Interim report of Notable-HCC: A phase Ib study of neoadjuvant PD-1 with stereotactic body radiotherapy in patients with resectable HCC

Mingming Li1, Li3, Jinyue Bu1, Bo Zhang1, Xueqin Shi1, Kai Cui1, Jing Liu1, Zhonghao Li1, Lei Zhao1

1Department of Hepatobiliopancreatic Surgery, Shandong Cancer Hospital Affiliated to Shandong First Medical University, Jinan, China. 2Department of Radiation Oncology, Shandong Cancer Hospital Affiliated to Shandong First Medical University, Jinan, China. 3Department of Graduate, Shandong First Medical University and Shandong Academy of Medical Sciences, Jinan, China.

Objective

1. So far, there is no neoadjuvant therapy recommended by major hepatocellular carcinoma (HCC) guidelines. In other malignancies, ICIs in the neoadjuvant setting have shown better outcomes than in the adjuvant setting, and the combination of radiotherapy to ICIs incrementally improves the systemic response to ICIs. This study shows the benefit and safety of SBRT + PD-1 in early-stage HCC.

2. Methods: Neoadjuvant SBRT was planned for patients with early stage resectable HCC, who were treated with SBRT at least 3 weeks before resection. PD-1 was administered concurrently with SBRT. The primary endpoint included the number of patients experiencing a surgery delay of more than 6 weeks, overall response rate according to the RECIST v1.1 and mRECIST criteria, pathologic response rates, and safety and tolerability of the combination of SBRT and PD-1.

Results and interpretation

1. Ten patients were enrolled, all were BCLC A stage. One patient was excluded due to protocol violation. Total follow-up time was 12 weeks.

2. All 9 patients completed neoadjuvant therapy and surgery. No surgery delay occurred. ORR reached 30% according to RECIST and 60% according to mRECIST. Pathological complete response (pCR) was confirmed in 1 patient, major pathological response (MPR) was confirmed in 2 patients. So far, the safety of neoadjuvant SBRT+PD-1 was satisfactory. Grade 1 to 2 treatment-related adverse events (TRAEs) mainly include elevated transaminase, but all were well-tolerated. One patient developed recurrence 9 months after surgery (RF ablation), all other 9 patients are still in disease-free survival.

3. Conclusion

- Neoadjuvant therapy strategies incorporating anti-PD-(L)1 antibody plus locoregional treatment (SBRT) has shown promising results in several types of solid tumors but not HCC.

4. Introduction

- Currently, no neoadjuvant therapies are recommended for patients with early stage HCC by the primary HCC guidelines (e.g., EASL, AASLD, ESMO).

- Notable-HCC (NCT05185531) is a single-center phase Ib study of neoadjuvant SBRT plus anti-PD-L1 tislelizumab in patients with early stage resectable HCC.

- Eligible patients were aged ≥18, with histologically confirmed, resectable HCC of BCLC stage A; the patients' ECOG PS were of 0 or 1, and had at least one measurable lesion by CT-scan or MRI defined by RECIST v1.1 and HCC-specific mRECIST criteria.

- Key eligibility criteria:
  - Age: ≥18 years
  - Histologically confirmed resectable HCC of BCLC stage A
  - At least one measurable lesion by CT-scan or MRI defined by RECIST v1.1 and HCC-specific mRECIST criteria
  - Performance status: 0 or 1
  - Creatinine increased ≥1.5× upper limit of normal

- The clinical significance of neoadjuvant SBRT in resectable HCC needs further exploration.

- Figure 1: Study design for Notable-HCC Mainland cohort

- Figure 2: Days between treatment initiation and surgery

- Figure 3: Radiographic and pathological responses to neoadjuvant SBRT and tislelizumab

- Table 1: Baseline characteristics of the patients enrolled

- Table 2: Treatment-related adverse events

- Table 3: Radiographic and pathological responses

- Figure S1: Study design for Notable-HCC Mainland cohort

- Figure S2: Days between treatment initiation and surgery

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- Table S1: Baseline characteristics of the patients enrolled

- Table S2: Treatment-related adverse events

- Table S3: Radiographic and pathological responses

- Patient primary endpoint:
  - Surgery delay >6 weeks
  - Major pathological response (MPR) defined by RECIST v1.1 and HCC-specific mRECIST criteria

- Table 4: Demographic and characteristics

- Table 5: Radiographic and pathological responses

- Number of patients (n=20)

- RECIST
- mRECIST

- Best overall response

- Complete response 0 (0%) 2 (20%)

- Partial response 3 (30%) 4 (40%)

- Stable disease 7 (70%) 4 (40%)

- Progressive disease 0 8

- Disease control rate 10 (100%) 1 (10%)

- Pathological response

- Major pathological response (>70%) 2 (20%)

- Complete pathological response 1 (1%)