A PHASE 2, MULTICENTER, SINGLE-ARM TRIAL OF CV301 PLUS ATEZOLIZUMAB (ATEZO) IN LOCALLY ADVANCED (UNRESECTABLE) OR METASTATIC UROTHELIAL CANCER (UC)

TPS494

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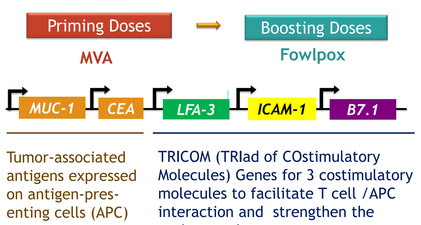
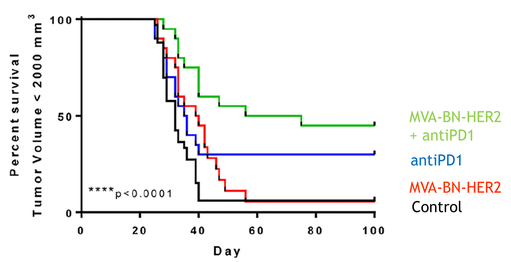
Background

CV301 is a replication deficient poxviral-based vaccine comprising a prime-boost strategy with two poxviral vectors, Modified Vaccinia Ankara (MVA) prime and Fowlpox boost, both encoding 5 human genes: CEA, MUC-1 and three costimulatory molecules (below).



Preclinical evidence suggests that CV301 can generate a tumor-specific T cell immune response, potentially increasing the clinical benefit associated with PD-(L)1 Inhibitors.



Foy SP et al. *PLOSONE* 2016; 11 (2): e0150084

Hypothesis

CV301 enhances the clinical benefit associated with inhibitors of the PD-1/PD-L1 pathway.

Objectives and Endpoints

Primary

Proportion of subjects with a confirmed Objective Response (OR) measured Complete Response (CR) + Partial Response (PR) Rate as per Response Evaluation Criteria in Solid Tumors (RECIST 1.1)

Secondary

- Progression-Free Survival (PFS)
- Overall Survival (OS)
- Duration of Response
- Safety of the treatment combination of CV301 with Atezo

Exploratory

Tumor Tissue

Analysis of biopsy tissue of pre- and post-treatment samples e.g.:

- Tumor-Infiltrating-Lymphocytes
- Programmed Death Ligand 1 (PD-L1) expressions
- Gene expression profiling for molecular subtyping
- Tumor mutational burden; MSI status
- T cell receptor clonality

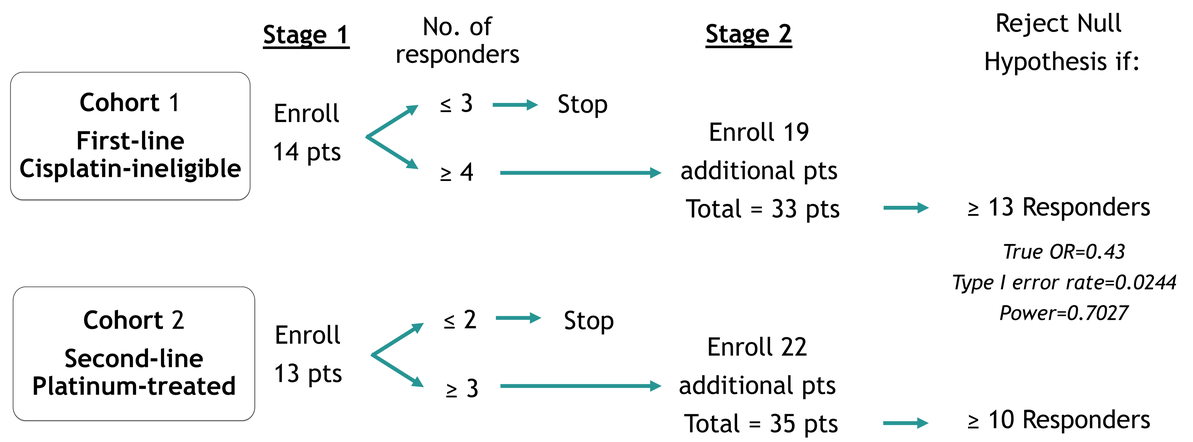
Blood

Analysis of peripheral blood mononuclear cells of pre- and post-treatment samples e.g.:

- Antigen-specific immune responses to CEA and MUC1
- Immunophenotyping of immune cell subsets
- Soluble biomarkers (e.g. cytokines and classical tumor markers)
- T cell receptor clonality

Blood samples are collected at screening, day 22, 64, 148 and 358.
Tumor biopsy is done at screening and optional on day 43, 64, 85 and 106.

Design & Statistics: Phase 2 Simon's two-stage design



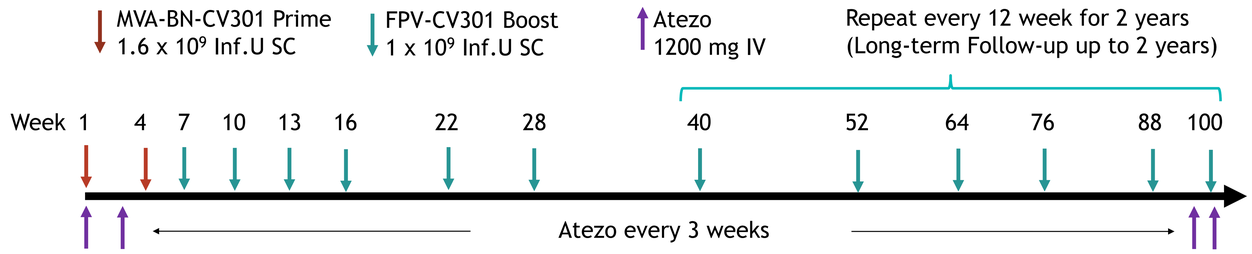
Key Eligibility Criteria

Patients with Locally Advanced/Unresectable or Metastatic UC including bladder, ureter, renal pelvis and urethra, life expectancy >12 weeks, measurable disease per RECIST v1.1, adequate organ function, FFPE tumor specimen available

Cohort 1: Ineligible for Cisplatin-containing chemotherapy (as first-line treatment). Untreated with chemotherapy for advanced stage and one of the following: ECOG PS 2, GFR between 20 and 60 mL/min, hearing loss or neuropathy ≥grade 2

Cohort 2: Previously treated with first-line platinum-based chemotherapy, anti-PD-1/L1 Naïve (second-line treatment). ECOG PS < 2, GFR ≥ 20 mL/min

Treatment Schedule



Trial Status

6 sites are open for recruitment; 3 patients are enrolled in Cohort 1 and 4 patients in Cohort 2, as of February 5th, 2019 (NCT03628716).

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