Recombinant human adenovirus type 5 combined with anti-PD-1 monoclonal antibody in the treatment of patients with advanced melanoma with previous immunotherapy failure: a single-site, single-arm, prospective study

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BACKGROUND

Although melanoma accounts for only 1% of all skin cancers, it is the most aggressive and dangerous type, with a strong tendency to metastasize and a very poor prognosis, accounting for 90% of all skin cancer deaths. Treatment for advanced melanoma after progression on immunotherapy is limited.

- H101, a recombinant human type 5 adenovirus with the deletion of E1B and E3 gene, which is the world's first approved oncolytic virus product in China, and has been reported to have anti-tumor activity in some solid tumors. OVVs can selectively replicate in cancer cells and lyse them, and then the viral infection spreads to and kills surrounding tumor cells, eventually leading to a reduction in the tumor volume.

In 2005, H101 was developed by Shanghai Sunway Biotechnology Co., Ltd., and approved by the State Food and Drug Administration for the treatment of advanced nasopharyngeal carcinoma.

Currently, there are 28 OVs under investigation worldwide (Table 1), with a total of 204 studies. Among them, about 50% of Phase I studies and 5.39% of Phase III studies. However, only two OVs have been approved, namely recombinant human adenovirus type 5 injection (Ancorine®, H101, Oncorine) and T-VEC (ProstAttak).

However, there was little evidence regarding the effect of H101 on advanced melanoma.

Table 1. 28 OVs under investigation

<table>
<thead>
<tr>
<th>Clinical stage</th>
<th>Product under development</th>
<th>Indications</th>
<th>Administration methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase III</td>
<td>A total of 7 OVs include Pexa-Vec (Phase III clinical suspension, unable to market as planned), ADV-TK, Reoysin (Canada), ProtAtak, CilG0070, E10A, Toca511</td>
<td>Bladder cancer, head and neck cancer, ovarian cancer, liver cancer, pancreatic cancer</td>
<td>Intravenous injection, intratumoral injection, intrapleural injection</td>
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<tr>
<td>Phase I- II</td>
<td>A total of 28 OVs such as EDS01, Orienx010, KH901, OH2, E10A, CAVATAK, MG1-MAGEA3, etc.</td>
<td>Melanoma, prostate cancer, lung cancer, NSCLC head and neck cancer</td>
<td>Intravenous injection, intratumoral injection</td>
</tr>
<tr>
<td>Clinical application</td>
<td>T3011, T601, M1 virus, etc.</td>
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Primary objectives

- We aimed to explore the effect and safety of H101 intra-tumor injection combined with anti-programmed death-1 (anti-PD-1) monoclonal antibody in the treatment of advanced melanoma with previous immunotherapy failure, and to further provide a new method for clinical treatment of melanoma.

Study Design

- A single-site, single-arm, prospective study.
- This study was registered on the Chinese Clinical Trial Registry (Registration No: ChiCTR2200055931).

Key Eligibility Criteria

- 18 years sages 75 years
- Histopathologically diagnosed as malignant melanoma
- According to the investigator’s judgment, the current physical condition and the expected diagnosis and treatment plan are suitable for the treatment plan of this trial
- Patients with advanced melanoma with previous immunotherapy failure
- At least one injectable lesion must meet the requirements of RECIST 1.1 and iRECIST measurable target lesions
- The longest diameter of the injectable lesion must be ≥10mm and ≤80mm
- Eastern Cooperative Oncology Group (ECOG) physical status score of 0-2
- The interval between the date of the first treatment of this study and the date of the last anti-tumor treatment is ≥14 days, and the adverse reactions of the previous anti-tumor treatment have recovered to baseline or below grade 1 (Common Terminology Criteria for Adverse Events (CTCAE) version 5.0) (except for alopecia and grade 2 anemia)

Figure 1. Study design

Patients with advanced melanoma with previous immunotherapy failure (N = 10, approx.)

- H101 injection dose is determined by the maximum tumor diameter: 5.0 × 10^11 virus particles (vp) (1 vial) for tumor diameter between 1cm and 4cm, and 1 × 10^12 vp (2 vials) for tumor diameter between 4cm and 8cm.

Primary Endpoints

- Objective response rate (ORR)
- Duration of response (DOR)
- Disease control rate (DCR)
- Overall survival (OS)
- Quality of life (QoL)
- Adverse events (AEs)

Secondary Endpoints

- Objective response rate (ORR)
- Duration of response (DOR)
- Disease control rate (DCR)
- Overall survival (OS)
- Quality of life (QoL)
- Adverse events (AEs)

Sample size

- It is estimated 10 patients with advanced melanoma with previous immunotherapy failure who receive treatment of H101 combined with anti-PD-1 monoclonal antibody are required.

Assessments

- Vital signs, physical examination, Eastern Cooperative Oncology Group (ECOG) score, blood routine, urine routine, fecal occult blood, biochemistry, coagulation function, color ultrasound of superficial lymph nodes, electrocardiogram, tumor assessment, quality of life score, concomitant therapy, concomitant medication, adverse events.

- The AEs are monitored according to the NCI Common Terminology Criteria for Adverse Events (CTCAE, Version 5.0).

Study Duration

Patients are now not yet recruiting and the estimated study duration is 3 years.

References


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