CHEMOPREVENTION OF HUMAN PROSTATE CANCER BY ORAL ADMINISTRATION OF GREEN TEA CATECHINS: A TRANSLATIONAL RESEARCH STORY

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INTRODUCTION

Clinical progression of Prostate Cancer (CaP) is variable: some tumours are indolent, others rapidly progress. Because, diagnosis is usually in elderly men, CaP is an ideal target for chemoprevention. We showed that Green Tea Catechins (GTC) possess anti-tumour activity, suggesting that it might be beneficial in the early stages of cell transformation. But an experimental confirmation in a real clinical setting was needed. High-Grade Prostatic Intraepithelial Neoplasia (HGPIN) is a pre-invasive stage of CaP for which no treatment options are available until CaP is diagnosed.

METHODS

We conducted a Phase II, placebo-controlled clinical trial to assess the efficacy of GTC in the prevention of CaP progression in HGPIN patients. 60 volunteers consumed GTC (600 mg per day tid; n=30) or placebo (n=30) for 1 year and received saturation biopsies at 6 months and one year. To assess whether CaP progression was prevented definitively or simply delayed by treatment, we performed an extra round of biopsies in patients two years after suspension of GTC treatment.

RESULTS

Only 1 tumour was diagnosed in the GTC-arm (3%); 9 cancers were found in the placebo-arm (30%). No related adverse effects were reported. In the follow-up study, biopsies taken two years after suspension of treatment showed one additional CaP diagnosis in the GTC-arm (total 2/30) versus two in the placebo-arm (total 11/30). Substantial data support the role of Clusterin (CLU) as mediator of apoptosis and inhibitor of cell proliferation. CLU gene is down-regulated during CaP progression, particularly in Gleason score higher than 7. We found that GTE administration induced CLU expression in patients responding to GTE treatment.

CONCLUSIONS

GTC had evidently cleared the pre-neoplastic lesions in a durable fashion, suggesting an early treatment effect. Overall, GTC treatment led to an 80% reduction in CaP diagnosis, also suggesting that an important decrease of sanitary costs is achievable. The finding that overexpression of CLU is associated with GTC administration may help to understand the molecular mechanisms underlying GTC action. Chemoprevention with GTC may open a new scenario in Western Countries for a novel and effective clinical approach for CaP, fulfilling a significant therapeutic and social need.