AdvanTIG-206: Anti-TIGIT monoclonal antibody ociperlimab + anti-PD-1 monoclonal antibody tislelizumab + BAT1706 vs tislelizumab + BAT1706 as first-line treatment for unresectable hepatocellular carcinoma

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Background

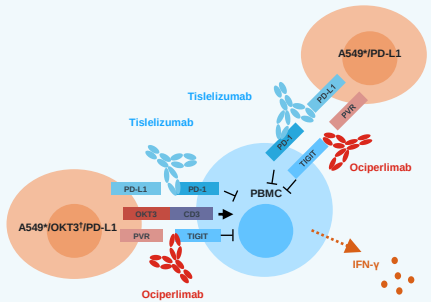
Unmet need in hepatocellular carcinoma (HCC)

- Liver cancer is one of the leading causes of cancer-related mortality, with 841,000 new cases reported in 2018[1]. HCC is the most common type of primary liver cancer worldwide[1]
- Tyrosine kinase inhibitors (sorafenib and lenvatinib) are approved in first-line treatment for unresectable HCC; however, life expectancy remains poor.[2–6] Furthermore, many patients experience adverse events leading to dose reductions and treatment interruptions[7–9]
- In the first-line setting, the combination of anti-programmed death-ligand 1 (PD-L1) therapy with anti-vascular endothelial growth factor (VEGF) therapy has improved overall survival and progression-free survival outcomes compared with sorafenib for patients with unresectable HCC[8]
- Despite improvements in clinical outcomes with PD-L1 combination therapy, new treatment options are needed to further improve overall survival and quality of life for patients with unresectable HCC

Introduction to ociperlimab, tislelizumab, BAT1706 and AdvanTIG-206 study

- T-cell immunoreceptor with immunoglobin and immunoreceptor tyrosine-based inhibition motif domain (TIGIT) is a co-inhibitory immune checkpoint receptor that is upregulated on T cells and natural killer cells in multiple solid tumors, which can cause tumor escape from immune surveillance[10,11]
- Ociperlimab is a humanized immunoglobin G1 (IgG1) monoclonal antibody (mAb) designed to bind to TIGIT with high specificity, blocking the interaction with CD155 (Poliovirus receptor [PVR]) and CD112 (PVR-L2) ligands on tumor cells[12]
- PD-L1 is an immune checkpoint protein that is overexpressed on the surface of tumor and immune cells in the tumor microenvironment.[13] Interactions between PD-L1 and programmed cell death 1 (PD-1) on T cells play an important role in suppressing antitumor activity[13]
- Tislelizumab is a humanized IgG4 anti-PD-1 mAb with high affinity and binding specificity for PD-1, and has demonstrated clinical activity in patients with previously treated, unresectable HCC[13–15]
- Dual targeting of tumors with anti-TIGIT and anti-PD-1 mAbs (**Figure 1**) has has shown synergistic inhibition of liver cancer growth in preclinical studies[16]
- BAT1706 is a proposed biosimilar of bevacizumab, an anti-VEGF antibody that has been shown to improve survival rates in HCC[17]

Figure 1. Dual targeting with anti-TIGIT and anti-PD-1 antibodies



Chen X, et al. Data presented at AACR 2021 (Abs 1854)
**PVR positive A549 cells; †anti-CD3 antibody clone; IFN, interferon; PBMC, human peripheral blood mononuclear cells; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; PVR, poliovirus receptor; TIGIT, T cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domain*

Conclusions

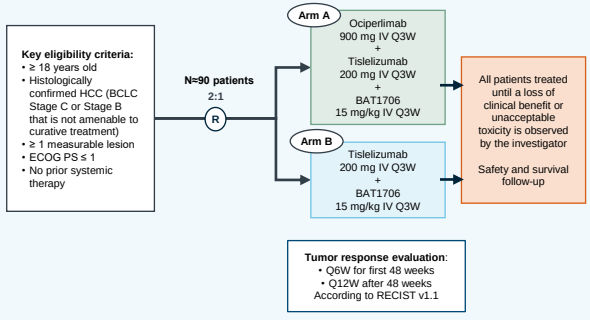
- **AdvanTIG-206** is a **Phase 2** study designed to investigate the **efficacy and safety of ociperlimab in combination with tislelizumab plus BAT1706,** and of **tislelizumab plus BAT1706,** as first-line treatments **in** patients with **unresectable HCC**

Methods

Study design and treatment

- AdvanTIG-206 is a randomized, multicenter, open-label, Phase 2 study (NCT04948697)
- Approximately 90 patients aged ≥ 18 years with histologically confirmed unresectable HCC, not amenable to curative treatment, will be enrolled (**Figure 2**)
- Eligible patients will be randomized 2:1 to:
  - **Arm A**: Ociperlimab 900 mg plus tislelizumab 200 mg and BAT1706 15 mg/kg intravenously (IV) once every three weeks (Q3W)
  - **Arm B**: Tislelizumab 200 mg plus BAT1706 15 mg/kg IV Q3W

Figure 2. Study design



BCLC, Barcelona-Clinic Liver Cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; HCC, hepatocellular carcinoma; IV, intravenous; ORR, objective response rate; Q12W, every 12 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks; R, randomized; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1

Endpoints and assessments

- The primary endpoint is objective response rate as assessed by the investigator according to Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1) (**Table 1**)
- Secondary and exploratory endpoints are also listed in **Table 1**
- Baseline tumor imaging will be performed ≤ 28 days before randomization
- Tumor response will be evaluated once every 6 weeks for the first 48 weeks of treatment, and once every 12 weeks thereafter, per RECIST v1.1
- Safety will be assessed through monitoring the incidence and severity of adverse events (graded according to National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0, vital signs and clinical laboratory results)
- Safety analyses will be performed using the safety analysis set (includes all randomized patients receiving ≥ 1 dose of the study treatment)
- Efficacy analysis will be performed using the intention-to-treat analysis set (includes all randomized patients)

Table 1. Endpoints of the study

AdvanTIG-206 endpoints	
Primary endpoint	• ORR assessed by the investigator according to RECIST v1.1
Secondary endpoints	• DoR assessed by the investigator • TTR assessed by the investigator • DCR assessed by the investigator • CBR assessed by the investigator • PFS assessed by the investigator • OS • Safety and tolerability • Serum concentrations of ociperlimab, tislelizumab and BAT1706 at specified timepoints • Immunogenic responses to ociperlimab, tislelizumab and BAT1706 evaluated through detection of antidrug antibodies
Exploratory endpoint	• Potential biomarkers associated with clinical response/resistance to study treatments

CBR, clinical benefit rate; DCR, disease control rate; DoR, duration of response; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; RECIST v1.1; Response Evaluation Criteria in Solid Tumors version 1.1; TTR, time to response

References

1. Bray F, et al. CA Cancer J Clin 2018;68:394–424
2. Bruix J, et al. Lancet 2016;389:56–66
3. Abou-Alfa GK, et al. N Engl J Med 2018;379:54–63
4. Kudo M, et al. Lancet 2018;391:1163–1173
5. NEXAVAR prescribing information. 2018 (accessed November 2021)
6. LENVIMA prescribing information. 2018 (accessed November 2021)
7. Llovet JM, et al. N Engl J Med 2008;359:378–90
8. Finn RS, et al. N Engl J Med 2020;382:1894–905
9. Iavarone M, et al. Hepatology 2011;54:2055–63
10. Manieri NA, et al. Trends Immunol 2017;38:20–8
11. Harjunpää H and Guillerey C. Clin Exp Immunol 2020;200:108–19
12. Chen X, et al. Presented at AACR 2021 (Abs 1854)
13. Desai J, et al. JITC 2020;8:e000453
14. Zhang T, et al. Cancer Immunol Immunother 2018;67:1079–90
15. Ducreux M, et al. Presented at WCGI 2021. (Abs 188)
16. Ostroumov D, et al. Hepatology 2021;73:1399–418
17. Siegel AB, et al. J Clin Oncol 2008;26:2992–8

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