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Eganelisib (IPI-549) Activity as a Macrophage Reprogramming Therapeutic Candidate in 1L Metastatic TNBC, 2L Metastatic Urothelial Cancer and Other Solid Tumors

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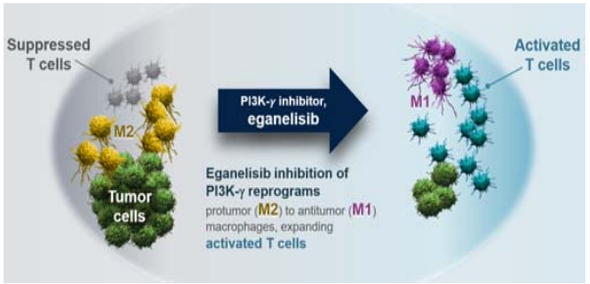
Eganelisib Introduction

- Oral, macrophage reprogramming therapeutic candidate
- Designed to address fundamental biologic mechanism of immune suppression in cancer
- Activates immune response resulting in up regulation of PD-L1 thus priming for checkpoint inhibition
- Growing body of evidence suggests that eganelisib improves patient outcomes over standard of care in areas of high unmet need

Eganelisib Mechanism of Action

PI3K-γ Inhibition Reprograms Macrophages to Turn Tumor Microenvironment from Immune Suppressed to Immune Activated



Increased IFN-γ Responsive Genes Including PD-L1[h]

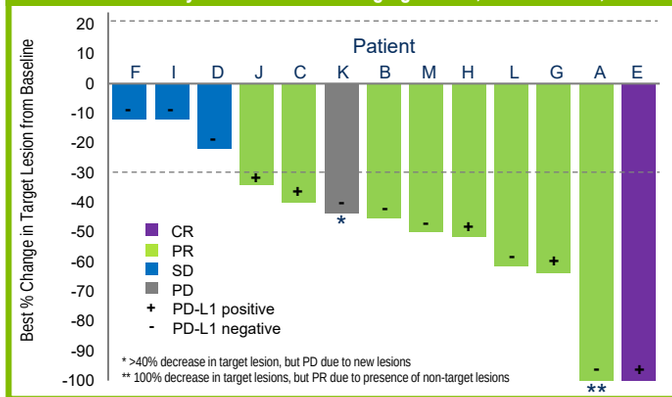
IFN-γ-responsive genes	Fold increase at C2D1	*P* value
PD-L1	**2.4**	**3.5×10^{-5}**
FCGR1B	1.8	1.5×10^{-3}
GBP2	1.5	5.6×10^{-4}
GBP5	2.3	1.3×10^{-4}
GBP1	2.0	1.9×10^{-4}
GBP4	1.7	9.4×10^{-4}

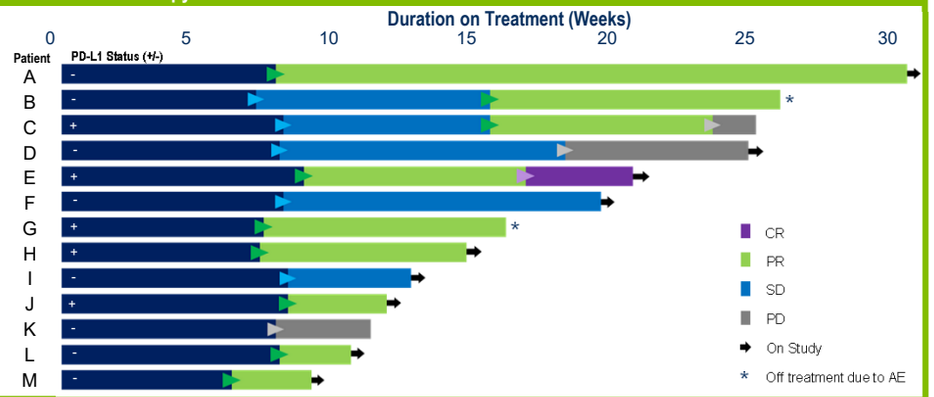
Consistent Evidence of Eganelisib Activity Across Six Different Tumor Types, Three Combination Regimens and Multiple Lines of Therapy in Over 130 Patients

Population		2L Urothelial Cancer		1L TNBC		Advanced TNBC	Advanced Ovarian	Melanoma (≤ 2 lines)	SCCHN (≤ 2 lines)
Study		MARIO-275[a]		MARIO-3[d]		ARC-2[e]	ARC-2[e]	MARIO-1[f]	MARIO-1[g]
Combination		Eganelisib + Nivolumab		Eganelisib + Tecentriq + Abraxane		Eganelisib + Etruma + Doxil	Eganelisib + Etruma + Doxil	Eganelisib + Nivolumab	Eganelisib + Nivolumab
Control Arm		Nivolumab + Placebo Control Arm				Etrumadenant (Etruma) + Doxil	Etrumadenant (Etruma) + Doxil	Progression on immediate prior CPI	Progression on immediate prior CPI
Industry Benchmark Approval Data		CheckMate-275 Benchmark Nivolumab Monotherapy		IMpassion130 Benchmark Tecentriq + Abraxane (n=450)					
		PD-L1 (-)	PD-L1 (+)	PD-L1 (-)	PD-L1 (+)				
ORR	Combo Arm	**26%** (n=23)	80% (n=5)	**50%** (n=8)	**100%** (n=5)	**25%** (n=8)	**75%** (n=4)	**21.1%** (n=40)	**20%** (n=20)
	Control Arm	**14%** (n=7)	40% (n=5)			**9%** (n=11)	**14%** (n=7)	Response/ DCR not expected	Response/ DCR not expected
	Industry Benchmark		**26%** (n=124)[b]	Not Reported/ Not Approved (n=266)	**58.9%** (n=185)				
DCR	Combo Arm	**57%** (n=23)	80% (n=5)						
	Control Arm	**14%** (n=7)	60% (n=5)						
	Industry Benchmark		**52%** (n=124)[b,c]						
PFS	Combo over Control Arm	PD-L1 (-)	ITT						
		0.54	0.83						

References:
a. Tomczak et al. ASCO GU 2021
b. Sharma et al. AACR Annual Meeting 2018
c. Infinity calculation from Sharma AACR 2018
d. Hamilton E et al. SABCS 2020
e. Gardner O et al. SABCS 2020
f. Postow et al. SITC 2020
g. Cohen et al. SITC 2020
h. Hong et al. SITC 2017

MARIO-3: Ph 2 Study Initial Data Evaluating Eganelisib, Atezolizumab, and Nab-Paclitaxel as 1L Therapy for TNBC[d]

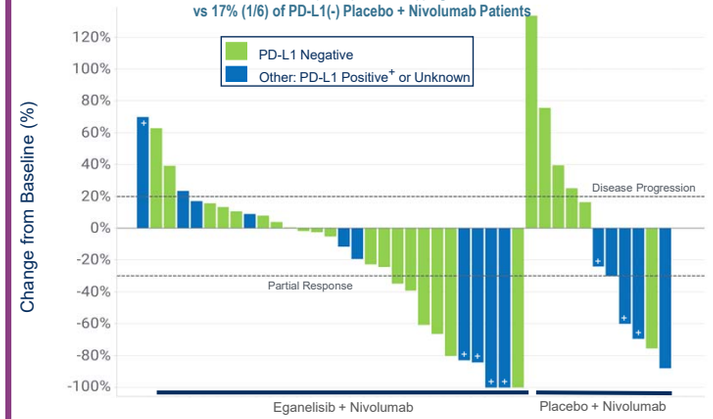




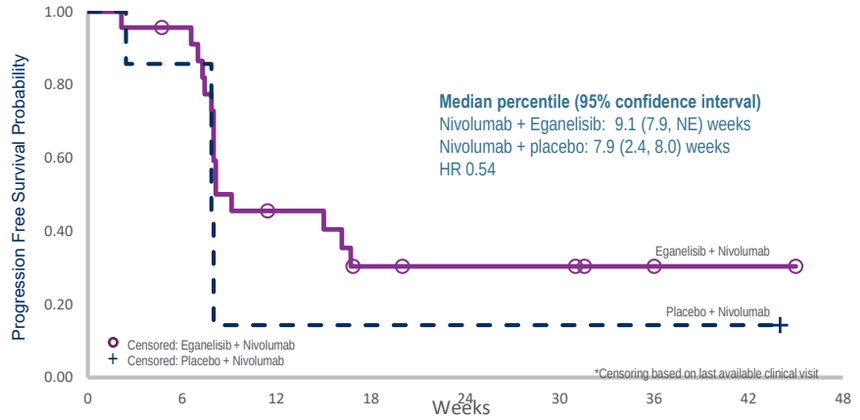
MARIO-275: Ph 2, Randomized, Placebo-Controlled Study to Evaluate Efficacy and Safety of Eganelisib Plus Nivo Compared to Nivo Plus Placebo in Urothelial Carcinoma Patients[a]

Best Percent Change in Tumor Volume of Target Lesion (N=40)

Reduction of Tumor Burden in 58% (11/19) of PD-L1(-) Eganelisib + Nivolumab Patients vs 17% (1/6) of PD-L1(-) Placebo + Nivolumab Patients

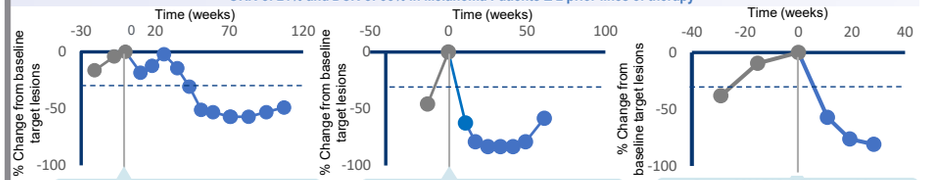


PD-L1 Negative Patients: Preliminary RECIST* PFS



MARIO-1: Ph 1/1b Study in Patients with Solid Tumors[f,g]

ORR of 21% and DCR of 53% in Melanoma Patients ≤ 2 prior lines of therapy

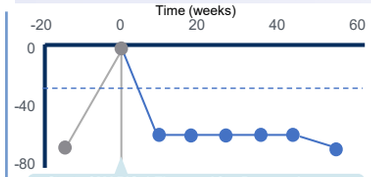


- Patient A with Stage III melanoma at study entry
- 57% tumor reduction in response to treatment with eganelisib + nivolumab
- PFS: > 25 months

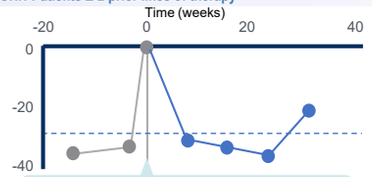
- Patient B with Stage IV melanoma at study entry
- 79% tumor reduction in response to treatment with eganelisib + nivolumab
- PFS: 14 months

- Patient C with Stage IV melanoma at study entry
- 76% tumor reduction in response to treatment with eganelisib + nivolumab
- PFS: 6 months

ORR of 20% and DCR of 40% in SCCHN Patients ≤ 2 prior lines of therapy



- Patient D with Stage IV SCCHN at study entry
- Refractory to pembrolizumab after 15 months
- 63% tumor reduction in response to eganelisib + nivolumab treatment
- PFS: 11 months



- Patient E with Stage IV SCCHN at study entry
- Refractory to pembrolizumab after 5 months
- 36% tumor reduction in response to eganelisib + nivolumab treatment
- PFS: 7 months

Conclusions and Next Steps

- Growing body of data showing that eganelisib is well tolerated[a,d,e,f,g] and active across six different tumor types, three combination regimens and multiple lines of therapy in over 130 patients.
- MARIO-1 results demonstrate the ability of eganelisib to overcome resistance to checkpoint inhibitor therapy.
- MARIO-275 results show adding eganelisib to nivolumab results in an improvement over standard of care checkpoint inhibitor monotherapy particularly in PD-L1 low patient population.
- Continuing to advance our MARIO-3 study (39 patients enrolled as of 22Apr2021) in 1L TNBC based on very encouraging early results with a 100% response rate in PD-L1 positive patients and a 50% response rate in PD-L1 negative patients for whom checkpoint inhibitors have not shown a benefit and are not approved.

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