INFECTION

First chlamydia vaccine trial in humans

Results of the first-in-human trial of a vaccine against *Chlamydia trachomatis* infections indicate that the use of the antigen CTH522 with either CAF01 liposomes or aluminium hydroxide (AH) as adjuvant is safe and well tolerated. Both vaccine formulations induced anti-CTH522 IgG seroconversion, but the formulation containing the liposomal adjuvant had an overall better immunogenicity profile than the one containing AH.

Chlamydia is the most common sexually transmitted bacterial disease, but an effective preventive medication is currently lacking. The recombinant antigen CTH522 is a version of the major outer membrane protein of *C. trachomatis*, which has shown promising results in animal vaccination studies. In this phase I, randomized, parallel, double-blind, placebo-controlled trial, women were randomly assigned to receive CTH522 (with either adjuvant CAF01 (CTH522:CAF01) or AH (CTH522:AH); $n = 15$, respectively) or saline ($n = 5$). Intramuscular injections were given at 0, 1 and 4 months, followed by intranasal administrations of CTH22 without adjuvant or placebo at 4.5 and 5 months. Previous studies with CAF01 showed that systemic administration followed by mucosal boosting is highly effective in inducing mucosal immunity and IgA and, although genital mucosa does not have immune inductive sites, intranasal immunization induced mucosal immunity also in the genital tract. The trial primary outcome was safety and the secondary outcome was humoral immunogenicity.

> “both vaccine formulations resulted in strong responses”

Overall, 91% of women received all five vaccinations. No treatment-related serious adverse events occurred. Mild injection site reactions were reported in all participants in the vaccine groups and in 60% in the placebo group; local reactions to intranasal administration were similar in the vaccination and placebo groups (all comparisons not statistically significant). In the CTH522:CAF01, CTH522:AH and placebo groups, 100%, 93% and 0% of women, respectively, had more than fourfold IgG seroconversion after the intramuscular immunizations. Post-hoc analysis showed that both vaccine formulations resulted in strong responses after the first immunization, which increased with each additional injection. Overall, the CTH522:CAF01 group had a faster seroconversion, higher IgG titres, a superior mucosal antibody profile and a more consistent profile of cell-mediated responses than the CTH522:AH group.

Clemens Thoma

ORIGINAL ARTICLE Abraham, S. et al. Safety and immunogenicity of the chlamydia vaccine candidate CTH522 adjuvanted with CAF01 liposomes or aluminium hydroxide: a first-in-human, randomised, double-blind, placebo-controlled, phase 1 trial. *Lancet Infect. Dis.* https://doi.org/10.1016/S1473-3099(19)30279-8 (2019)

FROM THE MEETING

Three times a charm for the third Prostate Cancer summit in Hamburg

Between 22 and 24 August 2019, Derya Tilki and Markus Graefen welcomed delegates to the third Hamburg Prostate Cancer Summit, organized by the Martini-Klinik, where a panel of internationally renowned experts convened to share their knowledge and insight as part of a programme that included discussions on key clinical issues of the day.

The meeting began with an engaging session of inspirational talks. Maha Hussain started with a presentation on standards of care, challenges, progress and personalized therapy in advanced prostate cancer. Mark Emberton followed by discussing what the future of prostate cancer management might hold, to conclude the first day of the summit.

An interesting session on screening, genomics and imaging kicked off day 2. Peter Albertsen discussed what we have learnt from screening for prostate cancer in the past three decades, commenting that the majority of cancers found are Gleason 6 disease and almost no Gleason 8, 9 or 10 cancers are identified by screening. Chris Evans then gave a very stimulating talk on genomics in prostate cancer, followed by Himisha Beltran who discussed germline tests, the characteristics of inherited disease and genetic counselling. The next presentation was a compelling one on the potential of high-resolution microultrasonography for imaging prostate cancer by Laurence Klotz. Mark Emberton and Peter Albertsen then had a lively debate on whether biparametric MRI is sufficient for prostate cancer detection, to finish the morning session.

PROSTATE CANCER

Prostate tumour pH affects macrophage function

Tumour acidosis might contribute to prostate cancer development by augmenting protumour functionality of macrophages in prostate cancer, according to new findings published in the *British Journal of Cancer*.

Metabolic changes are common in tumours, and cancer cells often engage glycolysis to satisfy metabolic requirements. This shift results in the generation of acidic compounds, including lactate, and acidification of extracellular spaces in the absence of adequate perfusion, which can advance an immunosuppressive microenvironment and macrophage phenotype. In a new study, researchers from the H. Lee Moffitt Cancer Center, Tampa, Florida, investigated whether low pH in the context of prostate cancer drives a protumour macrophage phenotype, also without lactate involvement.

First, the team tested the effect of an acidic environment on macrophage phenotype and function in vitro. Using conditions of pH 7.4 or pH 6.8, they found that mouse bone marrow-derived macrophages are driven towards a phenotype similar to tumour-associated macrophages (TAMs), demonstrated by gene expression, cytokine and functional analyses.

Next, the researchers tested this effect in vivo using mice with subcutaneous TRAMP-C2 xenografts and neutralizing tumour acidity with ad lib $NaHCO_3$. TAMs from mice whose tumour pH was neutralized had decreased levels of TAM markers, including *Arg1*, *Cd206* and *Fcgr2b*. Reduced CD206 expression was also seen in immunohistochemistry analyses. In a TRAMP transgenic prostate cancer mouse model without neutralization, tumour macrophage numbers, but not fibroblast numbers, corresponded with cancer progression. The highest