BACKGROUND

- CV9104 is a novel prostate cancer immunotherapy based on sequence-optimized, free and protamine-complexed mRNA encoding the antigens PSA, PSMA, PSCA, STEAP1, PAP and MUC1.
- Safety and immune responses to the predecessor therapy CV9103 encoding 4 of the antigens have been described previously.
- We assessed whether immunotherapy with CV9104 on top of standard of care (SOC) results in longer overall survival than placebo plus standard of care in patients with mCRPC.

METHODS

Study design
- Study scheme is presented in Figure 1.

Patient eligibility
- Men with chemo-naïve, asymptomatic or minimally symptomatic mCRPC progressing after castration or GnRH-analogue therapy, no visceral metastases, at least one 2nd-line antihormonal manipulation.

Endpoints
- The primary endpoint was overall survival (OS).
- The secondary endpoints were radiographic progression-free survival time (PFS1), PFS2 and rPFS5 (Figure 2), time to symptom progression and cellular and humoral immune responses.

Immune response
- Antigen specific cellular immune responses were measured ex vivo in pre- and post-treatment blood samples.

Statistical analysis
- The planned primary analysis was performed following 96 death events; for analysis of OS, a Cox proportional hazards regression model with adjustment for selected prognostic covariates was used.

RESULTS

Study design and treatment schedule
- Figure 1: Study design and treatment schedule.

Patients
- Between Nov 2012 and Dec 2013, 197 patients were randomized 2:1 to either CV9104 or placebo (corresponding to the ITT population).
- Baseline characteristics were balanced between treatment arms (Table 1).
- Drug exposure was similar in both treatment arms: median duration of treatment was 9.5 (CV9104) vs 10.4 (Placebo) months (Table 2).
- Use of 2nd subsequent therapies was fairly balanced (Table 2).

Immune response
- Table 1: Patient demographics and disease characteristics.

Table 2: First subsequent SOC therapies

Safety
- Incidence of Gr3 AEs (51.1% vs 59.7%) or SAEs (44.5% vs 43.5%) was similar in both arms.
- Mild to moderate injection site reactions and flu like symptoms were more frequent in the CV9104 arm.

CONCLUSIONS

- CV9104 did not improve overall survival compared to placebo in this patient population with mCRPC.
- There were also no significant differences in the rPFS endpoints and time to symptom progression.
- Injection site reactions and flu like symptoms were more frequent in the CV9104 arm; incidence of ≥ grade 3 AEs was balanced between the treatment arms.
- Cancer-mediated immunosuppression, tolerance to the prostate cancer self antigens and a suboptimal mode of administration for this protamine formulated mRNA vaccine as suggested by recent data may have contributed to this outcome.
- Further development of mRNA based cancer immunotherapies is ongoing with focus on improved formulations / modes of administration and combination with checkpoint blocking antibodies.

REFERENCES

3. Trial registration Clinicaltrials.gov identifier NCT 01817738.
4. Correspondence to uro@stent.net.