A phase 1/2 study of GB1275, a first-in-class CD11b modulator, as monotherapy and with an anti-PD-1 antibody in specified advanced solid tumors or with chemotherapy in metastatic pancreatic cancer (KEYNOTE A36)

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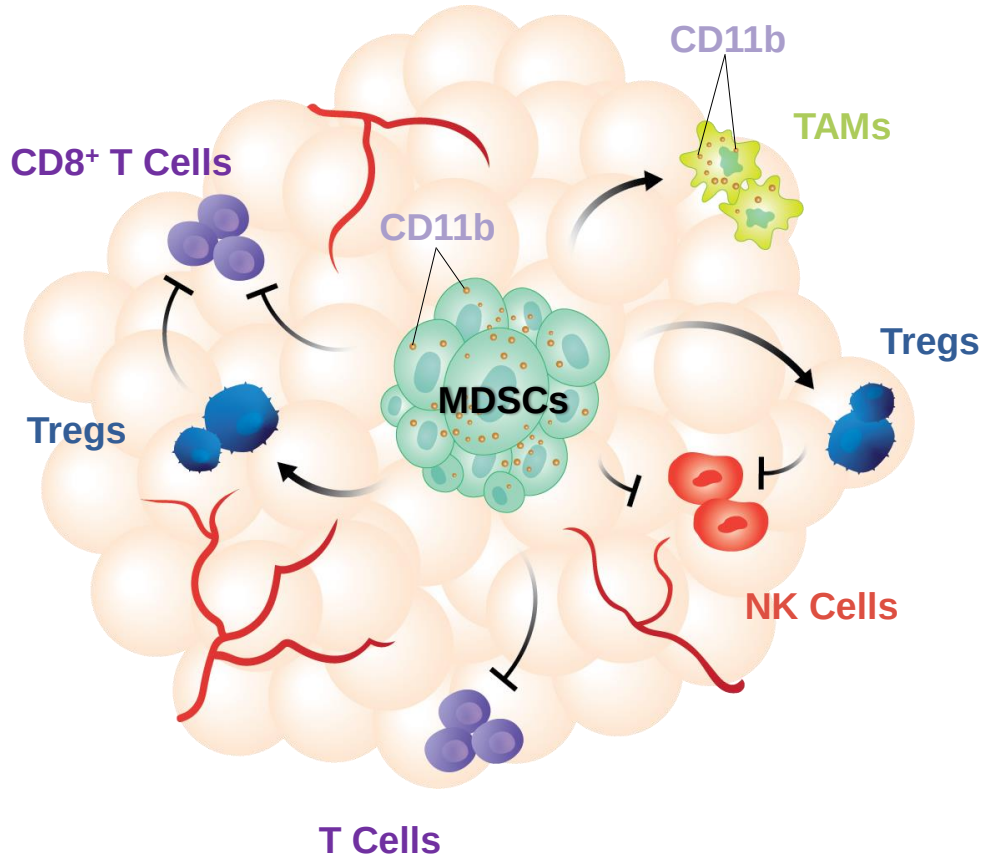
Introduction

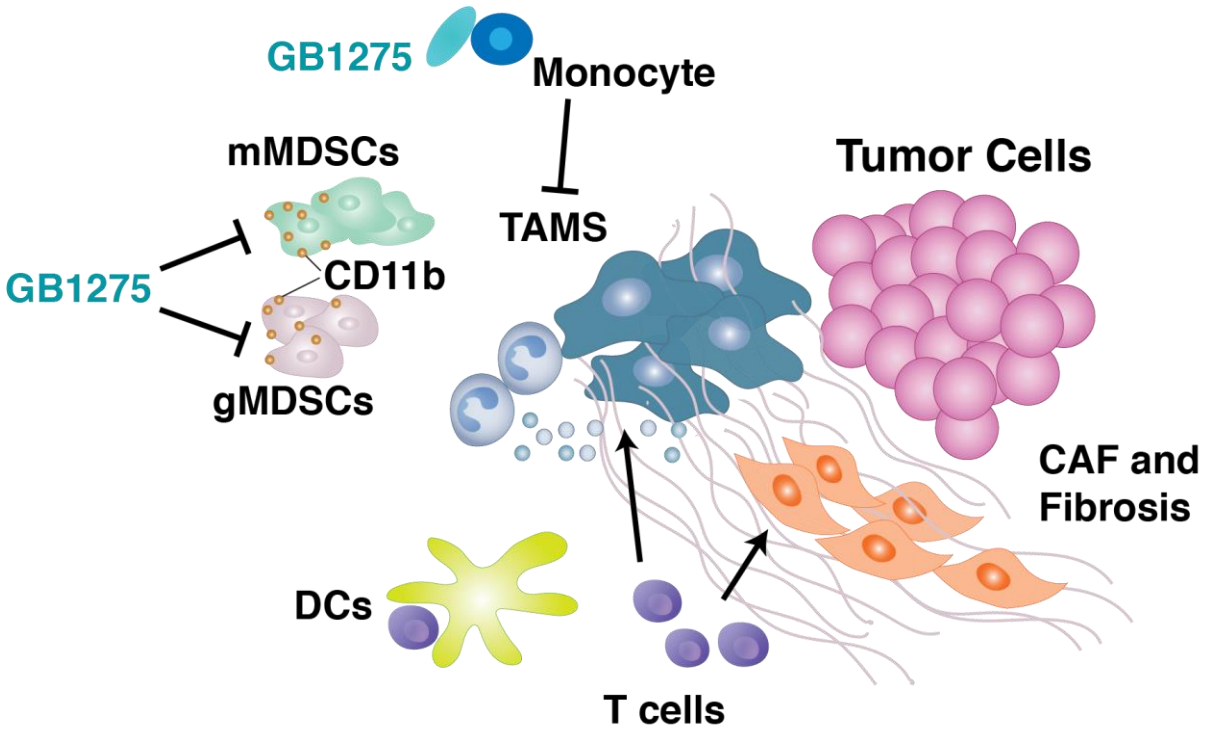
- CD11b is a cell surface integrin highly expressed on myeloid cells such as neutrophils, monocytes, and macrophages and is critical to cell adhesion and migration, and phagocytosis[1]
- Tumor influx of CD11b-expressing MDSCs and M2 TAMs creates an immunosuppressive TME associated with resistance to anti-PD-1 axis therapy[2-4]
- GB1275 is a first-in-class, CD11b modulator shown to reduce MDSCs and TAMs, repolarize M2 immunosuppressive TAMs to an M1 phenotype, and increase tumor infiltration of activated CD8+ T cells in vivo[5]
- This ongoing phase 1/2 study evaluates GB1275 alone and combined with an anti-PD1 antibody or standard of care chemotherapy in tumor types known to be IO-resistant



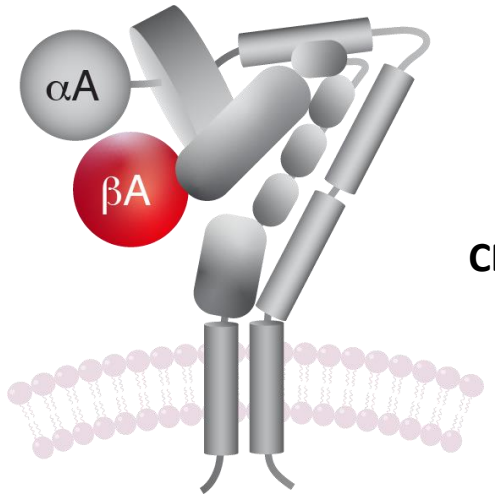
1. Arnaout MA. *F1000Res*. 2016;5. 2. Fleming V, *et al. Front Immunol*. 2018; 9:398. 3. Kumar V, et al. *Trends Immunol*. 2016; 37(3):208-220. 4. Mantovani A, et al. *Trends Immunol*. 2002; 23(11):549-555.
5. Panni R, et al. *Sci Transl Med*. 2019; 11: eaau9240. I/O, immuno-oncology; MDSCs, myeloid-derived suppressor cells; TAMs, tumor-associated macrophages; TME, tumor microenvironment

CD11b Modulation is a Novel MDSC / TAM-Targeting Approach

Tumor Microenvironment



GB1275 Mechanism of Action



CD11b receptor

Inactive

GB1275 is an allosteric small molecule modulator of CD11b

CAF, cancer-associated fibroblast; DCs, dendritic cells; gMDSCs, granulocytic myeloid-derived suppressor cells; mMDSCs, monocytic myeloid-derived suppressor cells TAMs

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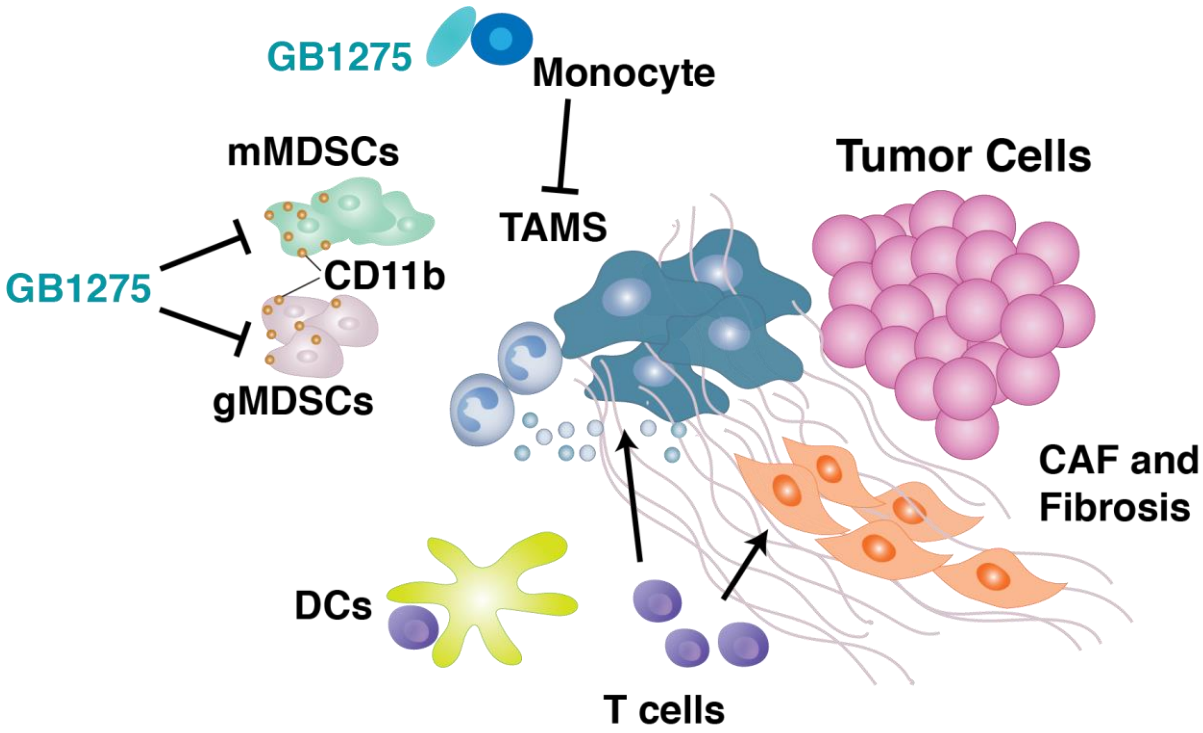

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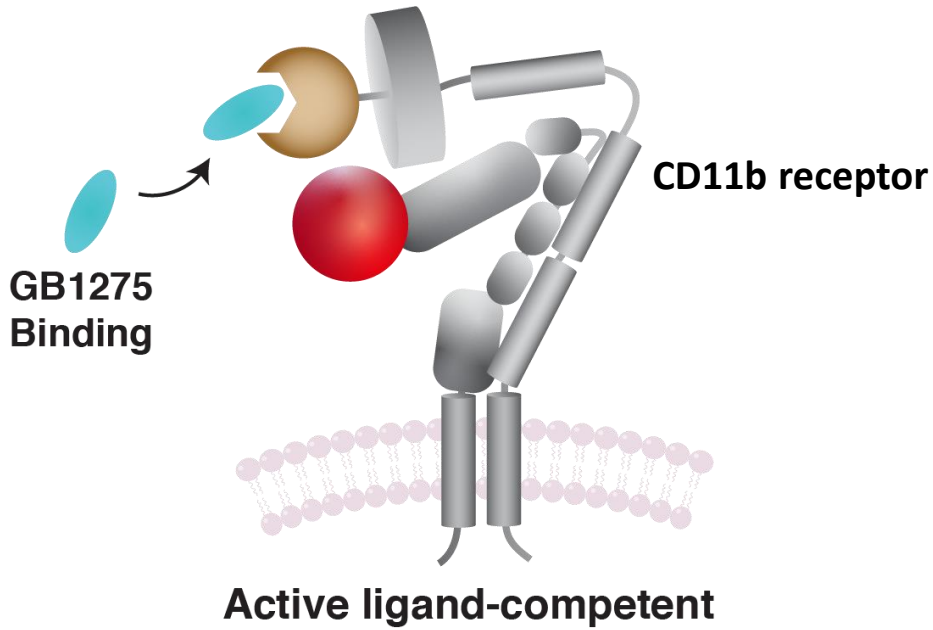

CAF, cancer-associated fibroblast; DCs, dendritic cells; gMDSCs, granulocytic myeloid-derived suppressor cells; mMDSCs, monocytic myeloid-derived suppressor cells TAMs

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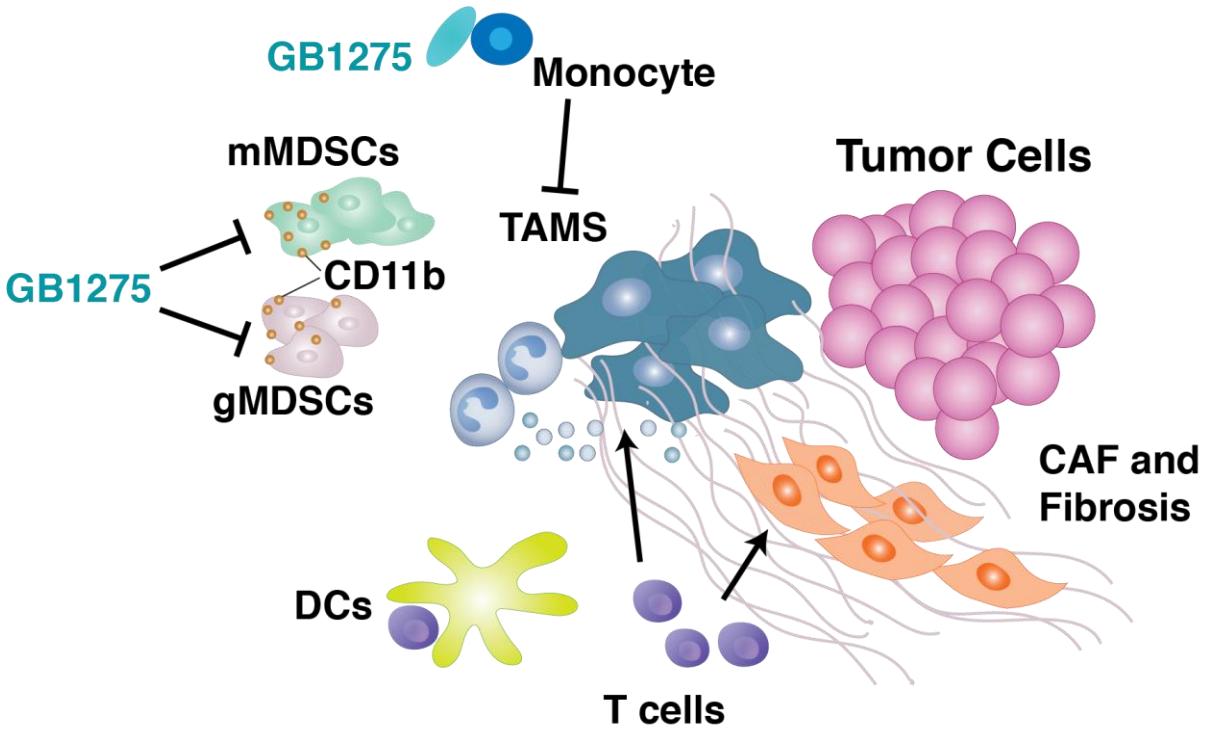

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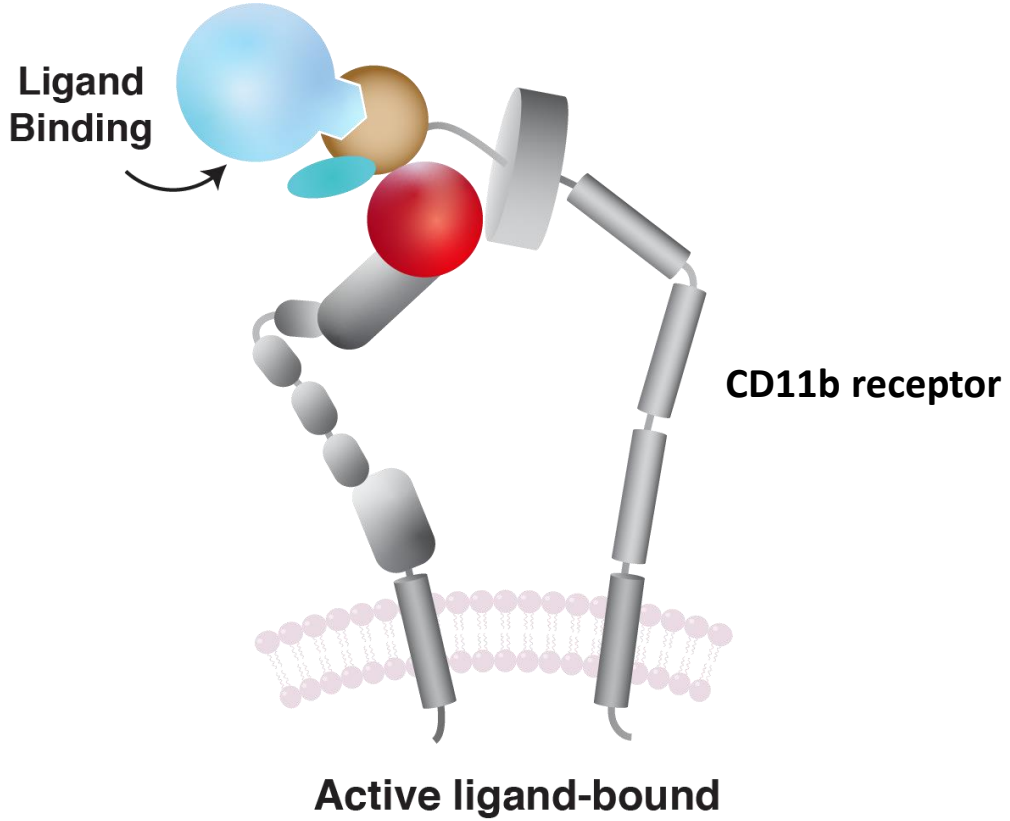
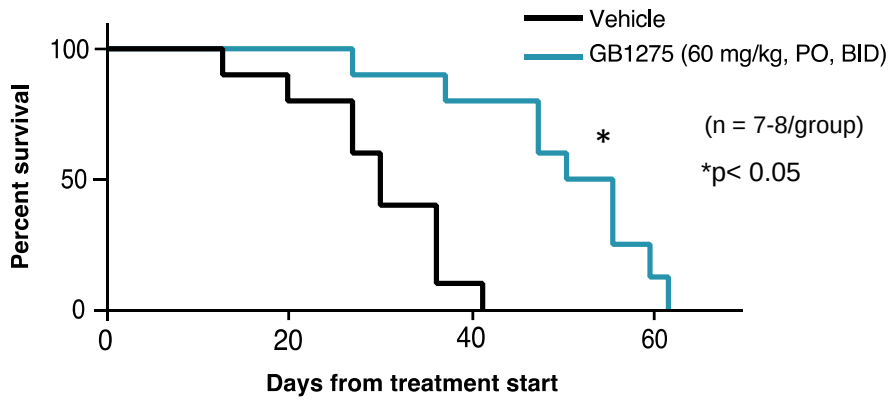


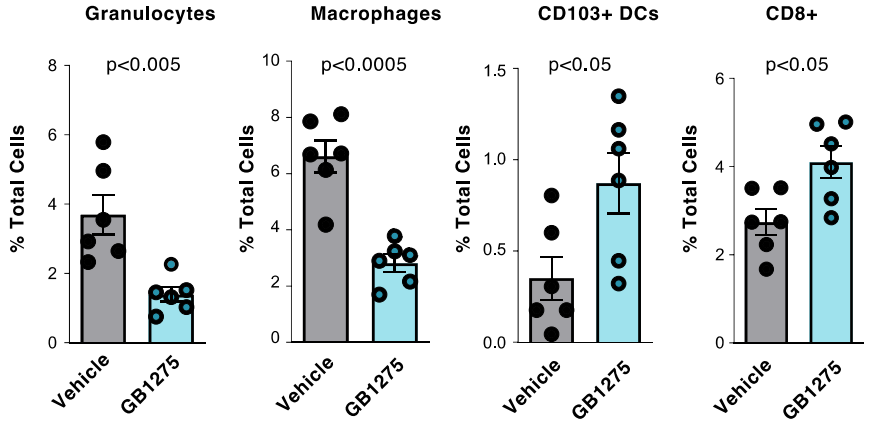
CAF, cancer-associated fibroblast; DCs, dendritic cells; gMDSCs, granulocytic myeloid-derived suppressor cells; mMDSCs, monocytic myeloid-derived suppressor cells TAMs

GB1275 Pre-clinical Data: Single Agent and Combination Activity in Orthotopic PDAC Model

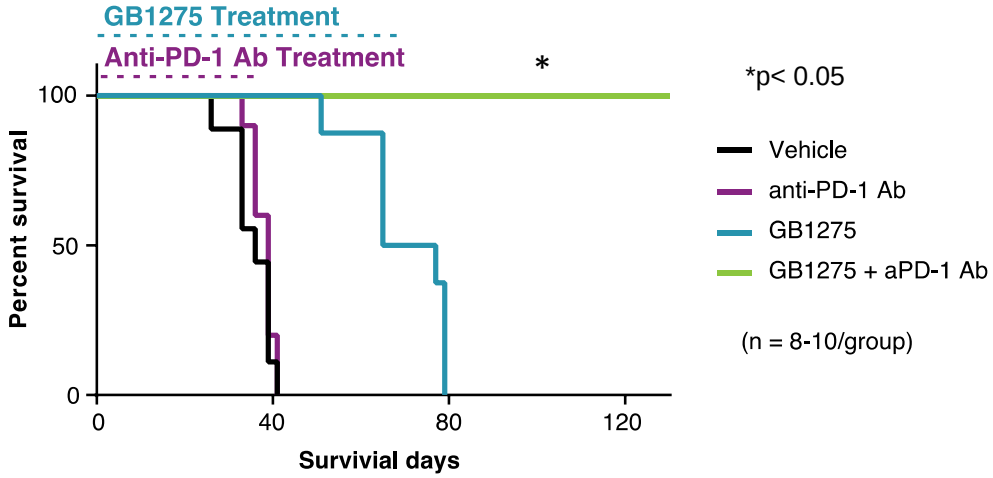
Survival: GB1275 vs Control



Tumor Biopsy: Biomarker Data

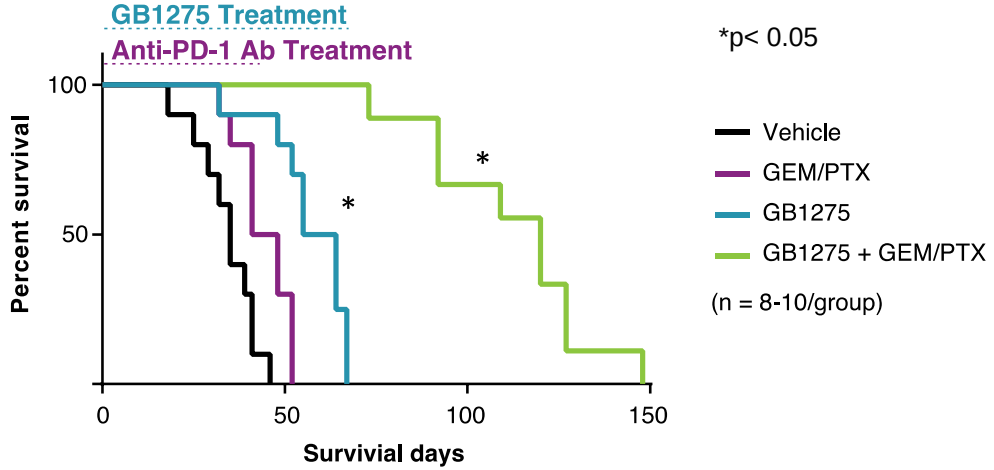


Survival: GB1275 + anti-PD1



Panni R, et al. *Sci Transl Med*. 2019; 11: eaau9240.

Survival: GB1275 + Chemo



GB1275 anti-tumor activity has also been shown in other preclinical models, such as breast cancer, melanoma, and colorectal cancer.

KEYNOTE-A36: Phase 1/2 Study of GB1275

Regimen A: GB1275 Monotherapy

- Dose 5
- Dose 4
- Dose 3
- Dose 2
- Dose 1

Regimen B: GB1275 +pembrolizumab

- Dose 5 + Pembro
- Dose 4 + Pembro
- Dose 3 + Pembro
- Dose 2 + Pembro
- Dose 1 + Pembro

Tumor Types (Refractory)

- MSS-CRC
- Pancreatic
- Gastric
- TNBC
- Prostate
- Esophageal

Regimen C (Safety Run-in)
Gemcitabine/nab-paclitaxel + GB1275
n ≈ 9

Ph 2 Expansion and Cohorts

PDL1 + Gastric/GEJ Cancer

Pembrolizumab + GB1275
n = 40

MSS-CRC

Pembrolizumab + GB1275
n = 26

1L metastatic Pancreatic Cancer

Gemcitabine/nab-paclitaxel + GB1275
n = 39

GEJ, gastroesophageal junction; MSS-CRC= microsatellite stable-Colorectal cancer; TNBC= triple negative breast cancer

Summary

- GB1275 is a first-in-class modulator of CD11b and disrupts multiple immunosuppressive myeloid cell subsets
- Preclinical data suggest differentiation from other approaches targeting immunosuppressive mechanisms
- Preclinical efficacy has been observed as single agent and in combination with chemo and anti-PD1 axis therapies
- Opportunity to target IO-resistant tumors: PDAC, MSS-CRC, CRPC, and those less responsive to IO: TNBC, and gastric and esophageal cancers
- In collaboration with Merck, Inc., Gossamer Bio, Inc. is examining GB1275 as monotherapy and in combination with pembrolizumab or chemotherapy in these IO-resistant tumors (NCT04060342)

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Thank you!

Questions?

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