Phase 1b Trial of ABBV-368 + Tilsotolimod in Combination With Nab-Paclitaxel and/or Budigalimab (ABBV-181) in Patients With Recurrent/Metastatic Head and Neck Squamous Cell Carcinoma

Poster #2195

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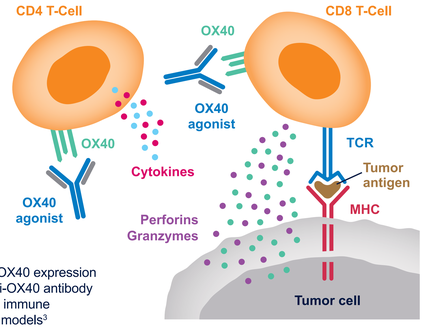
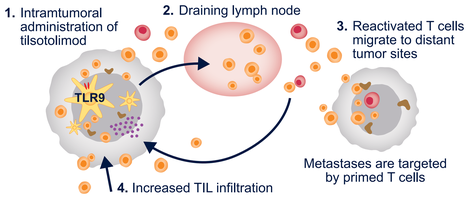
BACKGROUND

- Head and neck cancers account for approximately 4% of all cancers in the United States,[1] and patients with recurrent/metastatic head and neck squamous cell carcinoma (R/M HNSCC) have a poor prognosis, with a median survival in the second line of less than 7 months[2]
- Stimulation of the immune system to generate antitumor response represents a compelling therapeutic strategy, especially in patients with poor prognosis and limited treatment options
- OX40 is a type I transmembrane cell surface member of the tumor necrosis factor (TNF) receptor superfamily that plays a critical role in the enhancement of nascent immune responses and suppresses regulatory T-cell activity
- Preclinical studies have shown that TLR9 agonists can induce OX40 expression on CD4 T-cells in the tumor microenvironment; an agonistic anti-OX40 antibody can then be used to co-stimulate a tumor antigen specific T-cell immune response. This approach has led to tumor regression in mouse models[3]
- **ABBV-368** is a novel, immunoglobulin G1 anti-OX40 monoclonal antibody agonist that elicits tumor responses by stimulating effector T cells and inhibiting regulatory T cells[4]



MHC, major histocompatibility complex; TCR, T-cell receptor.

- **Tilsotolimod** is a synthetic toll-like receptor 9 (TLR9) agonist with immunostimulatory activity[5]
- **Budigalimab** (ABBV-181) is a humanized, recombinant immunoglobulin G1 monoclonal antibody targeting programmed cell death protein-1 (PD-1) modified to reduce Fc receptor interactions and limit effector function



NK, natural killer; TIL, tumor-infiltrating lymphocyte.

STUDY OBJECTIVES

1 PRIMARY

- To assess the safety, tolerability, and pharmacokinetics (PK) of ABBV-368 plus tilsotolimod; ABBV-368 plus tilsotolimod and nab-paclitaxel; and ABBV-368 plus tilsotolimod, nab-paclitaxel, and budigalimab (ABBV-181) in patients with R/M HNSCC

2 SECONDARY

- To assess the preliminary antitumor activity of ABBV-368 plus tilsotolimod; ABBV-368 plus tilsotolimod and nab-paclitaxel; and ABBV-368 plus tilsotolimod, nab-paclitaxel, and budigalimab in patients with R/M HNSCC based on Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1)

EXPLORATORY

- To assess the preliminary antitumor activity of ABBV-368 plus tilsotolimod; ABBV-368 plus tilsotolimod and nab-paclitaxel; and ABBV-368 plus tilsotolimod, nab-paclitaxel, and budigalimab in patients with R/M HNSCC based on immune RECIST (iRECIST)
- To evaluate pharmacodynamic and predictive biomarkers for association with PK, safety, and efficacy measures in patients with R/M HNSCC
- To evaluate the immunogenicity of ABBV-368, tilsotolimod, and budigalimab in patients with R/M HNSCC

STUDY DESIGN

Multicenter and International

3 Treatment Arms

Estimated enrollment: **69** patients

Phase 1b

R/M HNSCC

NCT04196283

Initiated on January 22, 2020

KEY PATIENT ELIGIBILITY CRITERIA

KEY INCLUSION CRITERIA

- ✓ Age ≥18 years and weight >35 kg
- ✓ Eastern Cooperative Oncology Group performance status of 0 or 1 and life expectancy of ≥3 months
- ✓ Histologically or cytologically confirmed R/M HNSCC of the oral cavity, oropharynx, larynx, or hypopharynx that previously progressed either during or after ≤3 prior treatment regimens administered in the recurrent or metastatic setting
- ✓ Must have received 1 immunotherapy regimen that included a PD-(L)1 inhibitor
- ✓ Must have ≥1 measurable target lesion per RECIST v1.1
- ✓ Must have ≥1 lesion accessible for intratumoral (IT) injection, and lesion(s) must be ≥2 cm in longest diameter
- ✓ Adequate liver and bone marrow function

KEY EXCLUSION CRITERIA

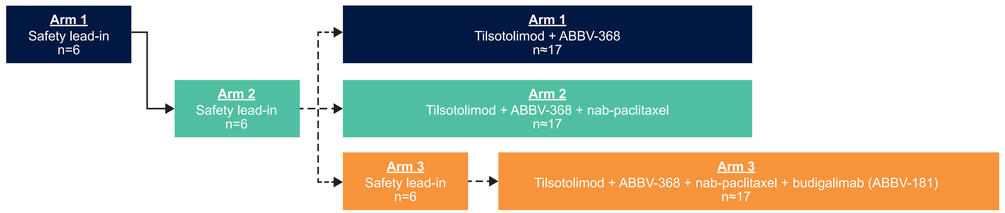
- ✗ Received prior treatment with OX40 or TLR agonists (excluding topical agents)
- ✗ Uncontrolled metastases to the central nervous system
  - Patients with brain metastases are eligible provided that there is evidence of clinically and radiographically stable disease for at least 4 weeks after therapy is administered and patients have not used prohibited levels of steroids for at least 4 weeks prior to first dose of the study drug
- ✗ History of clinically significant uncontrolled condition(s) including but not limited to the following: uncontrolled hypertension; Grade ≥3 peripheral neuropathy; active uncontrolled infection; symptomatic congestive heart failure; unstable angina pectoris or cardiac arrhythmia; and psychiatric illness/social situation that would limit compliance with the study
- ✗ Active autoimmune disease requiring therapy within the previous 2 years, with exceptions of vitiligo, type I diabetes mellitus, hypothyroidism, and psoriasis
- ✗ History of inflammatory bowel disease, pneumonitis, primary immunodeficiency, bone marrow transplantation, chronic lymphocytic leukemia, solid organ transplantation, interstitial lung disease, or active or latent tuberculosis without completion of standard-of-care treatment
- ✗ Positive test results for HIV or chronic or active hepatitis A, B, or C
  - Patients who have a history of hepatitis B or C and undetectable levels of hepatitis B viral DNA or hepatitis C viral RNA after antiviral therapy may be enrolled
- ✗ Received a live attenuated vaccine within 4 weeks of the first study dose

STUDY TREATMENT

THIS STUDY CONSISTS OF 3 TREATMENT ARMS:

1. Patients in **Arm 1** will receive intravenous (IV) ABBV-368 + tilsotolimod IT
2. Patients in **Arm 2** will receive IV ABBV-368 + tilsotolimod IT + IV nab-paclitaxel
3. Patients in **Arm 3** will receive IV ABBV-368 + tilsotolimod IT + IV nab-paclitaxel + IV budigalimab

Figure 1 – Study Design



STUDY ASSESSMENT AND STATISTICAL METHODS

- **Safety:** Safety and tolerability will be measured by monitoring adverse events (AEs), vital sign measurements, and clinical laboratory testing (hematology, chemistry, and urinalysis) as per the National Cancer Institute's Common Terminology Criteria for Adverse Events, version 5 (NCI CTCAE, v5)
- **Efficacy**: Objective response rate (ORR), clinical benefit rate (CBR), time to response (TTR), progression-free survival (PFS), and duration of response (DOR) will be assessed according to RECIST v1.1 and iRECIST; tumor assessments will be performed at baseline and multiple timepoints throughout the study until study completion
- **PK:** PK samples to assess serum concentrations of ABBV-368 and budigalimab and plasma concentrations of tilsotolimod will be obtained at multiple timepoints throughout the study
- **Biomarkers**: Biospecimens will be collected at specified timepoints to evaluate receptor occupancy and pharmacodynamic biomarkers in the blood and tissues
- **Immunogenicity**: Antidrug antibody (ADA) assays will be performed and reported as positive or negative

SUMMARY

- This multicenter, international Phase 1b study is investigating the safety, tolerability, and PK of ABBV-368 plus tilsotolimod in combination with other immune-modulating agents in patients with R/M HNSCC
- Preliminary efficacy (ORR, CBR, TTR, PFS, and DOR) based on RECIST 1.1 will be assessed as secondary endpoints
- Preliminary efficacy (ORR, CBR, TTR, PFS, and DOR) based on iRECIST, as well as pharmacodynamics and predictive biomarkers will be assessed as exploratory endpoints

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DISCLOSURES

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