Phase 1 trial of first-in-class anti-CD96 monoclonal antibody inhibitor, GSK6097608, monotherapy and in combination with anti–PD-1 monoclonal antibody, dostarlimab, in advanced solid tumors

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Abstract:

Patients will be given IV GSK6097608 alone or in combination with IV dostarlimab until disease progression, unacceptable toxicity, or withdrawal of consent.

Eligibility criteria:

- Adenocarcinoma, melanoma, squamous cell carcinoma, or other solid tumor types that have progressed after standard therapy for the specific tumor type, or which are inappropriate for standard therapy
- Measurable disease per RECIST 1.1
- Prior anti–PD-1 therapy is allowed if the last dose of anti–PD-1 therapy is given ≥4 weeks prior to first dose of study treatment
- The primary endpoint is safety (DLTs and AEs)

Study population:

- Adults (≥18 years old)
- Liquidating or solid tumors that have progressed after standard therapy for the specific tumor type, or which are inappropriate for standard therapy
- Measurable disease per RECIST 1.1
- Prior anti–PD-1 therapy is allowed if the last dose of anti–PD-1 therapy is given ≥4 weeks prior to first dose of study treatment

Study endpoints:

- Dose-limiting toxicity and adverse events
- ORR per RECIST 1.1
- PD-1 blockade

Study Design:

- Open label
- Multicenter
- Nonrandomized

Current Trial Sites:

Los Angeles, CA
Dallas, TX
Houston, TX
San Antonio, TX
Tokyo, Japan

References:


Abbreviations:

CD96: CD96 is an immune checkpoint that modulates T- and NK-cell activity to promote tumor immune evasion

CD226 axis:

- The CD226 axis plays an important role in NK- and T-cell biology and immunity.
- CD226 is an immune costimulatory molecule expressed on T- and NK-cell subsets.
- CD226 binding to ligands CD112 and CD244 on tumors and antigens presenting cells and stimulates an immune response.
- Growing preclinical (CD96) and clinical (PD-1) evidence underscores the importance of CD96, PD-1, and PD-L1 in promoting immune suppression and tumor evasion.

Methods:

Study design:

- In this open label, nonrandomized, sequential assignment trial (NCT04443551), patients will receive IV infusion of GSK6097608 every 3 weeks as monotherapy or in combination with IV dostarlimab.
- Patients will be given IV GSK6097608 alone or in combination with IV dostarlimab until disease progression, unacceptable toxicity, death, or withdrawal of consent.
- Based on the safety, pharmacokinetic, and pharmacodynamic properties of monotherapy, the combination arm will be opened.

Study population:

- Locally advanced, metastatic, or recurrent solid tumors
- Advanced disease per RECIST 1.1
- Measurable disease per RECIST 1.1

Outcome measures:

- The primary endpoint is safety (DLTs and AEs)
- Secondary endpoints include additional safety parameters, ORR, and PK

Study Endpoints:

- Primary
  - Dose-limiting toxicity and adverse events
- Secondary
  - ORR per RECIST 1.1
  - PD-1 blockade
  - PD-1 parameters of GSK6097608 and dostarlimab

Eligibility criteria:

- Adults (≥18 years old)
- Measurable disease per RECIST 1.1
- Prior anti– PD-1 therapy is allowed if the last dose of anti–PD-1 therapy is given ≥4 weeks prior to first dose of study treatment
- The primary endpoint is safety (DLTs and AEs)

Study Design:

- Open label
- Multicenter
- Nonrandomized

Current Trial Sites:

- The study is currently open and recruiting.

Disclosures:

- The authors have no relevant financial relationships to disclose.

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References: