WINTHER: An international WIN Consortium precision medicine trial using genomic and transcriptomic analysis in patients with advanced malignancies.

Jordi Rodon, Jean-Charles Soria, Raanan Berger, Wilson H. Miller, Vladimir Lazar, Eitan Rubin, ...Show More

Abstract Disclosures

Abstract

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Background: Precision medicine has focused mainly on matching drugs to tumor DNA alterations. However, not all individuals have tractable genomic alterations.We initiated the WINTHER trial to navigate patients to therapy based on either next generation sequencing (NGS) or transcriptomic analysis that compared tumor to normal tissue. **Methods:** Genomics (Arm A) was performed by NGS (N = 236 genes) (Foundation Medicine); transcriptomics (Arm B), by Agilent oligo-arrays (from fresh biopsies). A matching score was calculated for each patient (based on drugs received): for Arm A, number of alterations matched/total number of alterations; for RNA, by adding the reciprocals of the ranks of expression-matched drugs (using a transcriptomic algorithm). The clinical management committee (CMC) (lead investigators from the participating centers in 5 countries) suggested therapies, prioritizing genomic matches if available. The treating physician determined therapy given. **Results:** Overall, 303 patients consented; 107 (35%) received therapy consistent with CMC recommendations: 69 patients (64.5%) on Arm A (DNA-guided); 38 (35.5%), Arm B (RNA-guided). The median number of prior therapies was 3; median age = 59; median performance status = 1 (did not differ between arms). The most common diagnoses were colon, head/neck, and lung cancers. Adverse events after biopsy occurred in 1.2% of patients (1, (unrelated) convulsion; 2, pneumothorax). The rate of stable disease (SD) ≥ 6 months plus partial and complete response was 26.2%: Arm A, 23.2%; Arm B, 31.6%. Median progression-free survival (PFS) was 2.1 months (Arm A, 1.9; Arm B, 2.4). In multivariate analysis (hazard ratio (HR), 95% confidence interval (CI)), fewer prior therapies (0.63, 0.40-1.00, p = 0.048), better performance status (0.59, 0.37-0.92, p = 0.020) and a higher matching score (0.52, 0.33-0.82, p = 0.005) correlated with PFS. Higher matching score was also significantly associated with better overall survival (OS). (p = 0.012). **Conclusions:** Genomic and transcriptomic analysis were both useful for therapy selection. Higher degrees of DNA and RNA matching independently associated with longer PFS and OS. Clinical trial information: NCT01856296