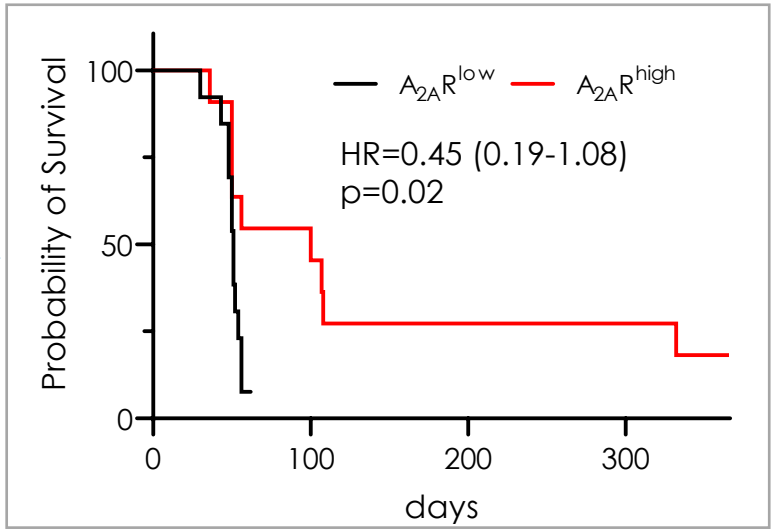


ROC Curve

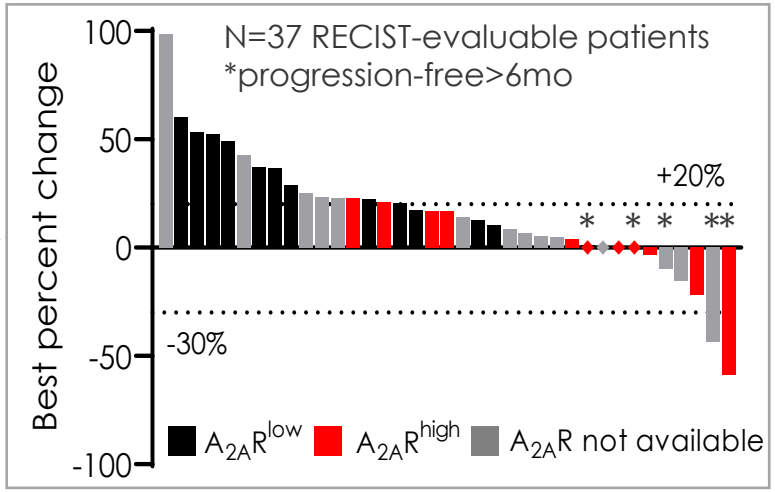


Optimal $A_{2A}R$ cut-off

Survival curve by high/low $A_{2A}R$ levels

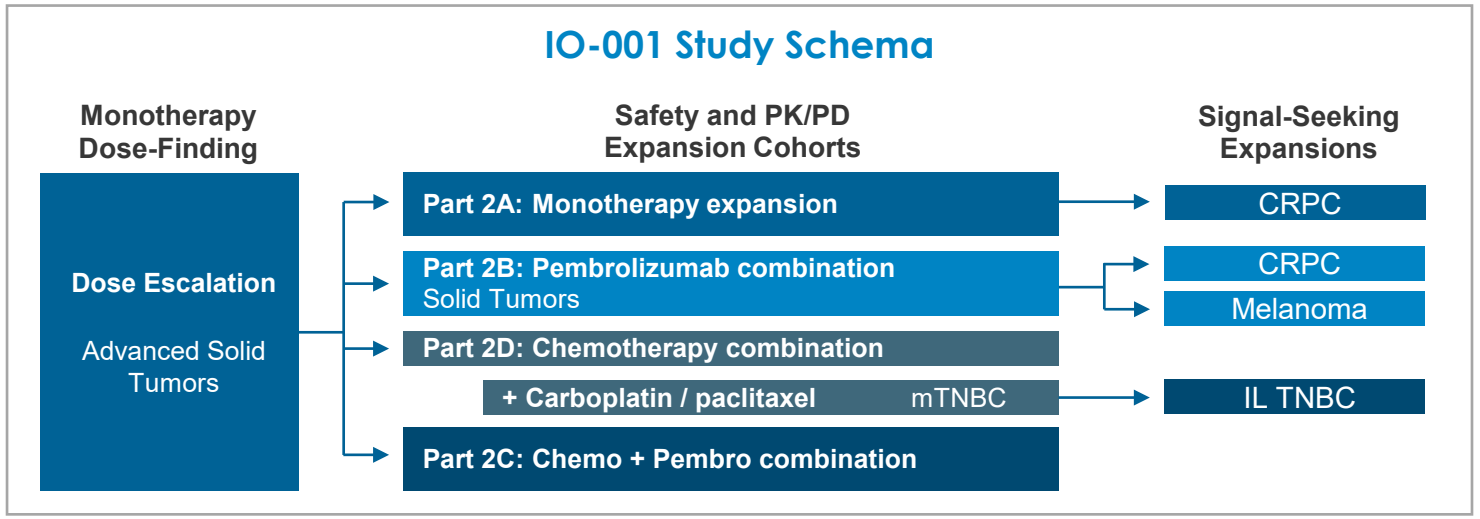


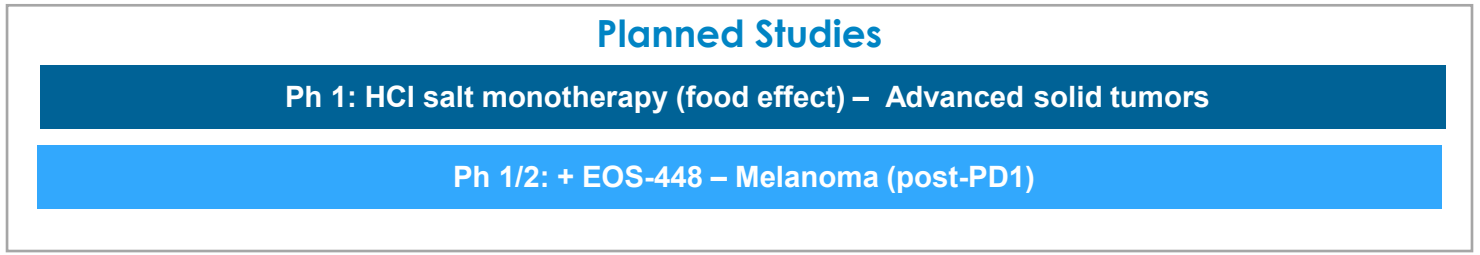
Best % Change in Tumor Lesion by High/Low $A_{2A}R$ levels



Inupadenant is tolerated well and shows signs of activity potentially associated with the expression of the A2A receptor within the tumor

- Inupadenant safety in this larger data set is **consistent with previously presented data.**
- 2 PRs and 3 SDs were **durable**.
- Analysis of pre-treatment tumor biopsies has identified that **$A_{2A}R$ may be associated with clinical outcome**. This provides new mechanistic insights, which we are continuing to investigate.
- **Expansion arms** in the ongoing study will evaluate activity in monotherapy, and in combination with either pembrolizumab, chemotherapy or both.
- **Future studies** will evaluate $A_{2A}R$ as a potential selection biomarker.





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