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PREDICTION OF TREATMENT EFFECTS FOR INDIVIDUAL CANCER PATIENTS USING DATA FROM RANDOMIZED CLINICAL TRIALS

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Aim: Results from randomized clinical trials (RCTs) evaluating the efficacy of chemotherapy are typically reported as relative risk or difference in median survival on a group level. Patients are most interested in their personal expected absolute treatment effect. Translating group level estimates to individual patients in clinical practice is challenging, as absolute treatment effects can vary substantially among individuals. We propose a method for individualized treatment effect prediction using data from RCTs, to identify cancer patients who benefit from specific treatments.

Methods: Data from the NVALT7 study, a randomized phase II trial comparing pemetrexed (P) with P plus carboplatin (C) in 240 patients with non-small cell lung cancer relapsing after platinum based chemotherapy (Smit et al. J. Clin. Oncol. 2009), were analyzed. Cox proportional hazards models, including routinely available patient and tumor characteristics, were developed for individualized prediction of the absolute effects of adding C to P in terms of absolute increase in overall survival (OS), progression free survival (PFS) and risk of grade 3/4 toxicity. Models were internally validated and an external validation in the GOIRC 02 2006 randomized phase II study is planned.

Results: The predicted individual benefit in OS of adding C to P ranged from -1.2 to 10.8 months. Patients with squamous tumors, particularly those with better performance status, lower leucocyte count and longer treatment free interval, had the highest predicted median OS benefit from addition of C (3.2 months), though with a wide range (1.4 to 10.8 months). The difference in predicted PFS for individuals ranged from 0.1 to 3.2 months. Internal validation showed a satisfactory model calibration and discrimination (c-index: 0.69/0.65 for OS/PFS). The predicted absolute risk increase (ARI) of toxicity with addition of C was similar in patients with ≤3 months predicted OS (ARI 5.0%) and those with longer predicted OS (ARI 5.2%).

Conclusions: Data from RCTs may be used to predict absolute treatment effects for individual patients before start of therapy. Individualized treatment effect predictions from validated models may guide treatment decisions in cancer patients by identifying those who benefit most in terms of OS and PFS and have low risk of toxicity.

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