# 1998P: Preliminary Results From a Phase I Study of T3011, an Oncolytic HSV Expressing IL-12 and Anti-PD-1 Antibody, for BCG-Failure Non-Muscle-Invasive Bladder Cancer

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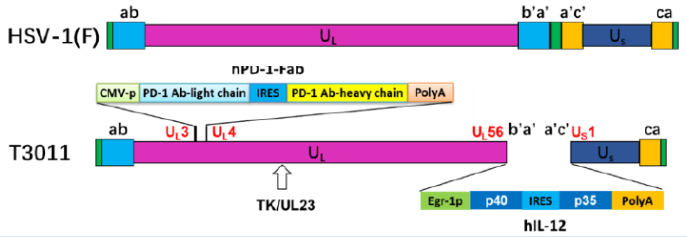
## Study Objective

- To evaluate the tolerability, safety, and preliminary efficacy of intravesical instillation of oHSV T3011 Injection in participants with high-risk BCG-failure NMIBC.

## Background

- T3011, a genetically modified HSV-1, selectively infects tumor cells while sparing normal cells.
- T3011 was inserted with biologically active IL-12 and anti-PD-1 antibody genes.
- Upon injection, locally produced IL-12 induces IFN-γ production, enhances the oncolytic activity of both NK cells and cytotoxic T lymphocytes, promotes anti-angiogenesis and inhibits tumor growth.
- PD-1 antibodies act as immune checkpoint inhibitors to augment tumor-killing activity of T-cells.

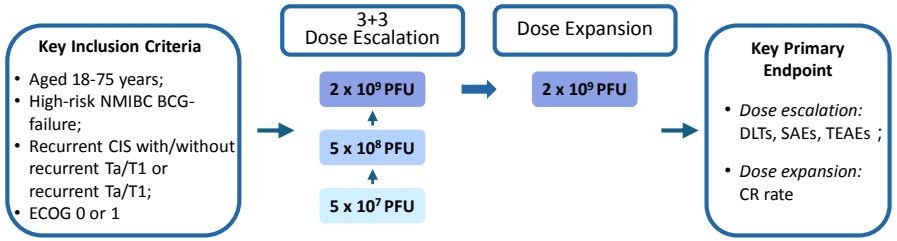
### Figure 1. T3011 Backbone Design




## Methods

- A phase I, open-label, dose escalation and expansion study of T3011 via intravesical administration to treat the patients with high-risk BCG-failure non-muscle-invasive bladder cancer (NMIBC). (NCT06427291)
- Eligible patients were treated with dT3011 via intravesical instillation as shown in Figure 2.
- T3011 was administered at three dose levels in 50 ml of solution, QW x 12 weeks followed by Q2W up to 1 year.
- Safety was evaluated according to CTCAE 5.0.
- A Complete Response (CR) was defined as negative results from both cystoscopy/biopsy and urine UroVysion FISH testing, which were assessed every 3 months.

### Figure 2. Study Design




## Results

### Patient Characteristics

- As of June 27, 2024, 17 patients (pts) received T3011 monotherapy. Baseline characteristics are shown in Table 1.

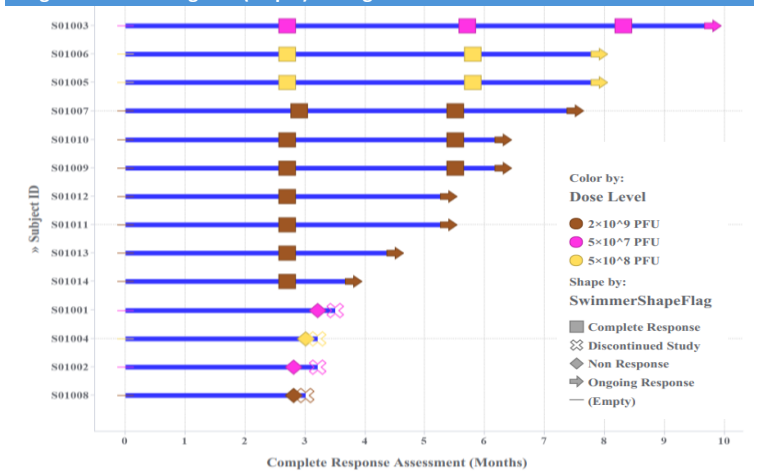
**Table 1. Baseline Characteristics**

| Characteristics | 5 x $10^7$ PFU | 5 x $10^8$ PFU | 2 x $10^9$ PFU | Total |
|---|---|---|---|---|
| **Age, years, N** | **3** | **3** | **11** | **17** |
| ≥ 65 years | 0 | 1 | 6 | 7 |
| **Sex, N** | **3** | **3** | **11** | **17** |
| Male | 2 | 2 | 5 | 9 |
| Female | 1 | 1 | 6 | 8 |
| **ECOG, N** | **3** | **3** | **11** | **17** |
| 0 | 0 | 0 | 0 | 0 |
| 1 | 3 | 3 | 11 | 17 |
| **BCG history, N** | **3** | **3** | **11** | **17** |
| Median (Range) | 20.0 (12~28) | 18.0 (15~21) | 10.0 (6~19) | 12.0 (6~28) |
| **High-Risk NMIBC, N** | **3** | **3** | **11** | **17** |
| CIS | 0 | 0 | 0 | 0 |
| CIS + Ta/T1 | 1 | 0 | 1 | 2 |
| Ta/T1 | 2 | 3 | 10 | 15 |

### Efficacy

- The overall 3-month CR rate for all pts irrespective of dose levels was 71.4% (10/14);
- The CR rate was 87.5% (7/8) at 2×$10^9$ PFU dose level;
- All responders after 3 months were able to continue T3011 therapy, 6 pts completed 6-month tumor assessment, and all remained in CR. 1 patient completed 9-month tumor assessment and continued to stay in CR.

**Figure 3. Swimming Plot (14 pts) for High-Risk BCG-failure NMIBC**




### Safety

- No DLTs were reported. DLT assessment period is first 4 weeks of the 12 weeks induction treatment period.
- MTD was not reached with no irAE/SAE/TRSAE.
- The common treatment related adverse events (TRAEs) (≥10%) included hematuria (35.3%), rash (11.8%), proteinuria (11.8%), pollakiuria (11.8%).

**Table 2. Safety Summary**

| Category | 5 x $10^7$ PFU (N=3) (%) | 5 x $10^8$ PFU (N=3) (%) | 2 x $10^9$ PFU (N=11) (%) | Total (N=17) (%) |
|---|---|---|---|---|
| **AEs** | 3 (100%) | 3 (100%) | 9 (81.8%) | 15 (88.2%) |
| **TRAEs** | 1 (33.3%) | 2 (66.7%) | 8 (72.7%) | 11 (64.7%) |
| **Grade ≥ 3 AEs** | 0 | 0 | 1 (9.1%) | 1 (5.9%) |
| **Grade ≥ 3 TRAEs** | 0 | 0 | 1 (9.1%) | 1 (5.9%) |
| **irAEs** | 0 | 0 | 0 | 0 |
| **SAEs** | 0 | 0 | 0 | 0 |
| **TRSAEs** | 0 | 0 | 0 | 0 |
| **AEs leading to treatment discontinuation** | 0 | 0 | 0 | 0 |
| **TRAEs leading to treatment discontinuation** | 0 | 0 | 0 | 0 |
| **AEs leading to dose suspension** | 0 | 0 | 2 (18.2%) | 2 (11.8%) |
| **TRAEs leading to dose suspension** | 0 | 0 | 2 (18.2%) | 1 (5.9%) |

**Table 3. TRAE Summary**

| Preferred Term | 5 x $10^7$ PFU (N=3) (%) | 5 x $10^8$ PFU (N=3) (%) | 2 x $10^9$ PFU (N=11) (%) | Total (N=17) (%) |
|---|---|---|---|---|
| **Hematuria** | 1 (33.3%) | 1 (33.3%) | 4 (36.4%) | 6 (35.3%) |
| **Rash** | 0 | 0 | 2 (18.2%) | 2 (11.8%) |
| **Proteinuria** | 0 | 1 (33.3%) | 1 (9.1%) | 2 (11.8%) |
| **Pollakiuria** | 0 | 0 | 2 (18.2%) | 2 (11.8%) |
| **Urinary tract infection** | 0 | 0 | 1 (9.1%) | 1 (5.9%) |
| **Micturition urgency** | 0 | 0 | 1 (9.1%) | 1 (5.9%) |
| **Diarrhea** | 0 | 0 | 1 (9.1%) | 1 (5.9%) |
| **Vomiting** | 0 | 0 | 1 (9.1%) | 1 (5.9%) |
| **Oedema peripheral** | 0 | 0 | 1 (9.1%) | 1 (5.9%) |

## Conclusion

- Intravesical T3011 was safe and well tolerated.
- T3011 also demonstrated promising anti-tumor efficacy in patients with high-risk BCG-failure NMIBC.
- MAD of 2×$10^9$ PFU of T3011 is determined to be employed for dose expansion.

Publication number:1998P; contact: fuscc2012@163. com