Effectiveness and safety of toripalimab, camrelizumab and sintilimab in a real-world cohort of hepatitis B virus associated hepatocellular carcinoma patients

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Abstract

Aims: The investigation regarding the clinical significance of programmed cell death protein-1 (PD-1)-targeted immunotherapy in Chinese patients is rare. This study evaluated safety and efficacy of PD-1 with Toripalimab, Camrelizumab or Sintilimab for Chinese Hepatocellular carcinoma (HCC) patients in a real-life cohort. Methods: We retrospectively analyzed HBV associated HCC patients treated with Toripalimab, Camrelizumab or Sintilimab in a retrospective cohort from Nov 2018 to Dec 2019. Efficacy was evaluated with objective response rate (ORR), disease control rate (DCR), progression-free survival (PFS), time to tumor progression (TTP) and overall survival (OS). Results: Seventy eight patients were finally included in the analysis: 26 for Toripalimab, 36 for Camrelizumab, and 16 for Sintilimab. Mean duration of follow-up was 22.7 ± 12.6 weeks and the mean Cycles of PD-1 at cut-off were 4.8 ± 2.7 for all patients. The ORR and DCR for the whole cohort were 17.9% and 73.1%, respectively. Overall, 21 (26.9%) patients had radiological disease progression and 6 (7.7%) patients died during follow-up. Median PFS was 40.7 (95% CI, 34.7-46.7) weeks, median TTP was 45.7 (95% CI, 40.5-60.0) weeks, and median OS was 51.1 (95% CI, 46.4-55.9) weeks. Most frequent drug-related AEs were Rash (19.2%), Hypertension (15.4%), Fatigue (12.8%), Paraesthesia (12.8%), and Diarrhoea (10.3%). Conclusions: Our findings suggest that: 1. PD-1-targeted immunotherapy with Toripalimab, Camrelizumab or Sintilimab yielded a promising outcome in Chinese HBV patients with HCC; 2. Immunotherapy was well tolerated generally and had manageable side effects, which is worth of popularization and application in clinical practice.

What is known about this subject

- HCC is often diagnosed at an advanced stage due to its obscurity, rapid proliferation and metastasis, where only systemic treatment can be offered.
- The investigation regarding the clinical significance of PD-1-targeted immunotherapy in Chinese patients is rare.
- Three PD-1 antibodies approved by the NMPA of China, Toripalimab, Camrelizumab and Sintilimab, have notable price advantage than Nivolumab and pembrolizumab.

What this study adds

- PD-1-targeted immunotherapy with Toripalimab, Camrelizumab or Sintilimab yielded a promising outcome in Chinese HBV patients with HCC.
- PD-1 therapy was well tolerated generally and had manageable side effects, which is worth of popularization and application in clinical practice.
Introduction

Hepatocellular carcinoma (HCC) is one of the leading causes of cancer related death worldwide, particularly in China, where HCC cases alone account for more than half of the estimated global total [1]–[4]. The overall survival of HCC varies considerably across the world, with Taiwan and Japan, where comprehensive surveillance programs afford early detection and curative therapy, having the best clinical outcomes. The outcomes in China, along with North America and Europe, however, are not as good. In these countries, greater than 60% of patients present to the hospitals with intermediate to advanced-stage HCC [5]. Unfortunately, to most of the late stage patients, only systemic and/or palliative treatment can be offered. The average survival time of these patients is usually less than 1 year [6]–[10].

Sorafenib is a multi-tyrosine kinase inhibitor (TKI) that inhibits proteins involved in angiogenesis and proliferation pathways implicated in the pathogenesis of HCC, such as vascular endothelial growth factor receptors (VEGFR), Raf-1 and B-Raf [11]. This drug was approved for advanced HCC treatment in 2007 following phase III SHARP trial [12]. It has been the only effective first-line systemic treatment option available for over a decade. It was not until the recent that a few other TKIs such as lenvatinib[13], regorafenib[14] and cabozantinib[15] have been approved for first- and second-line HCC treatment. Although the use of TKIs has significant overall survival (OS) benefits over placebo, its effects are not easily sustained. Many of the treatment regimens have been limited by primary and secondary resistance to the drugs; or failed due to severe treatment related adverse events (TRAЕ) forcing the discontinuation of the therapy [11].

Immune checkpoint blocker therapy has demonstrated encouraging efficacy in multiple cancer types, particularly melanoma and lung cancers. A rapidly growing list of blocking antibodies to immune checkpoints has been approved for cancer treatment [16]. HCC, now generally considered as an immunogenic tumor, may also be a good candidate for such therapy [17]. Programmed cell death receptor-1 (PD-1) is a transmembrane molecule found to be expressed on the surface of T and B lymphocytes, natural killer T cells, activated monocytes and dendritic cells. PD-1 molecule negatively regulates T cell antigen receptor (TCR) signaling by interacting with specific ligands, namely PD-L1 and PD-L2 [18]–[20]. Aberrantly upregulated PD-L1 expression has been found on many tumor cells, which is likely to result in tumor induced immune suppression via PD-1 signaling, and in turn, favors the growth and expansion of tumor cells. Overexpression of PD-L1 has been demonstrated to be significantly associated with tumor aggression and postoperative recurrence in HCC [21], [22]. Disrupting the interaction between PD-1 and its ligands, using monoclonal antibody (mAb), prevents the activation of its downstream signaling pathways, and restores the host anti-tumor immunity[23]. Nivolumab and pembrolizumab are potent mAbs specifically targeting PD-1. CheckMate-040 (NCT016558878), a phase I study of nivolumab treating sorafenib-intolerant/refractory advanced HCC patients resulted in 20% objective response rate (ORR) and a promising 1 year OS rate of 62% [24]. Similarly in an open-label, no-randomized phase II study, KEYNOTE-224 (NCT02702401), pembrolizumab treatment has demonstrated an ORR of 16.3% and 77.9% 6-month OS [25]. Most other PD-1 inhibitor trials for advanced HCC are still at their patient recruitment or preliminary analysis stages; however, these findings were supported by an Austro-German international multicenter real world study of 65 patients. In this study, the objective response rate or nivolumab (n=34) was 15% and pembrolizumab (n=31) was 10%, resulted in an overall ORR of the 12% for this retrospective cohort of PD-1 inhibitor therapy [26].

There are three domestically developed PD-1 mAbs approved in China since 2016: two humanized PD-1 antibodies toripalimab (JS-001, Shanghai Junshi Bioscience Co. Ltd.)[27], camrelizumab (SHR-1210, Jiangsu Hengrui Medicine Co. Ltd)[28]; and sintilimab, a fully human PD-1 mAb (IBI308, Innovent Biologics and Eli Lilly and Company)[29]. Although these three drugs have been shown to be efficacious in several cancer types, so far only camrelizumab has been trial (NCT02989922) in HCC patients, the ORR was 13.8% and the six-month overall survival was 74.7% in this study of 217 patients [28]. The ORR is comparable to the typical 10-20% in other PD-1 therapy trials [24], [25], [28], [30]. However, being domestically developed, the most notable advantage of these drugs to Chinese patients is the significantly lower cost (approx. $17.5k, $17.0k and $13.9k USD respectively), a fraction of nivolumab (approx. $63k USD) and pembrolizumab (approx. $87k USD). It is important to note that China’s large population of HCC patients consists of members from
vastly different socioeconomic backgrounds; the overall cost of a therapy is an important determinant in patients’ access to the appropriate treatments.

In China, more than 80% of HCC patients have a history of chronic hepatitis B virus (HBV) infection at the time of diagnosis. Persistent infection with HBV not only leads to chronic liver inflammation and drives the progression to HCC [31], it has also been shown to demonstrate many immunosuppressive properties. For example hepatitis B core antigen (HBcAg) is capable of inducing in vivo secretion of IL-10, a potent immunosuppressive cytokine [32]. Here, we are the first group to report the safety and efficacy of these PD-1 inhibitor drugs in a real world treatment cohort of HBV associated HCC patients in China, aiming to reflect the treatment reality in HCC outside of clinical trial programs and to share our experience for developing countries where the majority of HCC cases are associated with chronic HBV infection [3].

**Patients and Methods**

**Study design and patients**

This is a single center retrospective study of patients who received PD-1 inhibitor monotherapy with toripalimab, camrelizumab or sintilimab; or combination therapy with other modes of cancer treatments. Patients with chronic HBV infection, and radiologically or histologically diagnosed HCC were eligible. The approval for this retrospective study was obtained from the local institutional ethics committee. Written consents were obtained from patients prior to their enrolment into this study.

**Dosage PD-1 inhibitor therapy**

Toripalimab was given intravenously at 3mg/kg body weight or at a fixed dose of 240mg every 2 weeks. Camrelizumab was given at a fixed dose of 200mg every 2-3 weeks intravenously. Sintilimab was given at a fixed dose of 200mg every 3 weeks intravenously.

**Assessments**

Clinical and laboratory data were collected from all patients prior to PD-1 inhibitor therapy. Clinical data included age, gender, Barcelona Clinic Liver Cancer (BCLC) stage, Eastern Cooperative Oncology Group (ECOG) performance and Child-Pugh score. In addition, imaging data were collected based on abdominal computed tomography (CT) and/or magnetic resonance imaging (MRI), including tumor size, number, vascular invasion, and extrahepatic metastasis. Laboratory data included alpha-fetoprotein (AFP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), albumin, total bilirubin (TBIL), hepatitis B surface antigen (HBsAg), and prothrombin time (PT).

The patients underwent CT or MRI at baseline, 6-12 weeks after treatment initiation, and about every 3 months thereafter. Efficacy of treatment was measured by overall survival (OS) (defined as the interval between the first dose of PD-1 administration until death or the last follow-up), time to tumor progression (TTP) (defined as the time from first checkpoint inhibitor administration until the date that tumor progression was confirmed radiologically), and progression free survival (PFS) (defined as the time from first checkpoint inhibitor administration until radiological disease progression or death, whatever came first). Treatment related adverse events (TRAE) were recorded at every visit according to the US National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE v4.03) [33].

Tumor responses were evaluated according to the modified response evaluation criteria in solid tumor (mRECIST) [34]: (1) Complete response (CR), all enhanced imaging of the target lesions in the arterial phase disappeared; (2) Partial response (PR), the total reduction of the diameter of the target lesions (enhanced arterial phase) was >30%; (3) Stable disease (SD), the diameter of the target lesion did not reduce to that in PR and did not increase to that in disease progression (PD); (4) Progressive disease (PD), the diameter...
of the target lesion (enhanced imaging in the arterial phase) increased by at least 20% compared with the baseline value, or new lesions appeared.

Statistical Analysis

Statistical analysis was performed in SPSS Statistics for Windows (version 20.0, SPSS Inc., Chicago, IL, USA). Data were expressed as counts and percentages for categorical variables such as those in baseline characteristics, radiological tumor response and side effects. Kaplan-Meier survival curves were plotted for all groups. All statistical analyses were based on two-tailed hypothesis tests with a significance level of \( p < 0.05 \). Comparison between three PD-1 inhibitor groups were not performed due to the low sample size after the cohort is subdivided.

Results

Patients

Between November 2018 and December 2019, a total of 151 HCC patients received PD-1 targeted immunotherapy in our hospital (Figure 1). The data collection cut-off time was December 31, 2019. Seventy-six patients were excluded because of incomplete data (\( n=63 \)) or follow-up shorter than 6 weeks (\( n=13 \)). The remaining 75 patients were divided into 3 treatment groups based on the antibody used: toripalimab (\( n=26 \)), camrelizumab (\( n=33 \)) and sintilimab (\( n=16 \)). The demographic and laboratory characteristics at baseline are shown in Table 1. The mean duration of follow-up was 22.7 \( \pm \) 12.6 weeks for all patients, 31.3 \( \pm \) 7.4 weeks for toripalimab group, 15.1 \( \pm \) 9.7 for camrelizumab group and 23.3 \( \pm \) 14.7 for sintilimab group. The mean number of cycles of PD-1 therapy at cut-off were 4.8 \( \pm \) 2.7 for all patients, 5 \( \pm \) 1.9, 4 \( \pm \) 3 and 5.5 \( \pm \) 3.1 for toripalimab, camrelizumab and sintilimab groups respectively.

Efficacy

Seventy-five patients, who had at least one follow-up imaging result, were included in the assessment of tumor responses (Table 2). In the toripalimab group (\( n=26 \)), no patient had complete response (CR), 4 patients achieved partial response (PR), and 10 patients had stable disease (SD), resulting in an objective response rate (ORR) of 15.4% and disease control rate (DCR) of 53.8%. In the camrelizumab-treated patients (\( n=33 \)), the ORR and DCR was 12.1% and 78.8%, with 2, 2 and 22 patients had CR, PR and SD respectively. In the sintilimab group (\( n=16 \)), 1 and 4 participants achieved CR and PR, respectively. Nine patients had stable disease and 2 showed progressive disease (PD). The ORR was 31.3% and DCR was 87.5% for this treatment group. The overall ORR and DCR of this whole cohort was 17.3% and 72.0% respectively. Amongst the three groups, the sintilimab-treated patients appeared to have the best tumor responses, and the toripalimab group the worst. However, due to the heterogeneous nature of patients and these therapies, the data generated from this small cohort do not suffice to make any statistical conclusion.

The median progression-free survival (PFS) of this whole cohort was 40.7 (95% CI, 34.7-46.7) weeks (Figure 2, Table 2); and 28.1 (95% CI, 23.0-33.2) weeks, 30.0 (95% CI, 23.3-36.8) and 49.5 (95% CI, 38.8-60.2) weeks for toripalimab, camrelizumab and sintilimab, respectively (Figure 3, Table 2). Overall, 21 (28.0%) patients had radiological disease progression during follow-up. Median time to tumor progression (TTP) was 45.7 (95% CI, 40.5-60.0) weeks for the whole population (Figure 4, Table 2), and 30.6 (95% CI, 25.6-35.7) weeks, 32.5 (95% CI, 26.1-39.0) and 54.7 (95% CI, 48.5-60.9) weeks for toripalimab, camrelizumab and sintilimab, respectively (Figure 5, Table 2). Six patients (6/75, 8.0%) died during follow-up. The median overall survival (OS) was 51.1 (95% CI, 46.4-55.9) weeks for the whole population (Figure 6), and 37.9 (95% CI, 35.9-40.0) weeks, 40.0 (95% CI, 38.6-41.4) and 52.8 (95% CI, 43.8-61.7) weeks for toripalimab, camrelizumab and sintilimab, respectively (Figure 7, Table 2).
Safety

All recorded treatment related adverse events (TRAE) are shown in Table 3. Twenty-nine patients (29/75, 38.7%) experienced at least one adverse event (AE). Overall, the most frequent AEs were rash (15/75, 20.0%), hypertension (12/75, 16.0%), fatigue (10/75, 13.3%), paresthesia (10/75, 13.3%) and diarrhea (8/75, 10.7%). One patient died due to myocarditis, which was probably related to camrelizumab as it erupted after one cycle of treatment. A dose delay due to adverse events was required in 2 patients (2/26, 7.7%) treated with toripalimab, 4 patients (4/33, 12.1%) treated with camrelizumab and 1 (1/16, 6.3%) receiving sintilimab. Steroids or immunosuppressive drugs were used to treat an adverse event in 10 patients (10/75, 13.3%), of which 3 (3/26, 11.5%) were treated with toripalimab, 6 (6/33, 18.2%) with camrelizumab, and 1 (1/16, 6.3%) with sintilimab.

Discussion

At the time of preparing this manuscript, there are no reports available analyzing the efficacy and safety of toripalimab and sintilimab in treating HCC patients. A phase II/III trial (NCT03794440) of sintilimab combined with an anti-VEGF mAb Bevacizumab (IBI305) in HCC is still at its recruitment stage. In a randomized, multicenter phase 2/3 trial (NCT02989922) of camrelizumab (SHR-1210) in 217 patients with advanced HCC, the objective response rate (ORR) was 13.8%, six-month overall survival was 74.7%, and the median time to progression (TTP) and progression-free survival (PFS) was 2.6 and 2.1 months respectively [28]. In this retrospective observational study of 75 HBV-associated HCC patients, we have demonstrated the encouraging efficacy of toripalimab, camrelizumab and sintilimab (ORR 15.4%, 12.1% and 31.3%, respectively; overall ORR 17.3%), in a real world treatment setting, with well tolerated TRAE (overall 38.7% adverse event rate). Our findings are comparable to the results of the NCT02989922 camrelizumab trial, other PD-1 inhibitor therapy trials (KEYNOTE-224 and CheckMate-040) and real world observational data in advanced HCC patients [24]–[26].

Immune evasion through up-regulation of the PD-1 pathway is a pivotal mechanism in the progression of HCC. The efficacy of PD-1 checkpoint inhibitor therapy can be affected by the expression of PD-L in tumor cells, the number of different tumor specific neoantigens that the host immune cell can recognize, and the overall tumor micro environment (TME) [18], [30]. Using immunohistochemistry to characterize PD-L1 expression in selected tumor types has been suggested to be associated with the responsiveness of PD-1 treatment. However the role of such test has not been established in HCC [35]. Higher tumor mutational burden (TMB), results in a broadened display of tumor neoantigens, promoting a polyclonal, efficacious T cell effector response. PD-1 inhibitors generally have good responses in squamous cell carcinoma, cutaneous melanoma and lung cancers, whose TMB are above 10 mutations/megabase, with reported ORR ranges from 40% up to more than 70% in various clinical trial results [36]–[38]. In contrast uveal melanoma (UM) is a rare form of ocular tumor, which is believed to have one of the lowest TMB amongst all cancers [39]. Algazi et al. performed a meta-analysis focusing on UM patients receiving PD-1 inhibitor therapy, and reported only a 3.6% ORR and a median PFS of as short as 2.6 months [40]. HCC typically demonstrates a moderate TMB roughly of 2 mutations/megabase, underscoring the antigenic potential of HCC and perhaps also highlighting one of the reasons for the typical 15%-20% ORR in PD-1 therapy in HCC, considerably lower than that of the cancer types with high TMB. In murine models of HCC, the result of dual therapy combining PD-1 blockade with other angiogenesis inhibitor has shown to be promising [41]. In order to understand and attempt increase the efficacy of PD-1 efficacy in combined therapy for advanced HCC patients, a number of clinical trials have been set up: NCT03794440, sintilimab with bevacizumab (VEGF inhibitor); NCT03713593, pembrolizumab plus lenvatinib (VEGR inhibitor); NCT03764293, camrelizumab and tyrosine kinase inhibitor apatinib; and a number of PD-L1 inhibitor trials (NCT03298451, NCT03847428, NCT03443437). Liver has a critical role in maintaining a state of immune balance, due to its anatomical position and function as a ‘filter’ of blood clearing potential pathogens while maintaining nonresponsiveness to non-pathogenic antigens. Under normal biological conditions, the presence of a predominantly immunosuppressive microenvironment in liver might
affect disease control in patients with HCC [42]. In China, about 80% of the HCC patients also have HBV infection [31]. HBV core antigen has been shown to stimulate interleukin-10 (IL-10) secretion [32]. In HBV associated HCC patients, the presence of active HBV infection may further tip the immune balance towards more tolerance in the liver and also the whole body via potent immunosuppressive cytokines such as IL-10. In our cohort, all 75 patients have active HBV infections; nevertheless, the efficacy of PD-1 therapy is not significantly lower but similar to the published trials and observational studies where both HBV positive and negative patients were included. One of the possible drive to a potentially higher than usual ORR is that in our study, 14/75 (18.7%) of the patients are staged as BCLC B, while in most of these trials only patients who had progressed on or were intolerant to prior systemic treatments were included.

Besides the inherent biases in real world observational studies, there are several limitations. First, the mean duration of follow-up was short (22.7 ± 12.6 weeks). Second, this study was retrospectively designed, though objective endpoints (especially imaging data for tumor responses assessment) were elaborately and integrally recorded. Third, 76 of 151 patients were excluded from the final study, which might reduce the power of statistical analysis. But we believe the above data provide important experience on subgroups of patients frequently found in our everyday clinical practice and multi-disciplinary team (MDT) consultation. And despite all that, the strength of our study is the provision of unique real-life data on the safety and efficacy of PD-1-targeted immunotherapy with toripalimab, camrelizumab or sintilimab for HBV associated HCC patients, which might be the first study to evaluate PD-1 blockers in Mainland China.

In conclusion, our findings in this study support further applications of these drugs in HCC patients. Of course as non-randomized retrospective observational data, this study can only provide limited evidence to show that these drugs are efficacious and safe. It shall not be viewed as non-biased data and utilized in clinical decision making without further evidence base. What our study suggests is that toripalimab, camrelizumab and sintilimab, the three monoclonal PD-1 checkpoint blockers developed in China, appeared to have promising outcome in advanced HCC treatment with tolerable and manageable side effects, comparable to alternatives that are much more expensive, hence less assessable to Chinese patients: a multicenter, larger in scale, randomized controlled prospective study is needed to further understand the efficacy and safety of these drugs with or without other treatment modalities combined.

CONFLICT OF INTEREST/STUDY SUPPORT:

Specific author contributions: GS Y, XY H, M C and JZ C were involved in conception and design the study and interpretation of data. GS Y wrote the first draft of the article and did the statistical analysis. XY H, Q L, WC D, X C, YB G and JZ C made treatment decisions and manage the patients. PF Y and WX Y collected and recorded the data. All authors were responsible for re-drafting of the article and approved the final version.

Guarantor of the article: JZ C is the guarantor

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Potential competing interests: None

Statement of ethics: Approval for this retrospective study was obtained from the institutional ethics committee (NFEC-201903-Y1-01), and written informed consent was obtained from each patient before the procedure.

Data availability statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.
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Figure legends list

Figure 1. Patient recruitment flowchart

Figure 2. Kaplan-Meier curve showing progression-free survival for the whole cohort of patients treated with programmed cell death protein-1 (PD-1)-targeted immunotherapy

Figure 3. Kaplan-Meier curves showing progression-free survival for Toripalimab-, Camrelizumab and Sintilimab-treated patients

Figure 4. Kaplan-Meier curve showing time to progression for the whole cohort of patients treated with programmed cell death protein-1 (PD-1)-targeted immunotherapy

Figure 5. Kaplan-Meier curves showing time to progression for Toripalimab-, Camrelizumab and Sintilimab-treated patients

Figure 6. Kaplan-Meier curves showing overall survival for the whole cohort of patients treated with programmed cell death protein-1 (PD-1)-targeted immunotherapy

Figure 7. Kaplan-Meier curves showing overall survival for Toripalimab-, Camrelizumab and Sintilimab-treated patients
103 HCC patients treated with POI-based regimens between November 2018 and December 2019.

Excluded patients:
- Lack of follow-up (n=13)
- Incomplete data (n=6)

- Treated with toripalimab (n=28)
  - Toripalimab alone (n=4)
  - Prior molecular targeted chemotherapy (n=5)
  - Prior loco-regional therapy (n=1)
  - Prior combine molecular + loco-regional therapies (n=12)

- Treated with camrelizumab (n=50)
  - Camrelizumab alone (n=1)
  - Prior molecular targeted chemotherapy (n=6)
  - Prior loco-regional therapy (n=9)
  - Prior combine molecular + loco-regional therapies (n=10)

- Treated with arctemizumab (n=35)
  - Arctemizumab alone (n=3)
  - Prior molecular targeted chemotherapy (n=3)
  - Prior loco-regional therapy (n=0)
  - Prior combine molecular + loco-regional therapies (n=11)

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Progression-free Survival

Median 40.7 [95% CI, 34.7-46.7] weeks

Weeks
Progression-free Survival

Toripalimab: Median 28.1 (95% CI, 23.0-33.2) weeks
Camrelizumab: Median 30.0 (95% CI, 23.3-36.8) weeks
Sintilimab: Median 49.5 (95% CI, 38.8-60.2) weeks

Time to progression

Median 45.7 (95% CI, 40.5-60.0) weeks
Time to progression

Tortipalimab: Median 30.6 (95% CI, 25.6-35.7) weeks
Camrelizumab: Median 32.5 (95% CI, 26.1-39.0) weeks
Sintilimab: Median 54.7 (95% CI, 48.5-60.9) weeks

Cumulative Survival

Median 51.1 (95% CI, 46.4-55.9) weeks
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Table 1 Baseline_v3.docx available at https://authorea.com/users/318683/articles/448598-effectiveness-and-safety-of-toripalimab-camrelizumab-and-sintilimab-in-a-real-world-cohort-of-hepatitis-b-virus-associated-hepatocellular-carcinoma-patients

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Table 2 Response_v3.docx available at https://authorea.com/users/318683/articles/448598-effectiveness-and-safety-of-toripalimab-camrelizumab-and-sintilimab-in-a-real-world-cohort-of-hepatitis-b-virus-associated-hepatocellular-carcinoma-patients

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Table 3 AEs_v3.docx available at https://authorea.com/users/318683/articles/448598-effectiveness-and-safety-of-toripalimab-camrelizumab-and-sintilimab-in-a-real-world-cohort-of-hepatitis-b-virus-associated-hepatocellular-carcinoma-patients