# A phase II clinical trial of the phosphatidylserine targeting antibody, bavituximab in combination with pembrolizumab in patients with advanced hepatocellular carcinoma

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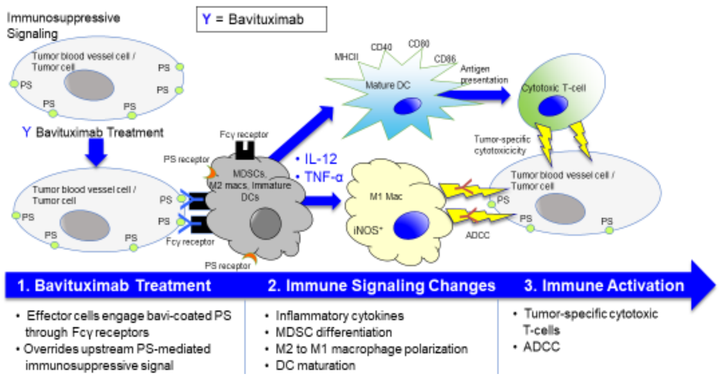
## BACKGROUND

- Phosphatidylserine is a highly immunosuppressive molecule typically expressed on the inner leaflet of the plasma membrane of normal cells.
- Phosphatidylserine and becomes externalized to the outer leaflet of the plasma membrane on cells that line tumor blood vessels, tumor cells, and exosomes in the tumor microenvironment creating a specific target for anticancer treatments.

### Bavituximab

- First-in-class chimeric monoclonal antibody in clinical development for cancer.
- Complexes with β2-glycoprotein 1 to inhibit immunosuppressive phosphatidylserine signalling.
- Can modulate the tumor microenvironment (TME) by driving innate and adaptive immunity.




## STUDY DESIGN & HYPOTHESIS

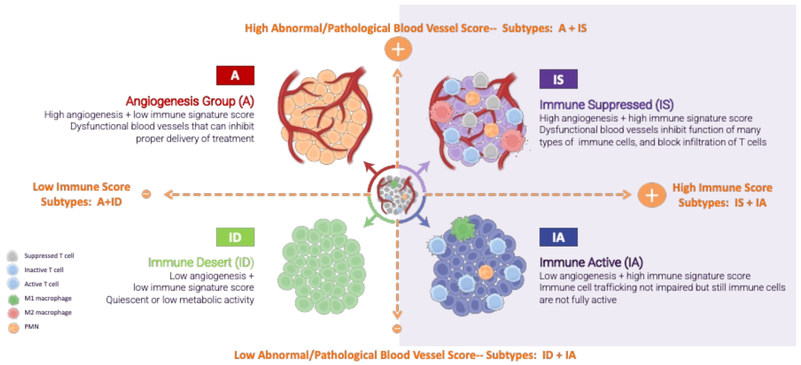
- Phase 2, single arm, clinical trial
- Sample size:
  - 28 evaluable patients
  - 3 or more of the first 15 patients should have a complete or partial response
- Hypothesis: the addition of bavituximab can increase the clinical activity of pembrolizumab for patients with advanced HCC

Locally advanced or metastatic HCC not amenable to locoregional therapy → Pembrolizumab: 200 mg IV once every 3 weeks; Bavituximab: 3 mg/kg IV weekly → Endpoints:
*Primary*: ORR
*Secondary*: OS, 6-months PFS, DOR, Safety
*Exploratory*: Correlative

## Xerna™ TME PANEL

- Pre-treatment tumor biopsies were analysed for RNA expression using a biomarker panel (Xerna™ TME Panel [OncXerna Therapeutics, Inc.]) to determine the dominant angiogenic and immunogenic biology in the patient's TME, and the findings were correlated with tumor response.
  - Xerna™ TME Panel is a qualitative in vitro diagnostic assay that uses next-generation sequencing to determine a gene expression profile from formalin-fixed paraffin-embedded samples.
  - The assay has been validated for Total RNA-Seq chemistry (Roche Kapa) in combination with the Illumina NextSeq 500/550 sequencer.
- A retrospective analysis was conducted to test the hypothesis that tumors with high immune score (immune active [IA] or immune-suppressed [IS] TME subtypes [biomarker-positive]) are more likely to respond to bavituximab + pembrolizumab than those with angiogenic (A) or immune-desert (ID) TME subtypes (biomarker-negative).

**Biomarker Panel Subtypes Based on Angiogenesis and Immune Signature Score**




## PATIENT CHARACTERISTICS (N=28)

| | |
|---|---|
| **Age, median, y (IQR)** | 64 (60-67) |
| **Sex** | |
| Female no. (%) | 4 (14.3) |
| Male no. (%) | 24 (85.7) |
| **Race** | |
| Asian no. (%) | 0 (0) |
| Black no. (%) | 14 (50) |
| White no. (%) | 14 (50) |
| **Ethnicity** | |
| Hispanic no. (%) | 2 (7.1) |
| Non-Hispanic no. (%) | 26 (92.9) |

## SAFETY

**Treatment-related Adverse Events**

| Adverse Event | Grade ≥ 3 No. (%) | All No. (%) |
|---|---|---|
| Rash | 1 (3.6) | 3 (10.7) |
| AST increase | 1 (3.6) | 3 (10.7) |
| Chills | 0 (0) | 2 (7.1) |
| Diarrhea | 1 (3.6) | 5 (17.9) |
| Fatigue | 0 (0) | 3 (10.7) |
| Platelet count decrease | 0 (0) | 2 (7.1) |
| Pruritus | 0 (0) | 3 (10.7) |
| ALT increase | 0 (0) | 2 (7.1) |

## EFFICACY

| Best Overall Response N (%) | All Patients[1] N =28 | Patients with Biomarker Data[2] | | |
|---|---|---|---|---|
| | | All N =19 | Biomarker + N = 8 | Biomarker - N =11 |
| Complete response[3] | 2 (7.1) | 1 (5.3) | 1 (12.5) | 0 (0) |
| Partial response[3] | 7 (25.0) | 5 (26.3) | 4 (50.0) | 1 (9.1) |
| Stable disease | 5 (17.9) | 3 (15.8) | 1 (12.5) | 2 (18.2) |
| Progressive disease | 14 (50.0) | 10 (52.6) | 2 (25.0) | 8 (72.7) |
| Objective response rate | 9 (32.1) | 6 (31.6) | 5 (62.5) | 1 (9.1) |
| Disease control rate | 14 (50.0) | 9 (47.4) | 6 (75.0) | 3 (27.3) |

*[1]Analysis based on evaluable patients per protocol; [2]All patients with available biomarker results; 9 patients did not have tissue available for testing and biomarker status could not be determined. [3]Responses were confirmed by radiographic assessment no sooner than 4 weeks from the time of initial response.*

## CONCLUSIONS

- Bavituximab plus pembrolizumab is well tolerated with no new safety signals.
- Bavituximab plus pembrolizumab induces objective tumor responses in a meaningful subset of HCC in the frontline setting.
- Retrospective analysis of tumor biopsies showed that responses were enhanced in Xerna TME biomarker-positive patients while higher PD rates were observed in biomarker-negative patients.

## ACKNOWLEDGEMENTS & DISCLOSURES

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- David Hsieh declares no conflicts of interest.

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