Complementary Medicine (CM) Use in Phase III Clinical Trials (P3T) Conducted by the Canadian Cancer Trials Group (CCTG)

J. Connor Wells, Aven Sidhu, Keyue Ding, Daniel Y.C. Heng, Frances A. Shepherd, Peter M. Ellis, Penelope A. Bradbury, Derek J. Jonker, Malcolm J. Moore, Lillian L. Siu, Karen A. Gelmon, Christos Karapetis, Jeremy Shapiro, Louise Nott, Christopher J. O'Callaghan, Wendy R. Parulekar, Lesley Seymour, Martin Smoragiewicz, Jose G. Monzon

Background
CMs are products used concurrently with conventional medicine, including natural products and homeopathy. CM use is prevalent amongst cancer patients, but the use in patients enrolled on P3T had yet to be studied. This study examined patient characteristics and outcomes of CM users enrolled in P3T conducted by the CCTG.

Methods
Data were acquired from six international P3T and included patients with metastatic breast (BR), colorectal (CRC), and non-small-cell lung cancers (LC) (MA.31, CO.17-20-23, BR.21-26). Medications were independently reviewed by two authors to identify CM; discrepancies reviewed by a third author, and the final list was approved by consensus. Patient characteristics associated with CM use were identified with Chi-square and logistic regression. Propensity score stratification was conducted to compare between CM users and non-users for overall survival (OS), grade 3+ adverse events (AE) and quality of life (QOL) scales (EORTC-QLQ-C30).

Results
3446 patients were included (17.7% BR, 44.4% CRC, 37.8% LC). Of 24908 medications, 651 (2.6%) were considered CM and 20.4% of patients were CM users. CM use in LC was associated ($p<0.05$) with ECOG performance status (PS) 0-1 (vs 2+), weight loss <5%, non-smoker, and Eastern Asian ethnicity. CM use in CRC was associated with age ≤65, PS 0-1 (vs 2+), fewer sites of metastases, and normal hemoglobin. CM use in BR was only associated with age <50.
CM use did not affect time to global deterioration of QoL (hazard ratio (HR) 1.07 ($p=0.22$, 95%CI 0.94-1.21)). CM use was associated with fewer AEs ($p=0.02$, 61.5% vs 50.0%) but worse subjective QoL pain, constipation, and role ratings. CM use HRs for OS in LC, CRC, and BC P3T were 0.80 ($p=0.005$; 95% CI (0.68-0.94)), 0.87 ($p=0.08$; 95% CI (0.75-1.02)), and 0.85 ($p=0.35$; 95%CI (0.61-1.19)), respectively.

Conclusions
The use of CM amongst patients enrolled in P3T is high. Patient's using CM tend to be younger and have better PS. Worse QOL indices were associated with CM use, although time to deterioration and incidence of AE were not. HR for OS in the lung cancer trials favoured CM users, however, this should be interpreted with caution given the retrospective/post-hoc nature of this study and the more favourable baseline characteristics.