

Letter to the Editor NOT referring to a recent journal article

Chemoprevention of Human Prostate Cancer by Green Tea Catechins: Two Years Later. A Follow-up Update

Prostate cancer (CaP) progresses slowly and clinical is usually diagnosed in very elderly men. Delaying disease onset by a few years would reduce incidence, which makes it an ideal target for chemoprevention strategies. We and others showed that both Green Tea Catechin (GTC) and EGCG possess anti-tumour activity *in vitro*, as well as *in vivo* in the TRAMP mouse model [1,2]. We suggested that administration of GTCs might be beneficial in the early stages of cell transformation but not later, when cancer had already developed.

We performed a clinical trial in 60 volunteers bearing HGPIN, the main pre-malignant lesion of CaP, to assess the efficacy of GTCs for chemoprevention, as published [3]. Volunteers consumed GTCs (600 mg per day tid) or placebo for 1 year. Subjects received two follow-up saturation biopsies [4], at 6 months and one year. Only 1 tumour was diagnosed in the GTCs-arm (incidence: 3%), while 9 cancers were found in the placebo-arm (incidence: 30%); no related adverse effects were reported.

Was CaP progression prevented definitively or simply delayed during treatment? We performed another round of prostate mapping in a subset of these patients. The mean follow-up from the end of GTCs dosing was 23.3 months for placebo-arm (range: 12-30) and 19.1 months for GTCs-arm (range: 12-30). Only 9 from the placebo-arm and 13 from the GTCs-arm underwent this third prostate mapping. Despite the high drop-out rate (57% and 55%, respectively), the two arms remained balanced and large enough for statistical analysis.

Figure 1 shows a Kaplan-Meier plot of study data. Three further cancer diagnoses appeared during

follow-up, two in the placebo arm and one in the GTCs-arm. The final difference in cancer prevalence is highly significant ($p < 0.01$) by χ^2 test analysis. These results suggest that the inhibition of prostate cancer progression achieved in these subjects after one year of GTCs administration was long-lasting. The early emergence of benefit observed at 6 months suggests a treatment effect on early lesions. Overall, treatment with GTCs led to an almost 80% reduction in CaP diagnosis, from 53% to 11%, suggesting that an important decrease of sanitary costs related to this disease could be achieved [5].

This chemoprevention approach in high risk patients would fulfil a significant therapeutic and social need, thus opening a new scenario for a novel and effective clinical approach for CaP. A larger confirmatory trial of these results is currently underway (Kumar N. et al, Moffitt Cancer Centre, Tampa Fl, USA; personal communication).

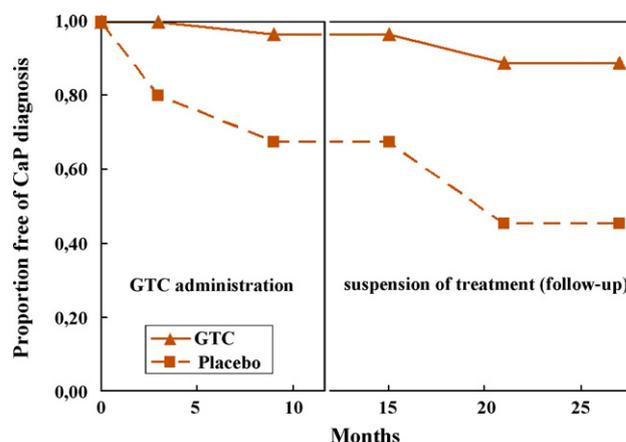


Fig. 1 – Kaplan-Meier analysis of final result showing the prevalence of prostate cancer at 6- and 12-mo check (previous study) as well as 2 years later following suspension of GTC administration (follow-up study).

Conflicts of interest: The authors have nothing to disclose.

References

- [1] Caporali A, Davalli P, Astancolle S, et al. The chemopreventive action of catechins in the TRAMP mouse model of prostate carcinogenesis is accompanied by clusterin overexpression. *Carcinogenesis* 2004;25:2217–24.
- [2] Gupta S, Hastak K, Ahmad N, et al. Inhibition of prostate carcinogenesis in TRAMP mice by oral infusion of green tea polyphenols. *Proc Natl Acad Sci USA* 2001;98:10350–5.
- [3] Bettuzzi S, Brausi M, Rizzi F, et al. Chemoprevention of human prostate cancer by oral administration of green tea catechins in volunteers with high-grade prostate intraepithelial neoplasia: a preliminary report from a one-year proof-of-principle study. *Cancer Research* 2006;66:1234–40.
- [4] Scattoni V, Zlotta A, Montironi R, et al. Extended and saturation prostatic biopsy in the diagnosis and characterisation of prostate cancer: a critical analysis of the literature. *Eur Urol* 2007;52:1309–22.
- [5] Sennfält K, Carlsson P, Varenhorst E. Diffusion and economic consequences of health technologies in prostate cancer care in Sweden, 1991–2002. *Eur Urol* 2006;49:1028–34.

Maurizio Brausi

Department of Urology, Carpi Hospital and AUSL Modena, Carpi-Modena, Italy

Federica Rizzi

Saverio Bettuzzi*

Department of Medicina Sperimentale, University of Parma, Parma, Italy and Istituto Nazionale Biostrutture e Biosistemi (I.N.B.B.), Roma, Italy

*Corresponding author.

Dipartimento di Medicina Sperimentale, Sezione di Biochimica, Università di Parma, Via Volturno 39, 43100 Parma, Italy.

Tel. +39 0521 903803; fax: +39 0521 903802.

E-mail address: saverio.bettuzzi@unipr.it (S. Bettuzzi)

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