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Abstracts

META-ANALYTIC, TRIAL-LEVEL APPROACH TO VALIDATION OF PROGRESSION-FREE SURVIVAL AS A SURROGATE ENDPOINT IN ADVANCED BREAST CANCER
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OBJECTIVES: Progression-free survival (PFS) has not been validated as a surrogate endpoint for overall survival (OS) for anthracycline-based (A) or taxane-based (T) chemotherapy in metastatic breast cancer (MBC). Using a meta-analytic trial-level approach, we evaluated the relationship between PFS and OS.

METHOIDS: A literature review identified all randomized, controlled A and T trials for MBC. Progression-based endpoints were classified by prescriptive definitions. Treatment effects were derived as hazard ratios (HR) for PFS (HRpfs) and OS (HRos) from trial data (constant rate assumption). The kappa statistic assessed overall agreement. HRos was predicted from trial HRpfs using fixed effects models that were internally validated. Sensitivity and subgroup analyses were performed for the constant rate assumption, PFS definition, year of last patient recruitment, and line of treatment. RESULTS: Inclusion criteria were met by 15 A and 16 T trials, allowing 17 A (n = 4155) and 17 T (n = 5509) comparisons. The direction of HRos and HRpfs agreed in 25% (A) to 50% (T) (negative) and in 62.5% (A) to 50% (T) (positive) (kappa = 0.71, p = 0.0029 (A); kappa = 0.75, p = 0.0028 (T)). HRpfs was a significant predictor of HRos for A (p = 0.0019) and T (p = 0.012) in the fixed effects models, with explained variance (R²) of 0.35 (T) and 0.49 (A). Cross validation showed that 97% of the 95% prediction intervals crossed the equivalence line. The direction of predicted HRos agreed with observed HRos in 82% (A) and 76% (T). Results were robust in sensitivity and subgroup analyses. CONCLUSION: This analysis suggests the treatment effect on PFS is significantly associated with the treatment effect on OS. However, prediction of OS based on PFS is surrounded with uncertainty: Half (A) to one third (T) of the OS treatment effect variance is explained by the PFS treatment effect variance. Using limited data, sensitivity and subgroup analysis did not explain result heterogeneity.

RESULTS FROM MABEL: QUALITY OF LIFE OF PATIENTS WITH METASTATIC COLORECTAL CARCINOMA (MCRC)
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OBJECTIVES: The MABEL study is an open label, uncontrolled, multi-centre, study of cetuximab in combination with irinotecan in patients with EGFR expressing mCRC and having progressed on a recent irinotecan-based treatment regimen. A study objective was to assess quality of life (QoL). This abstract will report on findings on 126 patients from 28 UK sites.

METHODS: QoL was assessed using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) and the EQ-5D. The EQ-5D questionnaire comprises 30 items, organised into global health status, functionality, symptomatology and single items. The EQ-5D questionnaire consists of the EQ-5D descriptive system and the Visual Analogue Scale (VAS). QoL changes were assessed on patients with a baseline and at least one post-baseline assessment. RESULTS: At the 6 week assessment, 88 [69.8%] patients completed at least one QoL item, with 71 [56.3%] patients at 12 weeks, and 41 [32.5%] patients at the end of the study visit. Given the loss of two thirds of data by the end of study, the following results will assess data over a 12 week period. Between baseline and 12 weeks the EORTC QLQ-C30 global health score increased slightly from 65.3 to 68.9. Symptomatic scales reported a similar trend with the exception of diarrhoea and financial difficulties single items. The EQ-5D index and VAS also reported a trend for a slight improvement between baseline (0.73 and 0.90 respectively) and 12 weeks (0.77 and 0.93 respectively.) CONCLUSION: It is important to consider these results in context of patient prognosis and treatment administered. The data suggests...